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Investigating the association between obesity and asthma among primary schoolchildren in Madinah, Saudi Arabia

Mahmoud A. Nahhas

Thesis presented in fulfilment of the requirement for the degree of Doctor of Philosophy

The University of Edinburgh
2014
بسم الله الرحمن الرحيم
Abstract

Background: Over the latter half of the last century, a dramatic increase in the prevalence of asthma has been observed. Over this same period there has been a substantial increase in the prevalence of obesity, this giving credence to the hypothesis that obesity and asthma may be causally associated.

Aim: The main aims of this thesis were to: i) estimate the prevalence of asthma, allergic rhinitis, and atopic eczema in primary schoolchildren in Madinah, Saudi Arabia; ii) investigate the association between childhood obesity and prevalence of asthma; and iii) investigate possible mechanisms that might explain any associations observed.

Methods: I undertook a pilot study aimed at testing the feasibility of conducting a large-scale descriptive epidemiological study of asthma and associated allergic disorders. This was followed by a two-stage cross-sectional survey, which was conducted to investigate the prevalence of asthma, allergic rhinitis, and atopic eczema in a sample of 5,188 schoolchildren, aged 6-8 years using an Arabic, validated version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Finally, I undertook an analytical study investigating the relationship between obesity and asthma. The cross-sectional study allowed for the identification of cases (i.e. those with a history of symptoms suggestive of asthma) and controls (i.e. those without a history suggestive of asthma). A sample of 632 cases and controls were recruited into a matched case-control study. Conditional logistic regression analysis, with appropriate adjustment for a range of potential confounders, was undertaken to explore the association between measures of obesity (in particular, body mass index (BMI)) and asthma. The possible aetiological roles of atopy and airway obstruction were studied by investigating the impact of sensitisation to common aeroallergens and measurements of lung function on the association between body mass index (BMI) and asthma.
Results: In the pilot study, I found that the asthma, allergic rhinitis, and atopic eczema were very prevalent in children in Madinah and that further epidemiological studies were therefore likely to be feasible. The overall prevalence of children with a history of symptoms suggestive of asthma was 23.6% (95% CI: 21.3, 26.0); the prevalence among boys was estimated at 24.4% (95% CI: 22.0, 26.9) and among girls at 21.9% (95% CI: 17.4, 27.1), respectively. After adjustment for a number of possible confounders, BMI was found to be a significant predictor of the odds of asthma in both boys (OR=1.11; 95% CI: 1.03, 1.19) and girls (OR=1.38; 95% CI: 1.23, 1.56). When sensitisation to allergens was included in the analyses, the effect of BMI on the risk of asthma was no longer evident in boys (OR=1.09, 95% CI: 0.99-1.19) or girls (OR=1.25; 95% CI: 0.96-1.60). When the effect of lung function measures were factored into the model, the association however persisted: boys: OR=1.10 (95% CI: 1.02, 1.18) and girls OR=1.37 (95% CI: 1.22, 1.54).

Conclusions: Asthma and related allergic disorders are very common in primary schoolchildren in Saudi Arabia. BMI is associated with symptoms suggestive of asthma in primary schoolchildren. This effect does not appear to be mediated through respiratory obstruction, but may, at least in part, be mediated through increasing the risk of allergic sensitisation. Prospective and more detailed gender-specific mechanistic studies are now needed to further investigate this association.
Declaration

I declare that this thesis was composed by me and is entirely my own work. It has not been submitted for any other degree or professional qualification.

Mahmoud Nahhas

May 2014
Dedication

To my parents, my teachers and my family
Acknowledgements

There are many people who have contributed to my development and the ideas within my thesis. To all of those teachers, colleagues, friends and relatives, I offer my heartfelt thanks.

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### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADEG</td>
<td>Annual Meeting of University Departments of General Practice in Scotland</td>
</tr>
<tr>
<td>AHR</td>
<td>Airway hyper-responsiveness</td>
</tr>
<tr>
<td>ATP</td>
<td>Adenosine 5'-triphosphate</td>
</tr>
<tr>
<td>BAT</td>
<td>Brown adipose tissue</td>
</tr>
<tr>
<td>BHR</td>
<td>Bronchial Hyper-responsiveness</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BTS</td>
<td>British Thoracic Society</td>
</tr>
<tr>
<td>CDC</td>
<td>Centres for Disease Control and Prevention</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CIA</td>
<td>Confidence Interval Analysis</td>
</tr>
<tr>
<td>CONSORT</td>
<td>Consolidated Standards Of Reporting Trials</td>
</tr>
<tr>
<td>DC</td>
<td>Dendritic cell</td>
</tr>
<tr>
<td>EIG</td>
<td>Edinburgh Immunology Group</td>
</tr>
<tr>
<td>EUSA</td>
<td>Edinburgh University Students’ Association</td>
</tr>
<tr>
<td>FEV1</td>
<td>Forced expiratory volume in 1 second</td>
</tr>
<tr>
<td>FRC</td>
<td>Functional residual capacity</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
</tr>
<tr>
<td>GBP</td>
<td>Great Britain Pound (£)</td>
</tr>
<tr>
<td>GEE</td>
<td>Generalised Estimating Equations</td>
</tr>
<tr>
<td>GENLIN</td>
<td>Generalized Linear Models</td>
</tr>
<tr>
<td>GINA</td>
<td>The Global Initiative for Asthma</td>
</tr>
<tr>
<td>GP</td>
<td>General practice</td>
</tr>
<tr>
<td>HSE</td>
<td>Health Survey for England</td>
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<tr>
<td>IgE</td>
<td>Immunoglobulin E</td>
</tr>
<tr>
<td>ISAAC</td>
<td>International Study of Asthma and Allergies in Childhood</td>
</tr>
<tr>
<td>LPS</td>
<td>Lipopolysaccharide</td>
</tr>
<tr>
<td>MHC</td>
<td>Major histocompatibility complex</td>
</tr>
<tr>
<td>M.O.E</td>
<td>Ministry of Education, Saudi Arabia</td>
</tr>
<tr>
<td>M.O.H</td>
<td>Ministry of Health, Saudi Arabia</td>
</tr>
<tr>
<td>M.O.H.E</td>
<td>Ministry of Higher Education, Saudi Arabia</td>
</tr>
<tr>
<td>MOOSE</td>
<td>Meta-analysis Of Observational Studies in Epidemiology</td>
</tr>
<tr>
<td>NHLI</td>
<td>The National Heart and Lung Institute</td>
</tr>
<tr>
<td>NR3C1</td>
<td>Nuclear Receptor Subfamily 3, Group C, Member 1</td>
</tr>
<tr>
<td>OHS</td>
<td>Obesity hypoventilation syndrome</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>OSA</td>
<td>Obstructive sleep apnoea</td>
</tr>
<tr>
<td>PEF</td>
<td>Peak expiratory flow</td>
</tr>
<tr>
<td>PRISMA</td>
<td>Preferred Reporting Items for Systematic reviews and Meta-Analyses</td>
</tr>
<tr>
<td>PROMs</td>
<td>Patient reported outcome measures</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<td>--------------</td>
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<tr>
<td>REC</td>
<td>Research Ethics Committee</td>
</tr>
<tr>
<td>RR</td>
<td>Relative risk</td>
</tr>
<tr>
<td>SA</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
</tr>
<tr>
<td>SINA</td>
<td>The Saudi Initiative for Asthma</td>
</tr>
<tr>
<td>SPT</td>
<td>Skin prick test</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>S.R</td>
<td>Saudi Riyal (currency)</td>
</tr>
<tr>
<td>STROBE</td>
<td>Strengthening The Reporting of Observational studies in Epidemiology</td>
</tr>
<tr>
<td>TGF-β</td>
<td>Transforming growth factor beta</td>
</tr>
<tr>
<td>Th</td>
<td>T helper</td>
</tr>
<tr>
<td>TNF</td>
<td>Tumour necrosis factor</td>
</tr>
<tr>
<td>TSFT</td>
<td>Triceps skin-fold thickness</td>
</tr>
<tr>
<td>TV</td>
<td>Tidal volume</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
</tr>
<tr>
<td>VAW</td>
<td>Viral associated wheeze</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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Chapter 1: An introduction to the epidemiology of obesity and asthma with an overview of patho-physiological mechanisms and causal pathways

1.1 Introduction

Technological advancements have made human life easier providing several comforts thereby making it possible for people to limit intense everyday physical activities. Many of these comforts have also resulted in people leading more sedentary lifestyles. The most important health concern is the increasing rate of obesity, which increases the risk of various long-term conditions.

Obesity has been on the rise throughout the past two decades.(1) Recent reports by the World Health Organization (WHO) have shown an increase in rates among the people of the whole world.(1) The United States (US) present some of the highest rates of obesity in all age groups(2) and they are followed by countries such as the United Kingdom (UK) and several European countries.(3) The increasing prevalence of obesity now also afflicts many low- and middle-income countries.(4, 5)

The rise of obesity is known to give rise to a variety of health problems, such as atherosclerosis,(6) several cardiovascular disorders, and heart disease;(7) decreased exercise tolerance; insulin resistance leading to diabetes; sleep disorders; respiratory diseases, such as obstructive sleep apnoea (OSA);(8, 9) as well as psychological and social problems.(10)

Childhood obesity is a particularly important issue of concern. Increasing rates of obesity in children are alarming because they may lead to the aforementioned health problems far earlier in life than is normally the case with associated adverse effects on the personal well-being of young people and associated increased costs of healthcare. Furthermore, obese children may develop psychological problems since they may also experience teasing, social exclusion, discrimination and prejudice from their peers.(10) The growing realisation that childhood and adolescent obesity is linked with the risk of obesity and morbidity in older age has led to increased interest in studying overweight and obese children.(11)
Understanding the factors that lead to obesity and its association with medical and psychosocial problems is very important for planning interventions to improve the quality of life of these children as they mature and to decrease the cost of healthcare.\textsuperscript{(12, 13)}

The possible role of obesity as a contributory factor for asthma is a topic worthy of detailed investigation given that several studies have yielded important evidence that obesity increases the risk of asthma both in children and adults.\textsuperscript{(14-16)}

1.2 Asthma

1.2.1 Definition of asthma

The first known description of asthma was recorded 3,500 years ago in an Egyptian manuscript called Ebers Papyrus.\textsuperscript{(17)} Hippocrates, the Greek physician, first used the word asthma five hundred years later to describe an illness; the word means 'laboured breathing' in Greek.\textsuperscript{(17)} Until recently, asthma has been used to describe any disorder with episodic, reversible, shortness of breath or dyspnoea, including ‘cardiac asthma’;\textsuperscript{(17)} however, the definition has now been changed to exclude shortness of breath secondary to cardiac disease and relates only to a disorder of the respiratory system.\textsuperscript{(17)}

The British Thoracic Society’s (BTS), Intercollegiate Guidelines Network (SIGN) British Guideline on the Management of Asthma\textsuperscript{(18)} adopted the definition of the International Consensus Report of 1992,\textsuperscript{(19)} which describes asthma as "A chronic inflammatory disorder of the airways which occurs in susceptible individuals; inflammatory symptoms are usually associated with widespread but variable airflow obstruction and an increase to a variety of stimuli. Obstruction is often reversible, either spontaneously or with treatment".

The National Heart and Lung Institute (NHLI) defines asthma as a “chronic lung disease that inflames and narrows the airway leading to wheezing, chest tightness and shortness of breath”.\textsuperscript{(20)} With no consensus definition of asthma available, the WHO defined asthma as a “disease characterized by the recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person”.\textsuperscript{(21)} The WHO also considers asthma an inflammatory condition of the lungs affecting the sensitivity of the nerve endings in the airways making them irritated resulting in swelling and narrowing of the air passages making it difficult for the diseased person to breathe. In another definition from an Expert Panel
Report, asthma is defined as “a health condition or disease marked with air flow obstruction, airway hyper-responsiveness (AHR) and airway inflammation characterised by the infiltration of eosinophil and T-lymphocytes resulting in breathing difficulties accompanied by cough, wheezing, and tightening of the chest”. (22) Certain identifiable conditions of asthma include increase in the thickness of the basement membrane, mucus production, denudation and smooth muscle hypertrophy of the airway. (23)

Genetic factors, age, gender, ethnicity, socio-economic status, and living conditions (e.g. parental smoking) may all contribute towards the risk of developing asthma. (23) Of particular interest is that asthma has recently been shown to be associated with obesity. (24-26) Indeed, it has been estimated that overweight and obese people may have a 50% increased risk of developing asthma when compared to those of normal weight. (27) A number of studies have shown positive associations between obesity and asthma. (28-32)

For the research undertaken in this thesis, I used a widely employed epidemiological definition of asthma, namely the validated definition developed by the International Study of Asthma and Allergies in Childhood (ISAAC). The ISAAC studies have been undertaken in three phases:

- Phase I (1992-1996) assessed the international prevalence and severity of asthma and related allergic disorders in school-aged children.
- Phase II (1998-2004) investigated aetiological (risk and protective) factors that may have contributed to the worldwide differences observed in Phase I. (33)
- Phase III (2000-2003) was a repetition of Phase I and additionally examined time trends in asthma and other allergic disease prevalence. (34)

The ISAAC Steering Group developed standardised core questionnaires on asthma, rhinitis and eczema. These questionnaires were agreed for international use at a workshop in Bochum, Germany on 8-10th December, 1991. The ISAAC questionnaires are standardised instruments that have been found to generate valid and reliable data on symptoms indicative of asthma. (35)

There are several approaches to identifying asthma, these ranging from the gold standard of clinician-diagnosed asthma to the more commonly employed approach in epidemiological
studies of basing case ascertainment on responses to a validated questionnaire. Different approaches can be used including enquiring about ‘ever wheezed’ and a history of ‘wheeze in the past 12 months’; the former has high sensitivity, but possibly less specificity than questions enquiring about recent symptoms, whereas the latter approach may be more of a marker of current asthma than the presence or absence of asthma per se. There is therefore no one correct approach as there are inevitable trade-offs that need to be considered when using different questions.

The development and validation of patient reported outcome measures (PROMs) is another important, but still evolving area in the assessment and evaluation of the quality of care for patients with different conditions such as asthma and other atopic diseases. These are however more concerned with assessing the impact of disease on individuals and responses to treatment, rather than identification of individuals with disease so these were really not appropriate for use as screening instruments.\(^{(36, 37)}\)

The disadvantages of the ISAAC questionnaire include, in particular: a) the fact that some languages (e.g. French, German) do not have an equivalent of “wheezing” and this therefore raises questions about the validity of the data as individuals may misinterpret such terms; b) the risk of recall bias; and c) problems resulting from low response rates.\(^{(35, 38-40)}\)

1.2.2 Patho-physiology of asthma

Asthma is an inflammatory disorder of the respiratory system.\(^{(41)}\) It is characterised by airway inflammation along with hyperreactivity and increased mucus secretion.\(^{(42, 43)}\) Atopy or the generation of specific-IgE to aeroallergens is an important pathological mechanism in many cases of childhood asthma.\(^{(44)}\) Asthma and atopy have been found to occur both simultaneously as well as independently.\(^{(44)}\) The likelihood of an individual developing allergies and asthma is influenced by their genetic constitution.\(^{(13, 44)}\) Although the genetic factors associated with atopy in relation to asthma are common allergic genes, several environmental factors play a major role in determining the expression of these genes and the development of asthma in atopic individuals.\(^{(43)}\) Exposure to tobacco smoke, air pollution and allergens, obesity and diet, exposure to infections, and microbial substances, can also promote allergic reactions as well as asthmatic responses.\(^{(45)}\) A study on paternal and maternal atopy as a risk factor, by Mandhane in 2005,\(^{(46)}\) revealed the influence of
paternal atopy contributing towards the onset of childhood asthma among males with maternal atopy being the contributing factor for female adolescent asthma.

Reversible inflammation and airway hyper-responsiveness (AHR) on exposure to a variety of environmental factors are two of the major characteristics of asthma.(43) The various inflammatory cells involved in asthmatic inflammation include:

- Mast cells that are involved in the acute bronchoconstriction in response to an allergen
- Dendritic cells that induce T-lymphocytes
- Eosinophils, the infiltration of which forms the basic characteristics of allergic inflammation and enhance AHR
- T-lymphocytes that express the various interleukins involved such as the IL-4, IL-5, IL-9, IL-13, IL-6 and IL-10, along with the TGF-β
- B-lymphocytes that secrete the IgE
- Platelets that aggregate in response to Th2-mediated inflammation
- Structural cells which serve as mediators of chronic inflammation.

All these cells secrete cytokines and chemokines which, along with certain lipid mediators and oxidation stress, increases the inflammatory response.(43)

The inflammation that occurs in response to external stimuli or triggers induces the epithelial cells to release growth factors which, in turn, end up thickening the basement membrane, and result in increased production of cytokines (TGF-β and PDGF) and other inflammatory mediators such as endothelins, causing inflammation in the airway. These changes result in oedema and hyperaemia of the bronchial mucosa leading to cough, wheezing, chest tightness and shortness of breath.
1.2.3 Descriptive epidemiology of asthma

Asthma is one of the most common chronic diseases in the world.\(^{(47, 48)}\) It is estimated that around 300 million people all over the world currently have asthma.\(^{(47, 48)}\) During recent decades it has become more common amongst both children and adults.\(^{(49, 50)}\) The increase in asthma prevalence in developed countries started in the 1960s and has subsequently raised concerns about the now considerable health and economic burden asthma has on individuals, families, health systems and societies.\(^{(51-53)}\)

In 1991 ISAAC was established to achieve uniform diagnostic criteria by using a simple and inexpensive standardised methodology.\(^{(54)}\) This has provided valuable data on the prevalence of childhood asthma.\(^{(55)}\) Phase 1 of this global study was conducted during the early- to mid-1990s, and involved more than 700,000 schoolchildren between the age of 6-7 years and 13-14 years; recruited by 156 centres in 56 countries. It revealed clear geographic variations in the prevalence of asthma symptoms, even within genetically similar groups of children.\(^{(55)}\)

The findings of the ISAAC studies have revealed a lot about the prevalence of asthma. We now know that the 12-month period prevalence of wheeze amongst both 6 to 7 year old and 13 to 14 year old children varies only a little within countries, but in contrast this varies widely between countries. In certain regions, asthma prevalence is generally lower in developing countries than in more affluent countries. For example, in Southeast Asia, the lowest prevalence rates of asthma symptoms were recorded in Indonesia and China, and the highest rates were in Japan, Thailand and Hong Kong.\(^{(55)}\)

The UK is considered to have one of the highest prevalence rates of asthma in the world. The prevalence was estimated to be 32.2% in 1994-1995, according to the ISAAC Phase I study, which was undertaken in 35,485 adolescents.\(^{(55-57)}\)

The national studies on the prevalence of asthma symptoms (wheezing), which were carried out in 1986 in the UK, reported that 6.6% of 16 year olds had wheezing in the past year\(^{(58)}\) and by 1995 this had increased to 32.3% among 12-14 year old children,\(^{(55)}\) using comparable questions. Amongst the younger age group, 6-10 years in the UK, the current prevalence of wheezing ranged from 7.6% in 1980\(^{(58)}\) to 20.2% in 1999,\(^{(59)}\) as assessed using comparable questions.
A cross-sectional study conducted in the UK reported a significant increase in physician-diagnosed asthma prevalence from 19.9% (1991) to 29.7% (1999) among 8 to 9 year olds. Another study reported an increase in current wheeze in both 6 to 7 and 13 to 14 year olds from 1995/1996 to 2001/2002 (6 to 7 year olds: girls 15.4-23.3%, boys 21.0-27.6%; 13 to 14 year olds: girls 21.8-21.4%, boys 18.0-23.2%) with the increase more prominent amongst boys. A third study showed an increase in lifetime asthma among (12-14) year olds from 20.6% - 25.9% (in 1995 and 2002). A study by Burr et al. reported an increase in reported asthma in 12 year olds from 5.5% in 1988 to 27.3% in 2003; a study by Upton et al. reported a doubling in the prevalence of asthma in adults from 3.0% - 8.2% (1972 and 1996); Rizwan et al. reported an increase in young children aged (5-11) years from 17.7% - 29.8% (1998 and 1991); Butland et al. in children aged (7 – 8) years from 12.9% - 17.8% in (1991 and 2002); and finally, Anderson et al. reported that asthma prevalence increased from the 1960s to early 2000s. In this latter study, asthma symptoms and prevalence were assessed through a combination of questionnaire-based surveys and the interrogation of large-scale general practitioner (GP) databases.

A cohort study reported an increase in the annual prevalence of physician-diagnosed asthma in women and men, respectively, from 3.0% (1990) to 5.1% (1999). Routine data sources and surveys for Scotland and England have also found asthma symptom prevalence to be increasing in the UK for all ages.

In Australasia, a study using the ISAAC questionnaire, reported a 7.3% decrease in the prevalence of physician-diagnosed asthma from 38.3% in 1992 to 31.0% in 2002 in children aged (8-11) years. However, another cross-sectional survey reported an increase in the prevalence of physician-diagnosed asthma for 15 and older, from 7.5% in 1990 to 12.2% in 2003, and furthermore for (8-11) year olds from 30.5% in 1992 to 38.6% in 1997.

An increase in asthma prevalence has been reported (using the ISAAC questionnaire) in Germany for both boys and girls aged 6-7 and 13-14 years.

In the US, the prevalence of asthma increased from 7.3% in 2001 to 8.4% in 2010, with 25.7 million people reported as having asthma (18.7 million adults over 18 years of age and 7.0 million children (0-17 years of age).
A very high prevalence of asthma among children (25.2%) and adolescents (15.9%) has been reported for the city of Tangara’ da Serra, Brazil;(76) however, this study found no important differences in prevalence between male and female populations.

Gaps in the epidemiological evidence do still exist; especially for some areas where little or no data have been collected. This includes parts of Asia, Africa and South America. In areas where asthma prevalence has only been reported in single cross-sectional studies it would seem prudent to endow resources to generate serial data. For example in some parts of Africa, Greece,(77) Nigeria,(78) United Arab Emirates,(79) Kuwait,(80) Palestine,(81) India,(82) Qatar,(83) and Saudi Arabia where no complete data are available.(47, 48)

Asthma is a public health problem not only in economically developed countries, but it also represents a growing issue in low- and middle-income countries. Around 300 million people currently suffer from asthma worldwide (47, 48) and it is in particular a common disease amongst children. Asthma is in many parts of the world still under-diagnosed and under-treated.(84, 85) It can result in significant reductions in the quality of life of both the affected individuals and family members.(84, 86-88)

A systematic review of the international literature of asthma by Anandan et al., in 2010 has clearly shown that there is no overall decline in the prevalence of asthma.(52) Furthermore, it reveals that, if anything, the prevalence of symptoms suggestive of asthma may still be increasing.(52)

1.2.4 Childhood asthma prevalence reported from studies in Saudi Arabia

In order to estimate the prevalence of asthma in Saudi Arabia, I searched MEDLINE database for relevant studies published from January 1980 to May 2013. Only epidemiological studies describing the prevalence of asthma in children in Saudi Arabia were eligible for this review. My search strategy is detailed in Appendix 1 These searches retrieved 67 potentially eligible studies. After de-duplication, 62 papers remained from which 54 papers were excluded as these did not meet the inclusion criteria. In the final stage, seven unique studies focusing on the epidemiology of asthma in children in Saudi Arabia were included in my literature review (see Figure 1.1).
As is evident from Table 1.1, there are major differences in how, when and in whom these studies were undertaken and this together with the methodological limitations of the existing evidence base and this is likely to have contributed to the considerable variations in the estimated prevalence of asthma in children. In order to help develop a more robust evidence base and also to generate the first data on asthma prevalence in Madinah, I decided to undertake a large-scale cross-sectional study using the ISAAC instrument. Such an approach would also support comparisons of asthma prevalence with other parts of the world.
Table 1.1: Studies on childhood asthma in Saudi Arabia

<table>
<thead>
<tr>
<th>Author, year, reference number</th>
<th>Year &amp; age of subjects (in parenthesis)</th>
<th>Location (city)</th>
<th>Population</th>
<th>Asthma definition used</th>
<th>Main findings</th>
<th>Main limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Al Frayh, Z Shakoor, M O Gad el rab and S M Hasnain (2001)</td>
<td>1986 &amp; 1995 (8-16 years)</td>
<td>(Jeddah – Riyadh) (Hail – Gizan)</td>
<td>1995 (n=1008) in (Hail &amp;Gizan) 1986 (n=2123) in (Jeddah &amp; Riyadh)</td>
<td>Questionnaire-based: history of wheeze; attack of breathlessness or tightness, cough</td>
<td>2,123 Schoolchildren (Jeddah/Riyadh), 55% boys-45% girls; 1,008 schoolchildren (Hail/Gizan), 56% boys, 44% girls Prevalence of asthma in 1986; 8% Prevalence of asthma in 1995; 23% Prevalence of Passive Exposure of asthmatics to tobacco smoke in 1986-17% Prevalence of passive exposure of asthmatics to tobacco smoke in 1995-35% Prevalence of passive exposure of children with asthma to tobacco smoke doubled over 9yr period (p&lt;.0001) Prevalence of asthma significantly increased between 1986 and 1995 (p&lt;.0001)</td>
<td>No adjustments for all relevant confounding risk factors or Consideration of effect modification 9 years difference between population studied (1986 in Jeddah and Riyadh, n=2,123); (1995 in Hail and Gizan n=1,008) No multivariate logistic regression analysis; precision of estimates only given in percentages with p values</td>
</tr>
<tr>
<td>Al-Ghamdi, A.A. Mahfouz, I.Abdelmoneim, M.Y. Khan and A.A. Daffallah (2008)</td>
<td>(2008) (11-78 years)</td>
<td>Asir region 2 primary healthcare centres in Al-Soka and Maraba</td>
<td>1325</td>
<td>ISAAC questionnaire-based on ever wheezed; wheeze in last 12 months; ever had asthma; sleep disturbance due to wheeze in last 12 months; wheeze on exercise in last 12 months; dry cough at</td>
<td>1325 schoolchildren consisting of 754-Al-Soka and 571-Maraba. Prevalence of asthma in the study population=12.3 % Prevalence of bronchial asthma at sea level was significantly higher than at high altitude (X2=46.6, P&lt;0.05) People living at sea level had 3 times the risk of developing asthma compared to people at high</td>
<td>Sampling issues (population selected without randomisation; “through a – house-to house survey”; no precision in age group (between 11 and 78 years old) or statistical analysis in terms of actual data with 95% CIs; no adjustment for major risk factors in asthma such as,</td>
</tr>
<tr>
<td>Study</td>
<td>Year/Duration</td>
<td>Setting</td>
<td>Participants</td>
<td>Questionnaire</td>
<td>Findings</td>
<td></td>
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<tr>
<td>Bener A, al-Jawadi TQ, Ozkaragoz F, al-Frayh A, Gomes J (1992)</td>
<td>1988–1990 (7–12 years)</td>
<td>Saudi Arabia (city not stated)</td>
<td>3041</td>
<td>A self-administered questionnaire-based diagnosis of asthma history of wheeze; diagnosed asthma</td>
<td>1581 boys and 1460 girls Prevalence of diagnosed asthma 6.8% Prevalence of history of wheeze 10.6% Prevalence rate of asthma in children with pets is 2x that of children without pets (OR 2.4; 95%CI: 1.8–3.1) Risk of chronic cough, chronic wheeze, allergic rhinitis and eczema was higher in children with pets than in children without pets</td>
<td></td>
</tr>
<tr>
<td>Harb Harfi, Kamel Al Abbad, Abbas H Alsaeed Trends in Medical Research (2010)</td>
<td>2007-2009 (6–14)</td>
<td>Riyadh city</td>
<td>1100 schoolchildren (815 boys and 285 girls)</td>
<td>ISAAC questionnaire-based: ever wheezed; wheezing in last 12 months; ever had asthma</td>
<td>The total prevalence rates for asthma, allergic rhinitis were noted to be 11.4% and 12.7% respectively. A total of 27.82% of children were allergically sensitive</td>
<td></td>
</tr>
<tr>
<td>N. Hijazi, B. Abalkhair, A. Seaton (1998)</td>
<td>1998 (12 years)</td>
<td>In two different city (Jeddah &amp; Rabegh-Mastourah) 1. Jeddah city 2. Rabegh-Mastourah Kulia, Hujer, Saber, Alabouak, Maghenia (rural area)</td>
<td>1020 urban Jeddah 424 rural</td>
<td>ISAAC questionnaire-based asthma ever; wheeze ever; wheeze last year, dry cough; wheeze with exercise; asthma diagnosed</td>
<td>1444 schoolchildren (1,020 in Jeddah and 424 rural area) 1097 Saudi nationality/347 non-Saudi nationality significantly higher prevalence of allergic symptoms in urban children compared to rural children and significantly higher prevalence of allergic symptoms in Saudi than in non-Saudi children.</td>
<td></td>
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</tbody>
</table>

Sample size ratio issues (1,020 urban and 424 rural children), no adjustment for potential confounders, such as parental tobacco smoke, exposure to environmental tobacco smoke, diet, pets in the house.

Night in last 12 months: altitude (crude OR = 3.27, 95%CI = 2.30–4.64) (adjusted odds ration = 3.94)

Proportion of people living in mud houses = 61.8% or in huts = 57.7% and keeping sheep in their houses was significantly higher at sea level (11.8%) than at high altitude (23.3%) (X2 = 364.6 and X2 = 87 respectively < 0.05). Tobacco smoking, diet, pollution, having pets in the house e.g. cat, dog.
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Location</th>
<th>Sample Size</th>
<th>Definition of Asthma</th>
<th>Prevalence of Questionnaire-Diagnosed Asthma (QDA)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kasim M. Al-Dawood, Journal of Asthma (2002)</td>
<td>1995 (6-15 years)</td>
<td>Al Khobar city</td>
<td>1482 schoolboys</td>
<td>Standardised and validated questionnaire-based definition of asthma; ever had an attack of wheezing (whistling noise that comes from the chest); shortness of breath with wheezing; clinician-diagnosed asthma</td>
<td>Cumulative prevalence of questionnaire-diagnosed asthma (QDA) was 9.5% Mean age=10.7±3.1 years Prevalence of household pets among QDA children=51% Prevalence of exposure to tobacco smoke at home=61%</td>
<td>14 years old cross-sectional study, internationally accepted ISAAC questionnaire for outcome measurements was not employed, no doctor-diagnosed asthma definition, no full adjustments for all confounding factors.</td>
</tr>
<tr>
<td>Mohammed O AL Ghobain, Mohamad S Al-Hajjaj, Mohamad S Al Moamary BMC Public Health (2012)</td>
<td>2009-2010 (16-18 years)</td>
<td>Riyadh city</td>
<td>3073 students (1504 boys and 1569 girls)</td>
<td>ISAAC questionnaire-based: lifetime wheeze, wheeze during the past 12 months and physician-diagnosed asthma</td>
<td>The prevalence of lifetime wheeze, wheeze during the past 12 months and physician-diagnosed asthma was 25.3%, 18.5%, 19.6%, respectively. Asthma and asthma-related symptoms are more common in boys than in girls, and also were associated with a high rate of rhinitis and hay fever</td>
<td>Major shortcomings in the handling of confounding, adjustments for major risk factors of asthma, other bias issues.</td>
</tr>
</tbody>
</table>
1.3 Obesity as a risk factor for asthma: an overview of epidemiological studies

Several epidemiological studies have investigated the association between obesity and asthma in both children and adult populations. Studies conducted among children 6-14 years of age have shown higher rates of asthma diagnosis among obese girls compared to boys. (26, 89, 90) However, a longitudinal study on obesity and asthma, which followed up children around 7-18 years old for a period of seven years, showed an increased asthma incidence among the overweight and obese boys compared to girls. (91) An association between interleukin-6 (IL-6), obesity and asthma has been reported by El-Shazly et al., (92) among Egyptian children. Increase in IL-6 was relative to the increase in BMI percentiles, which, in turn, was relative to the severity of asthma. Similarly, a link of obesity with asthma has been found more commonly in women than in men and this is believed to be due to differences in sex hormones. (26)

Delgado et al., (93) reviewed the epidemiological studies on obesity and asthma and found that several of the cross-sectional studies and most of the prospective studies have shown a positive association between obesity and asthma. Delgado’s et al. analysis of the relevant studies on paediatric populations concluded that most of the studies suggest that childhood obesity is associated with an increased risk of developing asthma both in childhood and later in adulthood. Overall, Delgado et al. concluded that “obesity can increase the prevalence and incidence of asthma, although this effect appears to be modest and depends on factors such as age and sex.” (93)

In a systematic review by Noal et al., 10 prospective studies were reviewed which investigated the relationship between childhood BMI and the risk of developing asthma in adolescence. (94) The authors concluded that obesity precedes, and is associated with, the persistence and severity of asthma.

A meta-analysis by Flaherman and Rutherford (2006) analysed 12 epidemiological studies which examined the effect of high body weight during middle childhood on developing subsequent asthma. (95) The authors concluded that children with high body weight, either at birth or later in childhood, were at increased risk of developing asthma. The authors identified from the reviewed studies an array of suggested patho-
physiological mechanisms which included diet, gastro-oesophageal reflux, and mechanical effects of obesity, atopy, and hormonal influences.

In most of the studies and reviews on children, inconsistent results about the involvement of gender have been found. Contrary to studies in adults, where the association between obesity and asthma is more evident among female participants, in populations of children it is not clear whether gender has an involvement in this association.

Based on the findings of previous cross-sectional studies in several Arab countries, it is possible to investigate trends in the prevalence of overweight status, obesity, and asthma among Arab populations are summarised in (Figure 1.2) it is evident that both obesity and prevalence of asthma have demonstrated a parallel increase in the last 25 years.

![Figure 1.2: Temporal evolution of the prevalence of overweight status, obesity status, and asthma in Arab populations (the data are from multiple studies from several Arab countries)](image)
1.4 Obesity as a risk factor for asthma: evidence from human and animal studies

1.4.1 Summary of evidence from human studies

Studies have shown an association between increasing respiratory function and BMI in obese people with asthma. Schachter investigated the relationship between lung volume and bronchial reactivity(96) by subjecting both asthma positive and asthma negative subjects to methacholine challenge and comparing changes in lung volume and bronchial reactivity. The findings suggest changes in bronchial reactivity can occur without any relationship to lung volume change in an obese individual. This suggests that the increase in symptoms of wheezing and shortness of breath in the obese should not necessarily be attributed to asthma in the absence of variable airflow limitation that is reversible spontaneously or with treatment, or with an increase in the existing AHR to a variety of stimuli.(96)

Guler et al. (2004) investigated the relationship between leptin level and parameters of atopy and asthma in pre-pubertal children.(97) The authors compared BMI, serum leptin levels, serum IgE levels, and response to skin prick test between children with asthma and healthy controls. A significant difference was observed in serum leptin level between the two groups. Atopic asthmatic subjects had significantly higher leptin levels than non-atopic asthmatic subjects, but BMI, gender and age were not found to be associated with asthma. Moreover, a significant, but weak, correlation was observed between leptin levels and IgE levels in the overall group of asthmatic children. This study suggests that leptin may play a role in atopic asthma and that BMI may not be the best indicator of body fat.(97)

Studies of twins provide a good opportunity for researchers to investigate the relationship between obesity and asthma. One such study sought to determine if polymorphic genes are responsible for the association and to estimate the magnitude of the genetic cause. The study investigated the association between BMI and asthma in monozygotic and dizygotic twins. Using modelling techniques to account for genetic and environmental effects, they found a strong association between BMI and asthma with 8% of the genetic component of obesity also apparently involved in the generation of asthma. The study concluded that the covariance between obesity and asthma is predominantly caused by genetic risk factors for both conditions.(98)
Although this study suffers from the weakness of using self-reported measures to determine both obesity and asthma, it suggests that gene-environment interactions may have a huge impact on the association between obesity and asthma.(98)

Sood and colleagues used multivariate logistic regression analysis on data from the Third National Health and Nutrition Examination Survey to test the hypothesis that adults with asthma have higher serum leptin concentrations compared to those who do not have asthma.(99) Results showed that adults with current asthma had higher mean unadjusted serum leptin concentrations compared to adults with no asthma.(99) Following adjustment for skin fold thickness, BMI and demographic characteristics, the association between leptin and asthma was stronger in women than in men. An important finding was that un-stratified mean BMI and triceps skinfold thickness were higher in those with current asthma compared to those who had never had asthma, but after adjustment for gender, there was no significant difference between mean BMI and skinfold thickness of men with current asthma compared to men without asthma. Overall, this study suggests that higher leptin levels are associated with asthma in adults and the relationship may be stronger in women. Another important finding from this study is that BMI and skin fold thickness used to assess body fat may reveal the association between leptin and asthma.

The influence of female reproductive hormones was studied by Barr et al. in (2004),(100) where the use of a post-menopausal hormone was shown to be associated with an increasing rate of newly diagnosed asthma. This research was undertaken from 1986 to 1996, generating 546,259 person-years of follow-up data, and it provided further evidence that female reproductive hormones can impact on the risk of developing asthma in adult women.(100)

Almqvist and colleagues (2007) conducted a randomised controlled trial (RCT) in five-year old children with a family history of asthma which found that omega-3 fatty acid supplementation and restriction of dietary omega-6 fatty acids did not prevent asthma, eczema, or atopy. They also conducted an observational cohort analysis to examine the relationship of all measures of omega-3 and omega-6 polyunsaturated fatty acids with outcomes at the age of five years in the whole birth cohort, regardless of randomisation group.(101) They showed that plasma levels of omega-3 or omega-6 fatty acids were not associated with wheezing, eczema, or atopy at the age of five
years, and overall, fatty acid exposure (plasma levels, dietary intake, and compliance with supplements) was not associated with any respiratory or allergic outcomes.

1.4.2 Summary of evidence from animal studies

A study by Fredberg and colleagues (1996) measured the rate of mechanical energy dissipation and the rate of actomyosin adenosine tri-phosphate (ATP) utilisation simultaneously in activated canine airway smooth muscle subjected to small periodic stretches as occur in breathing.(102) Their findings suggest that steady-state force maintenance (‘latch’) is a low friction state which may account for the inability of dogs with asthma to reverse spontaneous airways obstruction with a deep inspiratory effort.(102) (Figure 1.3)

Figure 1.3: The ‘latch hypothesis’
In the ‘latch hypothesis’, obesity leads to a decrease in functional residual capacity (FRC) and tidal volume (TV), resulting in decreases in smooth muscle stretch. The resultant latching of the smooth muscle leads to increased airway reactivity and irreversibility of obstruction. These effects may be enhanced by breathing around the closing volume, which is characteristic of morbid obesity (adapted from reference.(103)).

The development of animal models of obesity has advanced the frontiers of knowledge in basic research in an attempt to unravel the role of adipocytes in the causation of asthma. Apart from their role in fat and glycogen metabolism, adipocytes play a role in the immune system. One experimental study investigated the mechanism by which dendritic cells (DC) acquire the potential to function as immune cells. Mature DCs are highly active cells equipped for antigen uptake, migration and clustering and activation of T-cells.(103) To test the hypothesis that DCs may acquire fat and glycogen stores during maturation, Maroof and his colleagues studied DC development in mouse stem cells with and without increasing doses of IL-4 or lipopolysaccharide (LPS), both of which promote stimulatory ability of DCs for T cells.(103) They found, by electron microscopy, that immunostimulatory DCs, developing on exposure to IL-4 or LPS from mouse bone marrow stem cells, showed an increasingly altered morphology, with increasing amounts of intracellular fat and glycogen. These suggest that the DC cells play an intermediary role between diet and immune function.(103)

In a study on the allergic immune response in the lungs of male and female mice, the female mice showed a more pronounced type of allergic inflammation in the airway after ovalbumin sensitisation. Melgert et al (2005)(104) showed that a reduction in T-lymphocytes in the lungs of female mice is important for the allergic immune response.

The evidence for the role of genes in the relationship between obesity and asthma is obtained indirectly from animal studies because it is difficult to create animal models with the appropriate genetic makeup to provide the evidence.

One study sought to determine whether leptin, a hormone responsible for satiety, augmented allergic airway response.(105) The authors looked at airway
responsiveness and serum leptin levels in mice following ovalbumin sensitisation. One group of mice were given an infusion of leptin, while a control group were given a saline infusion. The group given leptin infusions showed increased levels of broncho-alveolar lavage fluid cells, cytokines, serum IgE, and increased responses in methacholine challenge which suggests serum leptin may play a role in the relationship between obesity and asthma. This provides further evidence in support of the theory that obesity is a pro-inflammatory state, since leptin is associated with increased level of immune cytokines and circulating immunomodulatory cells. Another study provided evidence of the impact of leptin on airway responsiveness.(106) The latter study showed that obese mice have innate airway hyper-responsiveness and increased pulmonary responses to ozone (an environmental asthma trigger).(105)

1.5 Potential mechanisms

The evidence gained from biomedical research has suggested at least five possible patho-physiological mechanisms (Figures. 1.4 and 1.5) which may explain the link between obesity and asthma.(107)

These mechanisms are:

1) A direct effect on functional respiratory mechanics
2) Immune and inflammatory responses
3) Activation of common genes
4) Hormones and gender
5) Diet, physical activity and fetal programming.(107)
Figure 1.4: Five possible mechanisms linking obesity and asthma
Figure 1.5: Further investigation of the five possible mechanisms linking obesity and asthma

1.5.1 Direct effects on functional respiratory mechanics

The respiratory dysfunction in asthma is characterised by reversible airflow limitation due to bronchoconstriction; both FVC and FEV1 are reduced. Several pathways leading to this state have been identified. These include bronchial hyper-responsiveness and immune and inflammatory damage to the lungs. Obesity has been suggested as a causative mechanism for asthma because of its effect on the mechanism of respiration. Obesity causes a direct decrease in the lung TV and a decrease in the FRC. The resultant reduction in lung volume reduces stretching of the lung smooth muscles. A property of smooth muscle is an intrinsic rate of excitation and contraction called the cycling rate. The reduction in smooth muscle stimulation leads to a downgrading of the cycling rate, which further reduces the tidal breaths worsening the respiratory condition. Therefore, the impact of obesity on the respiratory mechanism may predispose the lungs to a condition favourable to the development of asthma. By weakening respiratory smooth muscles,
obesity indirectly reduces FVC and FEV1, because these are dependent on the ability of the smooth muscles to stretch normally. Also, obesity is associated with relaxation of the lower gastro-oesophageal sphincter leading to reflux of the acidic gastric content into the oesophagus and trachea either by vagally mediated reflux or micro-aspiration,(32) with resultant bronchoconstriction of the lower airway passages. Therefore obesity could be the cause of gastro-oesophageal reflux commonly associated with asthma.(15, 32, 45, 107, 111)

1.5.2 Changes in immune and inflammatory responses

Obesity can be considered as a ‘pro-inflammatory’ state because of its association with several inflammatory markers such as TNF-α, interleukin 6 (IL6) and 1β (IL-6 and IL-1β) and C-reactive protein.(45, 112) These markers have also been linked to the etiopathogenesis of asthma. Also, leptin (Figure 1.6), a hormone produced by adipocytes and found in high concentrations in obese states, has been implicated in the stimulation of Th1-type immune response and pro-inflammatory cytokine release by adipocytes.(32, 45, 107, 111) Serum levels of leptin are significantly higher in patients with asthma compared to healthy people.(97)
Figure 1.6: Adiponectin, produced from adipocytes, interferes with the immune system resulting in decreased immunological tolerance (adapted from reference (112))

1.5.3 Activation of common genes

The polymorphisms exhibited by many genes in the human genome complex raise the possibility of different diseases being influenced by one or more genes. Researchers have identified specific regions of the human genome which are important in both obesity and asthma (Figure 1.7). These are located in several chromosomes, namely 5q, 6p and 12q. The short arm of chromosome 5(5q) contains the β2 adrenergic receptor gene ADRB2, which codes for the adrenergic β2 receptor.(111) This influences sympathetic nervous system activity and is important in regulating not only airway tone, but also resting metabolic rate. This region also contains the glucocorticoid receptor gene NR3C1 which codes for the glucocorticoid receptor. The receptor participates in the modulation of inflammation in obesity and in asthma.(111)
Chromosome 6 contains the genes that code for the major histocompatibility complex (MHC) and TNF-α. These proteins play a role in the immune and inflammatory components of both obesity and asthma. Chromosome 12q contains genes for inflammatory cytokines associated both with obesity and asthma.

![Figure 1.7: Combined effect of genes and environmental factors (i.e. reduced physical activity) on the generation of obesity potentially resulting in the generation of asthma (adapted from reference(45))](image)

Changes in physical activity levels may interact with genetic predisposition resulting in obesity which after that leads to the development of asthma.(45)

1.5.4 The influence of hormones and gender

Refractory asthma is associated with both obesity and female gender; and the female gender is also a common factor in severe asthma and conditions with severe fixed airflow obstruction.(107) These may suggest an underlying gender-specific mechanism in operation. Oestrogen is predominantly a female hormone and the aromatase enzyme responsible for converting androgens to oestrogens is found in adipose tissue.(32) Adipose tissue participates in immunomodulation by secreting...
pro-inflammatory cytokines (IL-6) and hormones (leptin) which stimulate the Th1 type immune responses. This mechanism has been implicated in the immunological mechanism associated with asthma.(14, 15, 32, 45, 107, 111) Although evidence from the Nurses’ Health Study suggests that exogenous oestrogen is an independent risk factor for development of incident asthma in adult women,(30) the exact mechanisms by which oestrogen results in hyper-responsiveness of the airways in asthma is unknown.(45) Oestrogen pathway genes may be the link between gender and the obesity–asthma association as suggested by some researchers.(111) Oestrogen has a potential role in the stimulation of nitric oxide synthesis along with its pro-inflammatory and anti-inflammatory effects that are implicated in the pathogenesis of asthma.(110) Oestrogen is also responsible for airway oedema, limiting the ability of the lung inflation to stretch the airway, resulting in AHR.(100)

1.6 Future research priorities

The available evidence, both from epidemiological and basic science studies indicates a possible association between obesity and asthma. These studies have suggested five main potential patho-physiological mechanisms through which obesity may increase the risk of asthma. Current knowledge on these mechanisms is incomplete. Impairment of lung function, due to a direct mechanical effect of obesity on the lungs, which then leads to asthma, is plausible, but the available studies(113-116) cannot unequivocally support such an effect. The role of obesity on triggering immunological responses, which in turn induce airway inflammation and hyper-responsiveness, also needs to be further investigated, in order to clarify the degree to which obesity triggers the immune system. The role of dietary factors in inducing immuno-inflammatory conditions and whether these conditions may lead to asthma also requires more thorough investigation.
1.7 Assessing causality

1.7.1 The concept of causality

The first and most challenging question to ask is what it means to say that "A causes B?" Expressed most simply, a cause is the first event i.e. "A" preceded the second "B" in time and seemed to be related to its occurrence. In epidemiology however, it is not enough to simply say that one thing causes another; a cause can be considered something that alters the frequency of diseases, health status or associated factors in population. Therefore, epidemiologists and scientists have developed terminology to describe the causal relationship between two events. They say that causes are necessary, sufficient, neither or both (discussed below).(117, 118)

Observational studies in epidemiology can be used to search for causation. Observational studies include: the study of the natural course of events that have occurred in the past, i.e. retrospective studies; the study of events when and as they occur, i.e. cross-sectional studies; and the study as they happen in the future, i.e. prospective studies. In an observational study, association is sought as well. Association refers to events that occur more frequently together than they would by chance. Although association is essential, consideration of distant and disassociated events affecting one common factor and how they eventually affect the outcome in a subject in question is also important. The web of causation represents a set of disassociated events that could be interrelated to each other resulting in a disease.(119) Causality or causal association is applied to ascertain how different circumstances or events are related to each other.(117)

1.7.2 Necessary and sufficient as concepts of disease causality

Assessment of causality requires critical thinking. To determine cause-effect relationships certain elements must be present in order for a disease to develop. Logically, a cause must always precede an outcome and could be termed as either sufficient or necessary.(117, 120) The element of causality that is essential is termed as ‘necessary’. This refers to the idea that a certain variable, be it a pathogen or an event, must always be present and must precede an effect, resulting in a cause-effect association. In the absence of a necessary cause, the disease cannot develop.
On the other hand, a cause is termed ‘sufficient’ when a particular variable inevitably produces an effect or at least initiates the effect. (117) Others have defined sufficient cause as a set of minimal conditions and events that inevitably produce disease. (121)

Each sufficient cause has a necessary cause as a component. For example, in a study of an outbreak of food-borne infection, it has been found that both the chicken salad and creamy dessert were sufficient causes of salmonella diarrhoea. However, it is the ingestion of the Salmonella bacteria that is the necessary cause of the diarrhoea. In a similar manner, there are also different components in the causation of tuberculosis, but the infection with Mycobacterium tuberculosis is a necessary cause (Figure: 1.8). A causal factor per se may be neither necessary nor sufficient, like tobacco use as a factor for cerebrovascular disease. (117)

![Figure 1.8: Causes of tuberculosis (adapted from reference (117))](image)

### 1.7.3 Establishing the cause of a disease

Causal inference is a term used for the process to establish whether the observed associations are likely to be causal and involve the use of guidelines and judgement.
The process of judging causation is often difficult and may be contentious.(117) The key steps in assessing the nature of the relationship between a possible cause and outcome are shown in (Figure 1.9).

Figure 1.9: Key steps in assessing causality between a possible cause and an outcome (adapted from reference (117))
In 1965, the British medical statistician Sir Austin Bradford-Hill established a set of minimal conditions for establishing cause and effect relationships in medicine; these conditions, known as the 9 Bradford-Hill criteria can prove very helpful in trying to decide whether an observed association is causal. The Bradford-Hill criteria are:

1) Strength of association
2) Consistency
3) Specificity
4) Temporality
5) Dose-response relationship
6) Biological plausibility
7) Coherence
8) Experimental evidence
9) Analogy.

**1.7.3.1 Strength of association**

A strong association between the possible cause and effect, as it is measured by the relative risk (RR) is more likely to be causal. However, this value could be influenced by confounding variables or bias. Therefore, a high risk ratio does not automatically establish causality. Relative risks (RR) > 2 are considered strong. For example, cigarette smokers have a doubling in risk of acute myocardial infarction compared to non-smokers.

Even if an association has been shown to be weak based on the computed RR, it still does not preclude it from being causal. This is because the strength of association depends on the relative impact of other possible causes. For example, in observational studies, the association between diet and risk of coronary heart disease (CHD) has been found to be weak; however there is now good evidence from RCTs that dietary modifications can reduce the risk of heart disease.
1.7.3.2 Consistency

Consistency is demonstrated when several studies have yielded the same result. Consistency of results is especially important when a variety of designs are used in different settings, as this implies that making the same mistakes is minimised. It should be noted however, that a lack of consistency does not exclude association. Different levels of exposures and other conditions may contribute to the reduction of the impact of the causal factors in certain studies. Furthermore, when the results of several studies are interpreted, the study with the best study design should be given the greatest weight. Meta-analysis is a technique that pools results of several studies that have examined the same issue, particularly RCTs, to obtain a better overall estimate of the effect. (117)

1.7.3.3 Specificity

If a suspected causal factor is limited to a particular disease only, this adds credibility to a causal claim. It has to be pointed out that a particular factor may be a cause for several diseases and, also, a disease usually has multiple causal factors. It is made clear that absolute specificity is rarely the case in disease aetiology (except in the case of some infections). However, the criterion of specificity becomes very strong for proving causality in the case where a certain factor is the most common risk factor of a disease and thus it is presented to be almost ‘specific’ to the disease in question.

1.7.3.4 Temporality

This relates to the key question of “Did the cause precede the effect?” (118). Temporality is crucial, because the cause must precede the effect. This is often self-evident; however, difficulties in establishing the temporal relationship often arise in case-control and cross-sectional studies, where the measurements of the possible cause and effect are made at the same time. Also, in cases where the cause is an exposure that can be of different levels, it is essential that a high enough level can be reached before the disease can occur. This also presents a difficulty in the establishment of the correct temporal sequence. Repeated measurements of the
exposure at more than one time point and in different locations may aid the researcher to strengthen the evidence. (117)

1.7.3.5 Dose-response relationship

Dose-response relationship occurs when changes in the level of the possible cause corresponds to changes in the prevalence or incidence of the effect. Hearing loss can be an example of dose-response relationship with noise. It has been shown that the prevalence of hearing loss increases with the noise level as well as with the exposure time. (117)

1.7.3.6 Biological plausibility

In simple terms, the association should make sense in terms of its adherence to the biological principles. Association may be proven to be causal based on current biological, medical, and epidemiological knowledge, as well as other scientific knowledge available. Logical analysis based on new knowledge, however, should not interfere with or restrict obvious and common-sense causal inferences. (120) A good example for this criterion is the consumption of Vibrio cholera-infested water leading to the development of cholera. In the 1830s the predominant view on the cause of cholera involved “miasma”, (125, 126) rather than contagion. (125) Contagion was not supported by evidence until John Snow’s work was published at a later date. (126) Pasteur and his colleagues later identified the causative agent as Vibrio cholera. This shows that the lack of plausibility may simply reflect the current lack of scientific knowledge. (117)

1.7.3.7 Coherence

The cause-and-effect interpretation of the results of a study should not seriously conflict with the generally known facts of the natural history and biology of a disease. (122)
1.7.3.8 Experimental evidence

Any related research that is based on laboratory experiments or “in vitro” animal models will make a causal inference more plausible.(122) An RCT is a prospective experimental study in which the effects of one or more interventions are assessed by dividing a research population on the basis of random allocation into one or more experimental and one or more control groups.(127) Biomedical experimental studies are laboratory studies which use experiments “in vitro” or on experimental animals, in order to test the hypotheses under study.

1.7.3.9 Analogy

When there is an already established cause and effect model for a particular disease, we might sometimes question whether a similar model could be applied to a disease under investigation as well.(122)

Apart from the above nine criteria of causation formulated by Bradford-Hill in 1965, modern epidemiology also considers another two criteria: reversibility and experimental evidence.

1.7.4 Reversibility

If the removal of a possible cause results in the reduction of the risk of having the disease, then there is a greater likelihood that the association is causal. For example, the cessation of cigarette smoking is associated with a reduced risk of having lung cancer when compared to the people who continue to smoke.(128, 129) This finding strengthens the likelihood that lung cancer is caused by cigarette smoking. However, if the cause leads to rapid irreversible changes in the host and later produces a disease regardless of the presence of a continued exposure, then reversibility cannot be a condition for causality.(117)
1.7.5 Study design

A variety of study designs have been utilised to assess causation (see Table 1.2) with varying success. Experimental evidence is however wherever possible, considered to be pivotal to making causal inferences. Moreover, the magnitude of the causal nature of the association is believed to be very strong in experimental studies. Thus, the results of such studies become the basis of inferences on the cause-effect association by providing substantial supporting evidence. This principle entails the demonstration of change in the outcome after the change in the exposure has been made under controlled conditions. Considering other designs:

- Cohort studies are the next best design, because bias is minimised especially when it is well-conducted.

- Case-control studies can provide consistency, sometimes temporality, specificity and often the strength of dose response.

- Cross-sectional studies are less suited to establish causation, because they provide no direct evidence on the temporal sequence of the exposure and outcome.

- Ecologic studies provide the weakest evidence for causality due to the increased risk of incorrect extrapolation to individuals from regional or national data.

### Table 1.2: Relative ability of different types of study to “prove” causation (adapted from reference (117))

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Ability to “prove” causation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomised controlled trials</td>
<td>Strong</td>
</tr>
<tr>
<td>Cohort studies</td>
<td>Moderate</td>
</tr>
<tr>
<td>Case-control studies</td>
<td>Moderate</td>
</tr>
<tr>
<td>Cross-sectional studies</td>
<td>Weak</td>
</tr>
<tr>
<td>Ecological studies</td>
<td>Weak</td>
</tr>
</tbody>
</table>
1.7.6 Judging the evidence

Although these guidelines have been developed, there are still no completely reliable criteria for establishing causality. Causal inference is usually non-uniform and tentative, and judgement must be made based on the available evidence. All these imply that uncertainty always remains. Furthermore, available studies are often conflicting with each other and due weight must be given when conclusions are to be inferred. In judging the different aspects of causation, the correct temporal sequence is essential and should be given the greatest weight. Once it is established, the next greatest weight should be appropriated to plausibility, consistency, and the dose-response relationship. The likelihood of a causal relationship is increased when a variety of studies lead to the same conclusion. It is also important to consider the evidence from well-designed studies, especially if they are conducted in different locations.\(^{(117, 120)}\)

The most important use of information derived from the study of disease causation is its potential in preventing the disease. If the causal pathways have already been determined, on the basis of the quantitative evidence from epidemiological studies, the decision about preventing a disease may be readily made. However, in situations where the causation pathway is not very well established but the impact is of great importance to public health, the “precautionary principle”\(^{(130)}\) may be applied. This principle involves implementing preventive actions as a safety measure to arrest disease transmission or development and is therefore called “precautionary prevention”.\(^{(130)}\)

1.8 Chapter summary

Technological advancements and modernisation have resulted in people leading a more sedentary life, this in turn has led to increased rates of obesity worldwide. Obesity is a state of health which constitutes a risk factor for several morbidities, such as cardiovascular diseases, diabetes, sleep disorders, and respiratory diseases.

Asthma is an inflammatory disease of the airways. The exact aetiology of asthma is unknown, but certain substances and physical activities can trigger the pathophysiological phenomena of asthma. Asthma triggers are classified into four broad
groups: irritating chemical substances; allergens; respiratory infections (particularly the viral ones); and exercise. In the last few decades, a parallel increase in the rates of obesity and asthma has been observed worldwide, giving credence to the hypothesis that obesity also constitutes a risk factor for asthma.

A number of epidemiological and basic science studies, both in human populations and in animal models, have indicated a positive association between obesity and asthma. Current research has suggested five possible patho-physiological mechanisms in order to explain the possible impact of obesity on the development of asthma. These mechanisms are summarised as: a direct effect on functional respiratory mechanics; immune and inflammatory responses; activation of common genes; hormones and gender; diet, physical activity and foetal programming.

Although several biomedical studies have been conducted, the above mechanisms have not yet been fully elucidated. There is also no clear view on whether these mechanisms act in the same way in children and in adults. For this reason, further studies on the topic are required. The investigation of causality between obesity and asthma should be carried out following the epidemiological criteria of causation, as defined by Bradford-Hill, and further developed for the modern era.

I decided to undertake an epidemiological investigation into the association between obesity and asthma in pre-pubertal children because no such investigation had previously been undertaken in Arab countries. I chose to undertake the fieldwork in Madinah because it provided a reasonably well-developed infrastructure for undertaking the proposed fieldwork. Furthermore, in view of my previous experiences of working as a Director of the School Health Department, I had the contacts and network that would help facilitate access to relevant ministers, head teachers and schools that would be important to execute the planned studies.

The chapter which follows will describe the pilot study in which I sought to assess the feasibility of undertaking a study investigating the relationship between obesity and asthma in primary schoolchildren aged 6-8 years in Madinah.
Chapter 2: Pilot study on the association between obesity and asthma in 6-8 year-old children in Madinah, Saudi Arabia

2.1 Introduction

In Arab countries generally and, more particularly in Gulf countries, there has been a remarkable change in lifestyle over the last few decades, leading to a subsequent change in the pattern of diseases. Obesity is one of the emerging health problems in the Arab countries that attract the attention of health professionals. Epidemiological studies among the populations of the Arabian Peninsula and the evaluation of the health risk of obesity have shown that the prevalence of obesity ranges between 16-25% in men and 17-48% in women.\(^{131}\)

Only a few empirical studies have been carried out in Saudi Arabia; these studies suggest that the prevalence of obesity and overweight in the general population has increased among Saudi people, both in males and females (see Figure 1.2).\(^{132-135}\)

Obesity is considered an avoidable risk factor for several chronic diseases such as diabetes mellitus, hypertension and ischemic heart disease.\(^{136, 137}\) There are a large number of studies hypothesising that obesity may contribute to the risk of developing asthma, but the exact nature of this relationship has not been fully clarified.\(^{138-140}\) Asthma, in turn, is one of the chronic disabling health problems in many countries all over the world.\(^{84}\)

The Kingdom of Saudi Arabia occupies most of the Arabian Peninsula, the original homeland of the Arab people. Saudi Arabia occupies 868,730 square miles (2,250,000 square kilometres) (Figure 2.1). It is bounded to the east by the Arabian (Persian) Gulf; and to the west by the Red Sea. It borders to the south and southeast with Yemen, Oman, the United Arab Emirates, and Qatar; and to the north and northeast with Jordan, Iraq, and Kuwait. Saudi Arabia has a hot desert climate with high humidity on the coastal fringes. Rainfall is scarce except in the area of Asir, where it is sufficient for agriculture on terraced farms and upper slopes and alluvial planes.\(^{141}\)
In Saudi Arabia about two million people suffer from asthma.\(^{(142)}\) The prevalence of asthma in schoolchildren varies among the different regions of the country.\(^{(143, 144)}\) The overall prevalence of childhood asthma across the entire country, as it has been estimated from studies based on questionnaires, varies between 10-20%. Some estimates of the prevalence in certain regions are as follows: 23% in Taif, 22% in Hail, 22% in Jazan, 16% in Qassim, 12% in Jeddah, and 12% in the Eastern Region.\(^{(143, 145)}\)

The Saudi Initiative for Asthma (SINA) pays particular attention to childhood asthma because it is considered to be one of the most common health problems responsible for school absenteeism and reduced participation in sports and other activities.\(^{(143, 146)}\)
Moreover, childhood asthma is a very important issue in Saudi Arabia, taking into account that children below 15 years old represent over 50% of the total population of the country. (141)

Madinah is a city in the Hejaz region of western Saudi Arabia, and the capital of Al Madinah Province. The Madinah region consists of seven cities: Madinah (the capital of the Province), Al Hunakiyah, Mahd Al Thahab, Al 'Ula, Bader, Khaybar and Yanbu. Madinah is the biggest city in this region (see Figure 2.2).

Figure 2.2: The 13 different Regions of Saudi Arabia (adapted from the Wikipedia the free Encyclopaedia Madinah city highlighted: http://en.wikipedia.org/wiki/File:Saudi_map.jpg)

Henceforth, the term Madinah will be used to denote the city rather than the province.
Despite, the abundance of high-calibre tertiary medical services in Saudi Arabia, the management of asthma in children and adults is poorly addressed by the healthcare services. Insufficient knowledge of asthma management, fears regarding the use of new drugs by healthcare professionals, and a lack of integrated services for tackling environmental hazards lead to insufficient asthma control within the Saudi population. As a result, beside the fact that the expenditure on healthcare has increased, the quality of life of asthma sufferers and their families remains sub-optimal.(148)

2.2 The value of a pilot study

A pilot study is an exploratory study that can help in designing future larger scale studies. Generally, a pilot study tests the methodologies and the research instruments to be implemented and makes a primary investigation of the study population under consideration.(149) Conducting a pilot study can help to reveal any problems or obstacles that could be avoided when designing the main, large-scale study. In addition, a pilot study gives a good idea of the facilities and the costs required for the implementation of the larger scale study.

The two epidemiological studies presented in Chapters 3 and 4 of this thesis involved the collection of data from a very large sample of participants, as well as performing a large number of procedures (i.e. questionnaires, spirometry measurements, skin prick tests (SPT) and anthropometric measurements). For this reason, a pilot study, which would test the feasibility and the difficulties of the suggested research procedures, was considered necessary. Moreover, since, to our knowledge, there are no studies on childhood asthma in Madinah, a pilot study was considered necessary in order to enable us to estimate the prevalence of childhood asthma and, therefore, decide on whether a larger scale study was feasible.

2.3 Aim and objectives

2.3.1 Aim

The aim of this pilot study was to test the feasibility of conducting two large-scale epidemiological studies investigating asthma and its potential association with obesity
among schoolchildren in Madinah, Saudi Arabia. The first was a cross-sectional study aiming to estimate the prevalence of asthma among schoolchildren. The second was a matched case-control study aiming to investigate any potential relationship between obesity and asthma. Therefore, the pilot study in this thesis included two phases: Phase I investigated the feasibility of the cross-sectional study and Phase II investigated the feasibility of the matched case-control study.

2.3.2 Objectives

The objectives of the pilot study were to:

- Determine the feasibility of conducting the two large-scale studies;
- Determine an estimate of the prevalence of childhood asthma in Madinah, so that we can decide if a larger scale study is justified;
- Decide on the appropriate methods and materials for the large-scale studies;
- Identify any obstacles that could occur when trying to conduct such studies;
- Estimate the logistics and the cost required for such studies;
- Investigate the social acceptability of carrying out such studies.

2.3.3 Research questions

I sought to answer the following questions:

1) Is it feasible to conduct two large scale epidemiological studies aiming to investigate asthma prevalence and the association between obesity and asthma among schoolchildren in Madinah, Saudi Arabia?
2) What is the prevalence of asthma among primary school-aged children in Madinah?
3) Is there an association between obesity and asthma in boys and/or girls in this population and if so what are the likely causal mechanisms?
2.4 Methods

2.4.1 Study design

The pilot study comprised two phases: Phase I, a two-stage cross-sectional survey; and Phase II, a case-control study.

Phase I of the pilot study employed a cross-sectional design, while Phase II included a case-control study. Only subjects fulfilling the criteria for inclusion as cases and controls were recruited from school areas known to have a high prevalence of asthma.

2.4.2 Study population and recruitment

The study population consisted of primary school students in Madinah, aged 6-8 years (both girls and boys). Since schoolchildren are an easily reachable group, the study was planned as a school-based survey. Permission was obtained from the education authorities of Madinah (General Directorate of Education); the School Health Departments, Ministry of Education; and from the respective school head teachers. Parents were asked to give their signed informed consent.

A list of all the primary schools in Madinah (n=614) was obtained from the General Directorate of Education. Eleven primary schools (six for boys and five for girls) from Madinah were randomly selected from a list of the schools in Madinah; the subjects from the selected schools were recruited using an invitation letter sent by General Directorate of Education to the head teachers (Appendix 2 includes all the invitation letters). All students aged 6-8 years in the selected schools were eligible for recruitment in Phase I. Students whose parents gave their consent for further measurements to be performed (i.e. spirometry, anthropometric measurements, SPT, and phlebotomy) were eligible for participation in Phase II of the pilot study. An information sheet was designed to collect data on school characteristics (for both boys and girls) e.g. school name, number of students etc. as well as for the collection of study information. This form was used in the pilot study as well as in the larger study. In Chapter 4 Appendix number 13,14,15 and 16.
2.4.3 My training and the training of the research team

Before starting the pilot study I attended the following training courses/workshops and gained practical skills that would be important for me to use in my fieldwork:

- A nurse asthma clinic at Dundee University Hospital, Dundee, Scotland on 18th of May 2008 on the management of asthma in schoolchildren.
- A one-day training course provided by the Education for Health, Warwick, England, UK “How to perform a Skin Prick Test” at the University of Edinburgh, on 1st of August 2008.

A two-day training programme was conducted in Madinah for the healthcare professionals (doctors and nurses) who assisted in the study. (Appendix 3) refers to the GANTT chart for the pilot study. The content of the training programme is described in detail in (Appendix 4). The training programme focused on the methods and techniques required for achieving correct, anthropometric measurements (i.e. weight height, waist circumference, and triceps skin-fold thickness), lung function measurements (spirometry), SPT and blood sample collection (phlebotomy). I supervised the staff who helped me during the field work.

2.4.3.1 The research team

Because of cultural preferences and religious sensitivities the research teams were organised separately for the boys and girls schools. The boys’ school team consisted of one male doctor, three male nurses and one male laboratory technician. The girls’ school team consisted of one female doctor, three female nurses and one female laboratory technician. These healthcare professionals had sufficient experience in conducting this type of studies and were recommended by the Department of the General Directorate of Education the Ministry of Education. After they were recommended to me, I contacted each of them personally and all of them agreed to participate in the study. I conducted personal interviews with them to explain the study and how they would participate in it. They all attended the training course,
which provided them with theoretical insights and practical skills to successfully carry out the research.

2.4.3.2 Training team

I led the training of the research teams and undertook this with the support of: Professor Mohamed El-Awdy (Professor of Community and Family Medicine at The University of Tibah); Dr. Samia Sabur (Consultant in Family Medicine, National Guard Hospital, Madinah); and Dr. Mohamed Alam (Consultant in Haematology, King Fahad Hospital, Madinah).

The course included background information on obesity, asthma, an overview of how to conduct cross-sectional and case-control studies, and consent procedures in children. There was furthermore practical training given in taking anthropometric measurements (i.e. height, weight, waist circumference, triceps skinfold thickness and calculating BMI), undertaking skin prick tests (SPT) to different allergens and performing spirometry to assess lung function. This training was provided over three days, this comprising of an initial two day training course and a third day for revision of key messages and assessment.

2.4.3.3 Assessment of the research team in Madinah

After demonstration, and under the supervision of experts, the trainees were asked to show their practical skills on how to conduct spirometry and interpret the outputs. The quality control and relevant protocols for this measuring of the lung function with spirometry were checked by the experts/trainers. Finally, on the third day of the training course and in the presence of Professor Aziz Sheikh, the revision and practical aspects of performing SPT and spirometry took place.

2.4.3.4 Feedback on the training of research team in Madinah

According to the feedback forms received from the healthcare professionals (n=10), the training course was found to be appropriate; 100% of the healthcare professionals
considered they had obtained relevant theoretical and practical skills. Also, the feedback forms demonstrated that the course was well-organised, materials were explained and demonstrated in a clear and understandable way. At the end of this course, most of the participants rated this training as excellent (Appendix 5).

2.4.4 The questionnaire

Collection of data for Phase I was based on the Arabic version of the validated questionnaire from the ISAAC.(150) ISAAC was an extensive worldwide epidemiological study of childhood asthma and allergies which involved nearly two million children from more than 100 countries worldwide.(151) The questionnaire used in ISAAC project was designed to include a minimum set of core questions about asthma, allergic rhinitis, and eczema (Appendix 6-A).(152) It was developed through review of several similar questionnaires used in other studies and through experience gained from pilot studies conducted prior to the beginning of the main project; it has been validated for use in many languages.(152)

Therefore, it is made clear that the ISAAC questionnaire has been specifically designed to investigate the prevalence of the aforementioned conditions among paediatric populations across the world. Moreover, it is a simple and low-cost tool that can be easily answered even by people with minimum education.(153)

Based on consideration of the above and aiming to make our findings comparable to those from international studies, the ISAAC questionnaire was selected for data collection in this thesis. The questionnaire was administered to the parents of each eligible child by the head teachers. Parents were asked to complete it at home and returned it to the school. The validated Arabic version of the ISAAC questionnaire was obtained from the University of Oman Medical School and it was used with permission.(150)

This questionnaire comprised two parts. The first part was the Arabic-translated version of the core ISAAC questionnaire, which comprised 21 questions related to the prevalence of symptoms of asthma, rhinitis and eczema in children. The information requested included: 1) parental reports of symptoms of these three conditions; 2)
parental reports of a clinician-diagnosed asthma, allergic rhinitis, or eczema; and 3) parental reports of any current symptoms (i.e. within the last 12 months prior to the study) of the three disorders in question (Appendix 6-B).

The second part of the questionnaire contained questions relevant to possible environmental exposures possibly leading to asthma and allergic disorders. These environmental questions were modified slightly to ensure that all questions were relevant to the Saudi context, e.g. housing conditions; pets and presence of animals at home; number of people in households, and parental smoking (Appendix 6-C).

Apart from the core questions of the ISAAC tool, there was another set of questions aiming to collect information about the socio-demographic status of the parents, as well as about lifestyle characteristics of the participating children (Appendix 6-C).

A consent form was sent to the parents; so that approval was taken for their children to participate in the study and also for measurements to be performed in Phase II. In addition, a separate data collection form was used for Phase II case-control girls and boys (Appendices 15 and 16) There was also an evaluation sheet addressed to the healthcare professionals (i.e. the research team) who assisted in the study, which was designed to elicit information about the research team’s perspective on the appropriateness of the questionnaire as a research tool (Appendix 5-B).

We used an Arabic version of the ISAAC questionnaire for the three diseases: asthma/asthma symptoms, rhinitis and eczema. Our goal was to evaluate the prevalence of asthma and asthmatic symptoms in children aged 6-8 years and to define the cases of asthma for a case-control study. For this reason, we focused only on asthma and symptoms of asthma outcomes in children aged 6-8 years.

2.4.5 Definition of cases

The identification of asthma cases for Phase II of the pilot study was based on question 1 of the ISAAC questionnaire: “Has your child ever had wheezing or whistling in the chest at any time in the past?”(Appendix 6-B, question 1). Studies suggest that symptoms of wheezing and whistling are fairly well-associated with bronchial hyper-responsiveness which is a hallmark of asthma.(154-157) As a
diagnostic criterion for asthma, I chose “ever wheezed”, because this question was one of the main stem questions in the ISAAC module. Additionally, this is likely to provide the most useful insights in relation to the lifetime prevalence of asthma in children.

2.4.6 Definition of controls

Subjects who gave a negative answer to question 1 of the ISAAC questionnaire were considered as not being likely to have asthma, and they were eligible for participation as controls for Phase II of the pilot study.

2.4.7 Anthropometric measurements

For Phase II of the pilot study, the following anthropometric measurements were taken as part of data collection: weight, height, skin fold thickness for peripheral and central areas of the body triceps skin-fold thickness (TSFT), and waist circumference (WC).

Weight and height were measured to enable calculation of the BMI. Weight was measured using a scale balance and height was measured by a vertical scale. BMI was defined as weight (in kg) divided by the square of height (in m²) and it is the most frequent measure of weight in relation to height. The value of BMI was used to determine obesity status using certain cut-off points, which are determined according to the distribution of BMI values in a target population.(158) Although BMI has been extensively used in obesity studies and it has been characterised as “the backbone of the obesity classification system and surveillance statistics an immensely valuable tool”, its use as a proxy of obesity has several disadvantages and it needs to be used with care.(158)

WC reflects total and abdominal fat levels and, as an indicator of adiposity, is not greatly influenced by height.(158) WC was measured using a steel measuring tape (Lufkin Executive Thinline Metric Tapes).
Skin fold thickness is used to quantify the amount of subcutaneous fat;(158) TSFT is considered as the simplest measure and it is frequently used.(158) Subcutaneous fat is taken as indicator of total fat of the body and, therefore, measuring TSFT is another indicator of obesity.(158) TSFT was measured by a skin fold calibre (Holtain Skinfold Caliper).

Standardised procedures for each of the measurements were followed strictly and these are described in Appendices 7-9.

2.4.8 Assessment of pulmonary function

For Phase II of the pilot study, spirometry was performed on the selected sample of students in order to assess pulmonary function. The following lung function indicators were measured: FEV1, FVC, and peak expiratory flow (PEF) and the FEV1/FVC ratio were calculated (Appendix 10). A portable spirometer was used and each child was instructed on how to blow air in to the spirometer. Measurements were performed with children in the standing position; the best reading of three successive measurements was recorded.

Spirometry is applied in order to assess lung function and it is particularly useful in differentiating obstructive airway disorders (such as asthma and chronic obstructive pulmonary disease from restrictive lung diseases (i.e. diseases in which there is no obstruction in the airways, but the size of the lungs is reduced).(159) As discussed in Chapter 1, one of the proposed mechanisms linking obesity with asthma suggests a direct effect of obesity on respiratory mechanics with a resulting impairment of the lung function. Thus, performing spirometry on the subjects in Phase II was considered useful to allow assessment of the impact of obesity on lung function.

2.4.9 Skin prick tests

Eligible children in Phase II of the pilot study were tested for immediate hypersensitivity responses to an array of aeroallergens. Such tests would indicate whether a child was vulnerable to allergy, i.e. whether the child was atopic; atopy is thought to be the strongest identifiable risk factor for asthma.(160) A positive test was
taken as a wheal with a mean diameter of at least 3mm greater than the saline control, 15 minutes after pricking the allergen into the right forearm. The following allergens were tested: house dust mite (Dermatophagoides pteronyssinus and Dermatophagoides farinae), desert weeds, cat, cockroach and pollen of Cynodon dactylon (Bermuda grass). These allergens were selected based on a review of previous studies in Saudi Arabia and worldwide (Appendix 11). (161-163) The above allergens were selected because exposure to them is commonly associated with the development of asthma.

2.4.10 Laboratory assays for a venous blood sample

Blood samples were collected from a small sample of children participating in Phase II of the pilot study for assessing the levels of immunological parameters. The following parameters were measured: C-reactive protein; adiponectin; leptin; Th1; Th2; T reg polyclonal IgE; IgE antibodies specific for D. pteronyssinus and for cockroach; for whole blood cultures stimulated with mitogen and relevant allergens for the measurement of the regulatory cytokines, IFN-γ, IL-13. (164) The above parameters are known to increase in asthmatic response and, as diagnostic tests, are characterised by high sensitivity and specificity. (107)

Phlebotomy was performed by trained members of the research team. From each subject, a blood sample of 10 ml was collected which was separated into two different tubes for obtaining serum and whole blood respectively. Serum samples were stored at -40°C and shipped frozen to Al-Borg Laboratory (Appendix 12).

Blood samples were analysed in the Central Laboratory of the Ministry of Health, in one of the biggest private laboratories in Madinah (Al-Borg Laboratory).

2.5 Data analysis

2.5.1 Data management

All data collected through the questionnaires or recorded through performance of measurements and laboratory tests were initially entered in Microsoft Excel. Data
cleaning was applied to investigate the datasets and to identify potential copy mistakes and missing values. Then data were analysed with the Statistical Package for Social Sciences (SPSS) version 14.0, under the supervision of Dr. Rob Elton, statistician, Allergy & Respiratory Research Group, Centre for Population Health Sciences, Medical School, The University of Edinburgh, UK.

2.5.2 Baseline characteristics

Analysis of baseline characteristics was performed to provide descriptions of the students studied. These characteristics include:

- Age
- Gender
- Resident in Madinah for at least one year
- Family history of atopy, eczema, rhinitis, vernal conjunctivitis and asthma.

2.5.3 Outcome variables

The key outcomes of interest were:

- Prevalence of asthma
- Prevalence of allergic rhinitis
- Prevalence of atopy (positive sensitisation to allergens through SPTs)
- Lung function measures
- Blood parameters
- Socio-demographic characteristics
- Lifestyle factors.
2.5.4 Statistical analyses

In Phase I, the relative frequency (i.e. prevalence %) of asthma, allergic rhinitis, and eczema was computed and the 95% confidence intervals (CIs) were calculated assuming the normal approximation of the binomial distribution. Relative frequencies and 95% CIs were calculated for each of the studied disorders separately, as well as for comorbidities.

In Phase II, means and SDs were calculated for continuous variables, i.e. the measures of obesity and the measures of lung function. Any missing values were ignored and the calculation of statistical measures was based on the rest of the dataset.

Although most respondents completed their questionnaires fully, there was a small amount of data missing for some variables from some respondents. Rather than omitting the whole case from analysis when this happened, cases were only omitted when the relevant variables were part of the analysis. This was achieved automatically in SPSS by setting these entries as missing.

2.6 Results

2.6.1 Results of the descriptive analysis of Phase I of the pilot study

All the eleven schools (five girls’ and six boys’ schools) approached for the pilot study agreed to participate.

Table 2.1 shows the number of children approached in each school (out of 614 primary schools in Madinah) and the number of children who declined and the children who participated in each of the two phases of the study. A total of 1,674 questionnaires were sent to the parents of the students and the response rate for Phase I was 77.9% (i.e. 1304 questionnaires were answered; 470 for girls and 834 for boys). Out of the 1304 students that participated in Phase I, 899 (68.9%) of them were eligible for participation in Phase II. Eligible participants were those whose parents gave their signed consent for all the measurements of Phase II i.e. anthropometric measurements, spirometry, SPT and phlebotomy.
Since the main aim of Phase II of the pilot study was to test the procedures of data collection, it was decided that only 10% of the eligible students would be selected for Phase II. Therefore, 90 students were randomly selected; in this sample, a proportion of 1:4 between cases and controls was applied, i.e. out of the 90 students, 18 were cases (according to question 1 of the questionnaire) and 72 controls. One of the selected cases was withdrawn during the study and, therefore, the number of controls was reduced to 68; this led to a final sample of 85 students participating in Phase II.

At the beginning of the pilot work, I thought that I may encounter difficulties to find sufficient numbers of cases for Phase II of our study. For this reason during the pilot study, I opted to recruit cases to controls in a 1:4 ratio. I thus recruited 90 students: 18 case and 72 controls. This preliminary work however revealed a high prevalence of asthma and I therefore opted for a 1:1 ratio in the recruitment of cases and controls in the subsequent work. This is because this has been shown to be the most efficient strategy in cases where there are no concerns about the ability to recruit cases or controls.(165)

Tables 2.2, 2.3, and 2.4 show the point prevalence of the three studied disorders in Madinah on the basis of the pilot study data. The prevalence of asthma in girls was estimated at 12.9% (95% CI 10.0, 16.0), while in boys at 19.8%. (95% CI 17.1, 22.5) The total prevalence of asthma among the participating students of Phase I of the pilot study was estimated at 17.4% (95% CI 15.3, 19.4). The prevalence of rhinitis in girls was estimated at 16.8% (95% CI 13.4, 20.2) and in boys at 26.7% (95% CI 24.0, 30.0). The total prevalence of rhinitis in both genders was estimated at 23.2% (95% CI 20.9, 25.5). The prevalence of eczema in girls was estimated at 8.5% (95% CI 6.0, 11.0) and in boys at 10.4% (95% CI 8.3, 12.5). The total prevalence of eczema was estimated at 9.7% (95% CI 8.1, 11.3).

The prevalence of children who demonstrated symptoms of more than one allergic disorder (Table 2.5) was estimated at 10.9%. The respective prevalence in girls was estimated at 7.6% and in boys at 12.8%. The prevalence of children who demonstrated symptoms of both asthma and rhinitis was estimated at 7.8% (girls: 4.5%; boys: 9.6%). The prevalence of children who demonstrated symptoms of both asthma and eczema is estimated at 3.8% (girls: 2.1%; boys: 4.7%). The prevalence of children who demonstrated symptoms of both rhinitis and eczema was estimated at
3.9% (girls: 2.3%; boys: 4.8%). The prevalence of children who demonstrated symptoms of all three allergic disorders (i.e. eczema, rhinitis and asthma) was estimated at 2.2% (girls: 0.6%; boys: 3.1%).
<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender of the students</th>
<th>Questionnaires sent to primary school-aged children (aged 6-8 years)</th>
<th>Refused to participate</th>
<th>Participated in Phase I</th>
<th>Declined to participate in Phase II</th>
<th>Agreed to participate in Phase II</th>
<th>Subjects recruited for Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>0022</td>
<td>Boys</td>
<td>92</td>
<td>25</td>
<td>67 (72.8%)</td>
<td>23</td>
<td>44 (65.7%)</td>
<td>8 (18.2%)</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>223</td>
<td>69</td>
<td>154 (69.1%)</td>
<td>44</td>
<td>110 (71.4%)</td>
<td>8 (7.3%)</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>135</td>
<td>18</td>
<td>117 (86.7%)</td>
<td>24</td>
<td>93 (79.5%)</td>
<td>8 (8.6%)</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>346</td>
<td>103</td>
<td>243 (70.2%)</td>
<td>72</td>
<td>171 (70.4%)</td>
<td>8 (4.7%)</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>202</td>
<td>50</td>
<td>152 (75.2%)</td>
<td>40</td>
<td>112 (73.7%)</td>
<td>8 (7.1%)</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>134</td>
<td>33</td>
<td>101 (75.4%)</td>
<td>38</td>
<td>63 (62.4%)</td>
<td>7 (11.1%)</td>
</tr>
<tr>
<td><strong>Total Boys</strong></td>
<td></td>
<td><strong>1132</strong></td>
<td><strong>298</strong></td>
<td><strong>834 (73.7%)</strong></td>
<td><strong>241</strong></td>
<td><strong>593 (71.1%)</strong></td>
<td><strong>47 (7.9%)</strong></td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>189</td>
<td>18</td>
<td>171 (90.5%)</td>
<td>67</td>
<td>104 (60.8%)</td>
<td>6 (5.8%)</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>49</td>
<td>11</td>
<td>38 (77.6%)</td>
<td>16</td>
<td>22 (57.9%)</td>
<td>8 (36.4%)</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>121</td>
<td>13</td>
<td>108 (89.3%)</td>
<td>25</td>
<td>83 (76.9%)</td>
<td>8 (9.6%)</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>56</td>
<td>12</td>
<td>44 (78.6%)</td>
<td>22</td>
<td>22 (50.0%)</td>
<td>8 (36.4%)</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>127</td>
<td>18</td>
<td>109 (85.8%)</td>
<td>34</td>
<td>75 (68.8%)</td>
<td>8 (10.7%)</td>
</tr>
<tr>
<td><strong>Total Girls</strong></td>
<td></td>
<td><strong>542</strong></td>
<td><strong>72</strong></td>
<td><strong>470 (86.7%)</strong></td>
<td><strong>164</strong></td>
<td><strong>306 (65.1%)</strong></td>
<td><strong>38 (12.4%)</strong></td>
</tr>
<tr>
<td><strong>Total number of children</strong></td>
<td></td>
<td><strong>1674</strong></td>
<td><strong>370 (22.1%)</strong></td>
<td><strong>1304 (77.9%)</strong></td>
<td><strong>405 (31.1%)</strong></td>
<td><strong>899 (68.9%)</strong></td>
<td><strong>85 (9.5%)</strong></td>
</tr>
</tbody>
</table>
Table 2.2: Prevalence of asthma parental reports according to the ISAAC questionnaire

<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender</th>
<th>Number of participants</th>
<th>Parental reports of ever having had wheeze</th>
<th>95% CI for the rate</th>
<th>Parental reports of diagnosed asthma</th>
<th>95% CI for the rate</th>
<th>Parental reports of symptoms of asthma in the last 12 months</th>
<th>95% CI for the rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0022</td>
<td>Boys</td>
<td>67</td>
<td>8 (12.1%)</td>
<td>(4.3, 20.0)</td>
<td>8 (11.9%)</td>
<td>(4.1, 20.0)</td>
<td>9 (13.4%)</td>
<td>(5.2, 22.0)</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>154</td>
<td>47 (30.9%)</td>
<td>(24.0, 38.2)</td>
<td>36 (23.4%)</td>
<td>(17.0, 30.1)</td>
<td>36 (23.4%)</td>
<td>(17.0, 30.1)</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>117</td>
<td>28 (23.9%)</td>
<td>(16.2, 32.0)</td>
<td>21 (18.0%)</td>
<td>(11.0, 25.0)</td>
<td>30 (25.6%)</td>
<td>(18.0, 34.0)</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>243</td>
<td>30 (12.4%)</td>
<td>(8.3, 16.5)</td>
<td>30 (12.4%)</td>
<td>(8.3, 16.5)</td>
<td>44 (18.1%)</td>
<td>(13.3, 23.0)</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>152</td>
<td>33 (21.7%)</td>
<td>(15.1, 28.3)</td>
<td>25 (16.5%)</td>
<td>(11.0, 22.4)</td>
<td>32 (21.1%)</td>
<td>(15.0, 28.0)</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>101</td>
<td>19 (18.8%)</td>
<td>(11.2, 26.4)</td>
<td>13 (12.9%)</td>
<td>(6.4, 19.4)</td>
<td>21 (20.8%)</td>
<td>(13.0, 29.0)</td>
</tr>
<tr>
<td>Total Boys</td>
<td></td>
<td>834</td>
<td>165 (19.8%)</td>
<td>(17.1, 22.5)</td>
<td>133 (16.0%)</td>
<td>(13.5, 18.5)</td>
<td>172 (20.6%)</td>
<td>(18.0, 23.3)</td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>171</td>
<td>15 (8.8%)</td>
<td>(4.5, 13.0)</td>
<td>17 (9.9%)</td>
<td>(5.4, 14.4)</td>
<td>27 (15.8%)</td>
<td>(20.3, 21.3)</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>38</td>
<td>5 (13.2%)</td>
<td>(2.4, 24.0)</td>
<td>2 (5.3%)</td>
<td>(-1.8, 12.4)</td>
<td>4 (10.5%)</td>
<td>(0.8, 20.2)</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>108</td>
<td>19 (17.6%)</td>
<td>(10.4, 24.8)</td>
<td>14 (13.0%)</td>
<td>(6.8, 19.3)</td>
<td>21 (19.4%)</td>
<td>(12.0, 27.0)</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>44</td>
<td>4 (9.0%)</td>
<td>(0.5, 17.5)</td>
<td>5 (11.4%)</td>
<td>(2.0, 20.8)</td>
<td>4 (9.1%)</td>
<td>(0.6, 18.0)</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>109</td>
<td>18 (16.5%)</td>
<td>(9.5, 23.5)</td>
<td>12 (11.0%)</td>
<td>(5.1, 17.0)</td>
<td>21 (19.3%)</td>
<td>(12.0, 27.0)</td>
</tr>
<tr>
<td>Total Girls</td>
<td></td>
<td>470</td>
<td>61 (12.9%)</td>
<td>(10.0, 16.0)</td>
<td>50 (10.7%)</td>
<td>(8.0, 13.5)</td>
<td>77 (16.4%)</td>
<td>(13.1, 20.0)</td>
</tr>
<tr>
<td>Total number of children</td>
<td></td>
<td>1304</td>
<td>226 (17.4%)</td>
<td>(15.3, 19.4)</td>
<td>183 (14.0%)</td>
<td>(12.1, 16.0)</td>
<td>249 (19.1%)</td>
<td>(17.0, 21.2)</td>
</tr>
</tbody>
</table>
### Table 2.3: Prevalence of allergic rhinitis symptoms, according to the ISAAC questionnaire

<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender</th>
<th>Number of participants</th>
<th>Parental reports of ever having had sneezing, runny nose, and blocked nose</th>
<th>Parental reports of ever having had sneezing, runny nose, and blocked nose in the last 12 months</th>
<th>Parental reports of ever having had hay fever</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n %</td>
<td>95% CI</td>
<td>N %</td>
</tr>
<tr>
<td>0022</td>
<td>Boys</td>
<td>67</td>
<td>14 (20.9%)</td>
<td>(11.2,30.6)</td>
<td>9 (13.4%)</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>154</td>
<td>57 (37.0%)</td>
<td>(29.4,44.6)</td>
<td>52 (33.8%)</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>117</td>
<td>32 (27.4%)</td>
<td>(19.3,35.4)</td>
<td>30 (25.6%)</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>243</td>
<td>60 (24.7%)</td>
<td>(19.3,30.1)</td>
<td>50 (20.6%)</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>152</td>
<td>31 (20.4%)</td>
<td>(13.9,26.8)</td>
<td>25 (16.4%)</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>101</td>
<td>29 (28.7%)</td>
<td>(19.9,37.5)</td>
<td>20 (19.8%)</td>
</tr>
<tr>
<td><strong>Total Boys</strong></td>
<td></td>
<td><strong>834</strong></td>
<td><strong>223 (26.7%)</strong></td>
<td><strong>(24.0,30.0)</strong></td>
<td><strong>186 (22.3%)</strong></td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>171</td>
<td>33 (19.3%)</td>
<td>(13.4,25.2)</td>
<td>28 (16.4%)</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>38</td>
<td>4 (10.5%)</td>
<td>(0.8,20.3)</td>
<td>3 (7.9%)</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>108</td>
<td>20 (18.5%)</td>
<td>(11.2,25.9)</td>
<td>18 (16.7%)</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>44</td>
<td>4 (9.1%)</td>
<td>(0.6,17.6)</td>
<td>4 (9.1%)</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>109</td>
<td>18 (16.5%)</td>
<td>(9.5,23.5)</td>
<td>16 (14.7%)</td>
</tr>
<tr>
<td><strong>Total Girls</strong></td>
<td></td>
<td><strong>470</strong></td>
<td><strong>79 (16.8%)</strong></td>
<td><strong>(13.4,20.2)</strong></td>
<td><strong>69 (14.7%)</strong></td>
</tr>
<tr>
<td><strong>Total number of children</strong></td>
<td></td>
<td><strong>1304</strong></td>
<td><strong>302 (23.2%)</strong></td>
<td><strong>(20.9,25.5)</strong></td>
<td><strong>255 (19.6%)</strong></td>
</tr>
</tbody>
</table>
Table 2.4: Prevalence of atopic eczema and eczema-related symptoms according to the ISAAC questionnaire

<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender</th>
<th>Number of participants</th>
<th>Parental reports of ever having had itchy rash</th>
<th>Parental reports of ever having had itchy rash in the last 12 months</th>
<th>Parental reports of ever having had eczema (medically diagnosed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n %</td>
<td>95% CI</td>
<td>n %</td>
</tr>
<tr>
<td>0022</td>
<td>Boys</td>
<td>67</td>
<td>4 (6.0%)</td>
<td>(0.3, 11.6)</td>
<td>4 (6.0%)</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>154</td>
<td>27 (17.5%)</td>
<td>(11.5, 23.5)</td>
<td>18 (11.7%)</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>117</td>
<td>8 (6.8%)</td>
<td>(2.3, 11.4)</td>
<td>8 (6.8%)</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>243</td>
<td>20 (8.2%)</td>
<td>(4.8, 11.7)</td>
<td>14 (5.8%)</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>152</td>
<td>15 (9.9%)</td>
<td>(5.1, 14.6)</td>
<td>17 (11.2%)</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>101</td>
<td>13 (12.9%)</td>
<td>(6.3, 19.4)</td>
<td>9 (8.9%)</td>
</tr>
<tr>
<td>Total Boys</td>
<td></td>
<td>834</td>
<td>87 (10.4%)</td>
<td>(8.3, 12.5)</td>
<td>70 (8.4%)</td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>171</td>
<td>11 (6.4%)</td>
<td>(2.8, 10.1)</td>
<td>6 (3.5%)</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>38</td>
<td>2 (5.3%)</td>
<td>(-1.8, 12.4)</td>
<td>2 (5.3%)</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>108</td>
<td>11 (10.2%)</td>
<td>(4.5, 15.9)</td>
<td>10 (9.3%)</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>44</td>
<td>2 (4.5%)</td>
<td>(-1.6, 10.7)</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>109</td>
<td>14 (12.8%)</td>
<td>(6.6, 19.1)</td>
<td>11 (10.1%)</td>
</tr>
<tr>
<td>Total Girls</td>
<td></td>
<td>470</td>
<td>40 (8.5%)</td>
<td>(6.0, 11.0)</td>
<td>31 (6.6%)</td>
</tr>
<tr>
<td>Total number of children</td>
<td>1304</td>
<td>127 (9.7%)</td>
<td>(8.1, 11.3)</td>
<td>101 (7.7%)</td>
<td>(6.3, 9.2)</td>
</tr>
</tbody>
</table>
Table 2.5: Children who have more than one type of allergic disorder

<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender</th>
<th>Number of participants</th>
<th>Children who have more than one allergic disorder (n %)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0022</td>
<td>Boys</td>
<td>67</td>
<td>5 (7.5%)</td>
<td>(1.2,13.8)</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>154</td>
<td>40 (26.0%)</td>
<td>(19.0,32.9)</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>117</td>
<td>11 (9.4%)</td>
<td>(4.1,14.7)</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>243</td>
<td>21 (8.6%)</td>
<td>(5.1,12.1)</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>152</td>
<td>18 (11.8%)</td>
<td>(6.7,16.9)</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>101</td>
<td>12 (11.9%)</td>
<td>(5.6,18.2)</td>
</tr>
<tr>
<td></td>
<td>Total Boys</td>
<td>834</td>
<td>107 (12.8%)</td>
<td>(10.5,15.1)</td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>171</td>
<td>12 (7.0%)</td>
<td>(3.2,10.9)</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>38</td>
<td>2 (5.3%)</td>
<td>(-1.8,12.4)</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>108</td>
<td>10 (9.3%)</td>
<td>(3.8,14.7)</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>44</td>
<td>1 (2.3%)</td>
<td>(-2.1,6.7)</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>109</td>
<td>11 (10.1%)</td>
<td>(4.4,15.7)</td>
</tr>
<tr>
<td></td>
<td>Total Girls</td>
<td>470</td>
<td>36 (7.6%)</td>
<td>(5.3,10.1)</td>
</tr>
<tr>
<td></td>
<td>Total number of children</td>
<td>1304</td>
<td>143 (10.9%)</td>
<td>(9.3,12.7)</td>
</tr>
</tbody>
</table>
Table 2.6: Prevalence of combined allergic disorders

<table>
<thead>
<tr>
<th>School Code</th>
<th>Gender</th>
<th>Number of participants</th>
<th>Asthma &amp; rhinitis</th>
<th>Asthma &amp; eczema</th>
<th>Rhinitis &amp; eczema</th>
<th>Asthma &amp; rhinitis &amp; eczema</th>
</tr>
</thead>
<tbody>
<tr>
<td>0022</td>
<td>Boys</td>
<td>67</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>0032</td>
<td>Boys</td>
<td>154</td>
<td>26</td>
<td>13</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>0042</td>
<td>Boys</td>
<td>117</td>
<td>10</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>0052</td>
<td>Boys</td>
<td>243</td>
<td>18</td>
<td>6</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>0062</td>
<td>Boys</td>
<td>152</td>
<td>14</td>
<td>9</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>0072</td>
<td>Boys</td>
<td>101</td>
<td>9</td>
<td>6</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Total Boys</td>
<td></td>
<td>834</td>
<td>80 (9.6%)</td>
<td>39 (4.7%)</td>
<td>40 (4.8%)</td>
<td>26 (3.1%)</td>
</tr>
<tr>
<td>0011</td>
<td>Girls</td>
<td>171</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>0851</td>
<td>Girls</td>
<td>38</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1001</td>
<td>Girls</td>
<td>108</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>1031</td>
<td>Girls</td>
<td>44</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0331</td>
<td>Girls</td>
<td>109</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Total Girls</td>
<td></td>
<td>470</td>
<td>21 (4.5%)</td>
<td>10 (2.1%)</td>
<td>11 (2.3%)</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Total number of children</td>
<td></td>
<td>1304</td>
<td>101 (7.8%)</td>
<td>49 (3.8%)</td>
<td>51 (3.9%)</td>
<td>29 (2.2%)</td>
</tr>
</tbody>
</table>
2.6.2 Descriptive results of Phase II of the pilot study

Table 2.7: Mean values (SD) of obesity measures in the sample of 85 children of Phase II of the pilot study

<table>
<thead>
<tr>
<th>Anthropometric measures</th>
<th>Both genders (n=85)</th>
<th>Boys (n=47)</th>
<th>Girls (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>122.52 (6.61)</td>
<td>122.63 (6.70)</td>
<td>122.39 (6.58)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>24.14 (5.11)</td>
<td>24.01 (5.04)</td>
<td>24.29 (5.26)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>15.93 (2.10)</td>
<td>15.83 (2.11)</td>
<td>16.05 (2.12)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>52.32 (6.90)</td>
<td>52.28 (7.48)</td>
<td>52.36 (6.21)</td>
</tr>
<tr>
<td>Triceps skinfold thickness (mm)</td>
<td>9.79 (3.63)</td>
<td>9.38 (4.34)</td>
<td>10.30 (2.46)</td>
</tr>
</tbody>
</table>

Table 2.8: Lung function tests in the group of 85 children of Phase II of the pilot study

<table>
<thead>
<tr>
<th>Lung function test</th>
<th>Both genders (n=85) Mean (SD)</th>
<th>Boys (n=47) Mean (SD)</th>
<th>Girls (n=38) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (Lt)</td>
<td>1.60 (0.33)</td>
<td>1.66 (0.33)</td>
<td>1.53 (0.33)</td>
</tr>
<tr>
<td>FEV1 (Lt)</td>
<td>1.26 (0.41)</td>
<td>1.38 (0.52)</td>
<td>1.20 (0.28)</td>
</tr>
<tr>
<td>PEF (Lt)</td>
<td>2.57 (0.77)</td>
<td>2.86 (0.68)</td>
<td>2.20 (0.72)</td>
</tr>
</tbody>
</table>

Out of the 85 children selected for Phase II, blood samples were collected for 72 (84.7%) of them. For seven children phlebotomy was difficult to perform, because these children were obese and it was therefore not easy for the phlebotomist to find the veins. The remaining six children were scared and refused the blood test. Moreover, there were major problems regarding the laboratory tests of blood samples. Several of the studied immunological parameters could not be measured in Madinah such as; leptin, Th1, Th2, IFN-γ, IL-4 and IL-6, because their quantification required specialised equipment which was not available in the clinical laboratories of Madinah and there was a huge difference in the cost. For the above reasons, blood tests were eventually excluded from the study and the respective findings of the pilot study are not presented here.
2.7 Discussion

2.7.1 Main findings

This pilot study has made an estimation of the prevalence of the studied disorders (i.e. eczema, allergic rhinitis and asthma) in the study population of concern, according to symptom reports by the parents of the participating children. Based on a sample of 1304 children (470 girls and 834 boys), the prevalence of asthma in girls was estimated at 12.9% (95% CI: 10.0, 16.0 %), while in boys at 19.8% (95% CI: 17.1, 22.5).

The above figures suggest that asthma is found at considerable levels among schoolchildren of Madinah and, thus, any attempt of conducting larger scale epidemiological studies is not meaningless. Asthma, allergic rhinitis, and to a lesser degree, eczema seem to constitute important health issues in schoolchildren and they need to be further investigated, both in respect to their prevalence rate and also in respect of their potential association with obesity.

High participation rates were observed in Phase I of the feasibility study (86.7% for girls and for 73.7% for boys); out of the 1,674 questionnaires sent, 1,304 were completed and returned to the research team. It is evident that more than 1,300 families showed interest to provide information about the health status of their children, which indicates that the study received a positive social acceptance by the parents; this is an encouraging message for designing and planning larger scale studies on this topic.

Phase II of the pilot study included a relatively small sample of participants (85 children; 38 girls and 47 boys). Out of these 85 children, 17 were reported by their parents as having had presented asthma symptoms in their life and they were considered as cases. The remaining 68 children were reported as never having had presented asthma symptoms and they were considered as controls. Because of the small number of cases in the selected sample, we considered that no accurate conclusions could be inferred by performing comparative analyses between cases and controls. Moreover, preliminary investigation of data showed that only 13 children (out of the 85) were obese or overweight (results not shown above) which suggests that there was not enough statistical power to reach accurate conclusions about any association between obesity and asthma. From the above figure, it was possible to estimate that the prevalence of childhood obesity in Madinah was about 15%.
Therefore, the analytical study in Phase II was basically performed in order to test the procedures and investigate the difficulties of carrying out a larger scale study of matched case-control design. The conclusions that were made from all the work done in Phase II are presented analytically in the next paragraph.

2.7.2 Strengths and limitations

This study benefits from the large sample size of participants, since 1304 boys and girls from 11 schools constitute an adequate pilot sample to draw conclusions before proceeding to the main study.

I obtained data on rhinitis and eczema outcomes in our population. However, since the main aim of this study was the assessment of asthma and symptoms of asthma in children, I focused only on asthma outcomes in this study.

The study analysed ad hoc data, collected with the ISAAC questionnaire, an internationally validated tool, developed specifically for studying asthma in childhood. Moreover, the study used anthropometric and physiological data that also occurred from ad hoc measurements. These measurements were performed by a team of healthcare professionals, who had previously received adequate training. The training course of the research team was supervised by Professor Aziz Sheikh.

The major disadvantage of the study is that the definition of asthma cases was based on parental responses and not to medical examination and physician diagnosis. This includes the problem of recall bias and consequently classification bias.

A disadvantage of the ISAAC questionnaire is that it has not been validated as a tool for identifying asthma in the age-group of 1-4 years; (153) nevertheless, this does not constitute a problem in the context of my fieldwork since the study population consisted of children 6-8 years old.

Another issue of consideration about the ISAAC questionnaire is the concern that language and culture on the reporting of symptoms have been poorly explored (153) and, therefore, bias in the correct identification of cases may be encountered among populations of different nations and cultures. Such an issue is unlikely to affect the findings in this work, but it may
cause problems when the results are to be compared with those of similar international studies.

The term ‘wheeze’ (and its Arabic equivalents) may not have been understood by all parents raising the possibility of misclassification error. That said, I feel this is unlikely in the context of my study, for the following reasons:

- The Arabic version of the ISAAC questionnaire uses the widely understood term ‘safeer’ to denote ‘wheezing’ (rather than the more linguistically accurate but less widely understood term ‘azeez’)

- Parents were given the option of contacting me about any questions they were unclear about, and whilst they phoned me about a number of other issues and questions, no-one contacted me about this particular question.

- Finally, the findings of a study of the accuracy of the Arabic version of three asthma screening instruments – including ISAAC – which demonstrates that questions using the term ‘wheeze ever’ had greater sensitivity than other terms (e.g. shortness of breath or cough) and comparable specificity; interestingly, this study also demonstrated that use of the questions ‘wheeze ever’ had comparable sensitivity and specificity to asking about ‘asthma ever’. (166)

Finally, it has been suggested that some answers given in the questionnaire can be misinterpreted leading to a false positive identification of asthma cases. (153) Taking into account that such a problem is inherent in any retrospective collection of data which is based on a history of self-reported symptoms, we consider this disadvantage as unavoidable.

### 2.7.3 Insights obtained through conducting the pilot study

The work in the pilot study was valuable in understanding research procedures and getting an idea of the difficulties that may be encountered. The main points to be considered are the following ones:

- The training programme for the healthcare professionals achieved its intended purpose, as it was conducted over two days with the active participation of the trainees. The skills of the trainees were assessed by the end of the second day.
• The research protocols were acceptable to the healthcare professionals of the research team as shown by their evaluation of the training course (Appendix 5).

• The response rate for Phase I of the pilot study was 77.9% (1304 participants responded out of 1673). The response rate for Phase II was 68.8%. These figures represented response rates which offered a very encouraging point for conducting large-scale studies.

• The questions asked in the ISAAC questionnaire were easily answered by parents. In 2% (n=27) of the approached children, there were difficulties in answering the questionnaire due to the death or illiteracy of the parents. In that case, the questionnaire was answered by the oldest brother or sister of the participating child.

• Collection of blood samples was challenging because most of the parents were not willing to give their consent for their children receiving phlebotomy as indicated in the consent form attached to the questionnaire. However, for those children for whom we had consent, phlebotomy was not found to be a difficult procedure, since it was successful in the 84.7% of participants (i.e. 72 children out of 85).

• There were major problems regarding the laboratory tests of blood samples. Several of the studied immunological parameters could not be measured in Madinah such as; leptin, Th1, Th2, IFN-γ, IL-4 and IL-6, because their quantification required specialised equipment which was not available in the clinical laboratories of Madinah and there was a huge difference in the cost. As an alternative, we decided to send blood samples to a large private laboratory in Alexandria, Egypt. This highly specialised laboratory was able to perform the tests, but there was a need for a special order of reagent kits, since the required tests were not performed on a routine basis.

• The cost per sample was estimated at about £87.51, which was found to be not affordable. The overall cost of processing the specimens was estimated at around £6,563.86 (£87.51 per child) and the above figure was expected to increase taking into account the travel expenses to Egypt.

• All the above difficulties in the collection and analysis of blood samples were considered to be serious drawbacks for a future case-control (or any kind of analytical) study aiming to assess laboratory data. Therefore, I had to accept limitations in my ability to investigate some of the potential causal mechanisms of interest. Ideally, I would also have liked to have studied these relationships at tissue,
cellular, and biochemical levels. However, assessment of pulmonary and anthropometric measurements should not be considered as being of low value.

- The anticipated sample size for the large-scale studies needed to be reduced due to limitations in the available resources: time, money, and collaborators of the research team. Analytical details about the sample size estimation are described in Section 2.7.4.
- An issue that needed to be considered was the time schedule for the large-scale studies. In order to perform anthropometric measurements, pulmonary function tests, skin prick tests, and blood tests, for example, for 1000 students we would need at least 50 working days (a research team would be able to examine a maximum of 20 students daily).

2.7.4 Sample size calculation for the large scale case-control study

Based on the estimated prevalence of asthma from the results of the pilot study, an estimation of the minimum sample size required for the large scale case-control study was performed.

According to data from the General Directorate of Education in Madinah, the total number of boys, 6-8 years old, in all primary schools of Madinah was, at the time of the study, 69,619 students. The total number of girls, 6-8 years old, in all primary schools of Madinah was 81,974 students. Thus, there were totally 151,593 students, 6-8 years old, who were eligible to be recruited in the study.

Initially some power calculations were carried out for a design in which four controls were to be recruited for every case, but it was realised that this was not appropriate for a situation where the logistical effort of collecting data was equal for cases and controls, so we decided to adopt a 1:1 ratio in the final design.

The pilot study suggested that the prevalence of asthma was around 15% and therefore a sample of around 5,000 children needed to be recruited into the cross-sectional study in order to recruit sufficient numbers of cases (>600) to give 80% power to detect a mean difference of around 0.4 in BMI between cases and the same number of controls based on a SD of three units for BMI. This was thought to represent an acceptable compromise between good power and a realistic number of subjects to allow data collection for the case-control phase in a reasonable time frame.
There were 33,270 boys (59.7%) and 22,412 girls (40.3%) aged 6-8 years in primary schools in Madinah (i.e. a total of 55,682 students). All students aged 6-8 years were long-term residents in Madinah (i.e. for at least one year) and enrolled in the selected schools that were eligible to participate. The reason for choosing this strict criterion was to keep maximum homogeneity of study population (children), eliminate all possible bias in the conduction of our study. For example, Madinah has different climate and lifestyle compare to other parts of Saudi Arabia, particularly rural population. This environmental and lifestyle factors can play an important role in the development of asthma or asthmatic symptoms in those children who newly moved with parents to Madinah to live and study.

These data were provided by the General Department of Education in Madinah, Saudi Arabia. The possible explanations for this gender imbalance between boys and girls in this region could be elucidated as:

Firstly, women’s schooling at all levels in Saudi Arabia remained under the Department of Religious Guidance until 2002, and was heavily influenced by religious conservative scholars, who teach religious rituals. The teaching of girls usually takes place in private tutorials in the homes of professional Quran readers. Education for girls stopped at puberty, “when strict seclusion at home began and veiling in public became mandatory”.(163) Secondly, the patriarchal nature of Saudi society, social norms, local traditions, and the structure of the system of public education led to striking differences in boys’ and girls’ school attendance. Thirdly, there were differences in net enrolment in primary education for boys and girls, and the trend favoured boys. In accordance to Shari’a law female education is segregated from male education. And finally, the high dropout rates in schools for girls eventually have led to gender disparity in education in these schoolchildren. The female illiteracy level in Saudi Arabia (10 years and above) reached 20.2% in 2007, as compared to the male illiteracy rate, which was around 7.3%. Statistics in Saudi Arabia demonstrated that the number of girls at all school levels increased from 272,054 in 1974-75 to 2,121,893 in 2004-05. The percentage of girls at all school levels increased from 33% in 1974-75 to 48% in 2004-05 (see Figure 2.3). Thus, the above mentioned factors may help to explain the gender imbalances between boys and girls school enrolment.(167, 168)
Figure 2.3: Percentage of girl students at all school levels (1974–75 and 2004–05) (Source: SAMA, 2008, Ministry of Education, p. 374)

2.8 Conclusions

The estimated prevalence of asthma, allergic rhinitis, and eczema in schoolchildren of Madinah is found at high levels such that larger scale epidemiological studies are likely to be both justified and feasible. Data collection for the above disorders from parental reports using the ISAAC questionnaire seemed to receive social acceptance among the people of Madinah.

An analytical study of case-control design for investigating potential association between obesity and asthma in Saudi children is of great interest, since the prevalence of childhood asthma is at considerable levels and also because very few studies on this topic have been conducted in Saudi Arabia. Such a study is feasible to be conducted in Madinah. The healthcare professionals of the research team have gained very good experience on performing the appropriate measurements and most of the parents would be very willing to answer to the questionnaires and, thus, an adequate sample of participants should be expected.

The only difficulty that should be seriously considered is with blood tests. Performing phlebotomy on children aged 6-8 years has proved to be a difficult task, since a lot of the parents would not be willing to give their consent and most of the children would be scared to
be punctured. Moreover, blood tests will highly increase the cost of the study, since most of the immunological parameters require much specialised analyses and consequently very expensive reagents and consumables, as well as highly skilled personnel. Due to the highly specialised nature of the required blood tests, the latter need to be performed in a laboratory outside Madinah, something which will further increase the cost of the study and will expand the time schedule for data collection.

2.9 Chapter summary

Childhood asthma is one of the most common child health problems, in Saudi Arabia,(145, 148) contributing towards school absenteeism and reduced participation in sports and other activities. Moreover, childhood asthma emerges as a very important issue in Saudi Arabia, taking into account that children below 15 years old represent more than 50% of the total population of the country. Its prevalence in the entire country has been estimated at 10-20%;

The pilot study aimed at testing the feasibility and applicability of conducting two large-scale epidemiological studies designed to investigate asthma and its potential association with obesity among schoolchildren in Saudi Arabia. The first one was a cross-sectional study and the second one was a matched case-control study on a study population of primary school students in Madinah, Saudi Arabia, aged 6-8 years (both girls and boys).

An Arabic version of the validated ISAAC questionnaire was used for data collection A total of 1674 questionnaires were sent to the parents of the participating students and the response rate was 77.9%. A sample of 85 students (38 girls and 47 boys) was selected for Phase II of the pilot study.

The prevalence of asthma in girls was estimated at 12.9% and 19.8% in boys. The total prevalence of asthma in both genders was estimated at 17.4%. The prevalence of rhinitis in girls was estimated at 16.8% and in boys at 26.7%. The total prevalence of rhinitis in both genders was estimated at 23.2%. The prevalence of eczema in girls was estimated at 8.5% and in boys at 10.4%. The total prevalence of eczema was estimated at 9.6%.

Measures of obesity (i.e. weight, height, skin fold thickness for peripheral and central areas of the body, and waist circumference) were applied to the sample of 85 students in Phase II. Spirometry was performed on 85 students who were tested for immediate hypersensitivity
responses to an array of aeroallergens, using SPTs. Blood samples were collected from 72 children (out of the 85) to assess the levels of immunological parameters.

Most of the questions of the ISAAC questionnaire were very easily answered by the parents. No serious problems were encountered with the procedures of getting measurements from children (anthropometric data, phlebotomy, SPTs). Most of the problems encountered were with the blood samples for determining immunological parameters. A large number of parents were however unwilling to give consent for their children being punctured; moreover, it was found that the cost of performing blood tests was unaffordable, because the required reagents were very expensive and also because samples needed to be sent to a laboratory abroad.

The prevalence of childhood asthma, allergic rhinitis, and atopy were estimated as being highly prevalent among primary schoolchildren in Madinah. A larger scale matched case-control study was therefore considered feasible to undertake, with the exception of undertaking blood tests for investigating immunological parameters as these were both unacceptable to a large proportion of children/parents and because these were very expensive.

In the following chapter, the two stage cross-sectional survey to determine the prevalence of asthma and other allergic disorders in children of 6-8 years of age, in Madinah, Saudi Arabia will be discussed.
Chapter 3: Two stage cross-sectional survey to determine the prevalence of asthma and other allergic disorders in 6-8 year-old children in Madinah, Saudi Arabia

3.1 Introduction

Asthma, eczema and allergic rhinitis are all diseases of inflammation. Several factors in the immediate indoor and outdoor environment of human residences may lead to allergic disorders and such factors may become difficult to control. Atmospheric pollution, changes in the climate, lifestyle factors, and changes in the biological environment are some of the contributory factors for these phenomena. Asthma has become a threat to the well-being of many children and adults. Asthma is a chronic airway disorder that may become severe and sometimes lead to fatalities. It is believed that the burden of asthma is usually underestimated. Until the 1980s, most of the prevalence studies were from the developed countries. From the 1980s to the 1990s there were a few studies comparing the prevalence across the different regions of the world. As discussed in Chapter 1, ISAAC developed a standardised and coordinated approach with simple methodology that enabled the collection of comparable data from children including non-English speaking populations. The resource pool from ISAAC has helped to make worldwide estimates of asthma prevalence through standardised measurements.

The impact of asthma is multifaceted. The impact on society in the form of school absenteeism, extensive expenditure for the families, and the consequent psychological and social impact, are considerable. Apart from the global rise of the prevalence of asthma and consequent hospitalisations, the case fatality due to asthma is also reported to be increasing (in the USA only in poor minority groups), however asthma deaths have declined in many countries in the world because of better management of asthma. Acute asthma exacerbations continue to occur, with particularly frequent exacerbations related to disease severity. This poses financial stresses for the healthcare system, something which may become unbearable in a poor country or regional setting. There are reports that the burden of asthma in Saudi Arabia follows the international increasing trend. Table 3.1 summarises all recent studies about asthma prevalence in Saudi Arabia.
3.2 Regional variations

There is a great variation in the prevalence of asthma and allergy among the different regions of Saudi Arabia. A study by Hijazi and Abalkhail showed that there was a significantly higher prevalence of allergic symptoms in urban children compared with rural children in Jeddah. Another study regarding the Asir region showed that the prevalence of asthma in areas at sea level was 19.5% and in areas at higher altitude was 6.9%. (178)

Moreover, another study comparing the symptoms of asthma in urban and rural Saudi Arabia in 1998 showed that a greater number of allergic symptoms were found in urban than in rural children (OR=1.78; 95%CI: 1.45, 2.18) and in Saudi national children, rather than in non-Saudi children (OR=1.50; 95%CI: 1.23, 1.82). (178) A survey on the socio-demographic profile of children with asthma in Al-Majmaah province in the middle part of Saudi Arabia showed that male children represented 69% of cases. (181)

The incidence and prevalence of asthma and allergies is increasing in both the western and developing countries. For example, in the United Kingdom, a study has shown a rising incidence of asthma up to 32.2% between 1994 and 1995. (38, 52) Similarly, from 1982 to 1992 in the USA, the prevalence of self-reported asthma increased by 42%. (52, 173, 182)

Al-Dawood et al. (2002) remarked that, although a large volume of clinical and epidemiological research is being carried out within affected populations, the aetiology and risk factors of these conditions remain unexplained and poorly understood. (144) However, since the last decade observational research has been undertaken and valuable information on modifiable risk factors has become available. Moreover, research evidence has been incorporated into several of the current guidelines for asthma control (e.g. The Global Initiative for Asthma (GINA) Australian, BTS guidelines). (183, 184) However, information on risk factors is mostly available from other countries and Saudi Arabia needs to fill the gap on this matter. The locally operating risk factors may be dust mite, automobile exhaust, global warming and changes due to weather, changed lifestyle etc.
3.3 Aims, objectives and research questions

3.3.1 Aims

The aims of this study were to:

- Determine the prevalence of asthma, eczema, allergic rhinitis in Madinah, Saudi Arabia, in school age children.

- Identify any locally operating risk factors for asthma among primary schoolchildren in Madinah.

- Identify, from the studied sample of children, cases and controls for a subsequent matched case-control study (Phase II, see Chapter 4).

3.3.2. Objectives

The objectives of the study were to:

- Collect data about parental-reported asthma, eczema, and rhinitis in school age children, in Madinah, Saudi Arabia.

- Estimate the physician diagnosed, parental reported, and the overall prevalence of asthma in the study population.

- Describe the prevalence of asthma in children in respect to the socio-demographic and lifestyle attributes of their parents.

3.3.3 Research questions

I sought to answer the following research questions:

- Is it possible to determine the prevalence of asthma, eczema, allergic rhinitis in school-age children in the city of Madinah, Saudi Arabia?
• Could any locally operating risk factors for asthma among primary schoolchildren in Madinah be identified? Would it be possible to identify any local risk factors for asthma among primary schoolchildren in Madinah?

• From the studied sample of children, can cases and controls for a subsequent matched case-control study be identified? (Phase II, see Chapter 4).

3.4 Methods

3.4.1 Ethical considerations

In Saudi Arabia there were at the time of planning this study no regulatory bodies such as a Research Ethics Committee (REC) which could provide formal ethical review and approval before initiating a study. Also, there was no suitable in-house ethics review process in the Centre for Population Health Sciences at The University of Edinburgh. Nonetheless, I drew on existing guidance on the ethics of undertaking research in children and used this when planning my study.(185, 186) In addition, permission was obtained from the education authorities of Madinah (General Directorate of Education); the School Health Departments, Ministry of Education; and from the respective school head teachers. Furthermore, parents were asked to give their signed informed consent (Appendix 2) and children were given the option of withdrawing from any aspect of the study that concerned them. To ensure confidentiality of data, all children were given a unique identifier; then all personal details were removed. The files containing all personal identifiers were kept in an encrypted password protected file.

3.4.2 Design

We conducted a two-stage cross-sectional survey of primary school students, aged 6-8 years, who were permanent residents of Madinah for at least 1 year (see Section 3.5.4) We restricted our sample to children aged 6-8 years old as this enabled sampling of children in the first three classes of primary schools. The two stages involved sampling and recruiting schools and then sampling and recruiting children from the selected schools. The methodology of the study was piloted by the research team in Madinah, Saudi Arabia in 2008; the collection of data was carried out in April 2009.
3.4.3 Study sample and sampling frame

Our sampling strategy aimed to recruit a representative group of students, so that by studying this sample we would be able to generalise findings to the wider population of primary school-aged students of Madinah. Since schoolchildren are an easily reachable group, the study was planned as a school-based survey.

A list of all government and private primary schools in Madinah was obtained from the General Directorates of Education in the Madinah region (i.e. both boys’ and girls’ departments respectively); these primary schools were responsible for providing education for children aged 6–12 years. Schools were then stratified according to the geographical area (i.e. north, east, south, west and centre of Madinah) and gender (i.e. boys and girls) and a sample of 38 schools (i.e. 9 girls’ schools and 29 boys’ schools) was randomly selected for participation by the respective General Directorates of Education.

There were 33,270 boys (59.7%) and 22,412 girls (40.3%) aged 6–8 years old in primary schools in Madinah (i.e. a total of 55,682 students). All students aged 6–8 years who were long-term residents in Madinah (i.e. for at least one year) and enrolled in the selected schools were eligible to participate (see Figure 3.2). This decision was taken in order to provide a broadly homogenous population in relation to exposures to environmental risk factors, which was considered particularly important in relation to the case control study in which risk factors for the development of asthma were being investigated.

3.4.4 Recruitment of schools

The General Directorates invited the schools to participate with a letter of explanation (Appendices 13 and 14), addressed to the head teachers, outlining the purpose of the study and the procedures that were to be employed.

All 38 invited schools agreed to participate (100% recruitment rate). One of the girls’ schools was however subsequently excluded because of some authoritative obstacles and resulting communication problems we could not recruit controls from one of the girls’ schools. Accordingly, we omitted this school from the analysis. There were therefore in total 37 schools (i.e. 8 girls’ and 29 boys’ schools) included in the final analysis. Figure 3.1 displays the spatial distribution of the 37 selected schools on a topographic map of Madinah.
Figure 3.1: Recruitment of 37 boys' and girls' schools in Madinah (adapted from Al Madinah Tourist Map: http://www.sacred-destinations.com/saudi-arabia/images/maps/medina-city-map-wp-pd-900.jpg)
3.4.5 Recruitment of children and methods of data collection

In the second stage of the cluster sampling, students aged 6-8 years in primary school, that is from the first three classes, who were long-term residents in Madinah (i.e. for at least one year), and enrolled in the 37 selected schools, were invited to participate in the study. (Figure 3.2) describes diagrammatically the number of eligible students in each step of the cluster sampling. The parents of these children were sent, via the school, a letter explaining the rationale for the study and what it entailed, a consent form and the Arabic version of the ISAAC questionnaire that was used in the pilot study (see Section 2.4.4). The students were asked to return the completed questionnaire from their parents to their teachers. No reminders were issued to non-responders. The class teacher collected the questionnaires and returned them to the research team. These documents were compiled in booklet form (blue for boys and pink for girls) and only those which were fully completed and where full consent was given through the signed consent form were used for analysis. The afore-mentioned signed consent form was used for both the cross-sectional survey and also the case-control study (as described in Chapter 4) (Appendices 15 and 16).

The standard ISAAC questionnaire was used; this included recording the child’s name, age, school; socio-demographic data, indoor environmental risk factors, diet and eating habits, and parents were asked to answer the core questionnaire for wheezing and asthma (module 1.1) such as:

- Has your child ever had wheezing or whistling in the chest at any time in the past?
- Has your child had wheezing or whistling in the chest in the last 12 months?
- How many attacks of wheezing has your child had in the last 12 months?
- In the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?
- In the last 12 months, has wheezing ever been severe enough to limit your child’s speech to only one or two words at a time between breaths?
- Has your child ever had asthma?"; “In the last 12 months, has your child’s chest sounded wheezy during or after exercise?
In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?
Figure 3.2: Sampling frame and recruitment of schools and students
3.5 Data handling and analysis

3.5.1 Data coding and extraction

I undertook the coding of data and this was independently checked by a second person. Any questionnaire containing missing information for one or more sections was excluded. Qualitative variables were listed as dichotomous or in a rank order and appropriate coding was done. The coding was carried out in consultation with a statistician.

Data were coded according to schools, gender and the questions in the questionnaire. Codes were applied to label the study variables. Missing variables were also coded.

3.5.2 Data entry and processing

Data entry was performed using an Excel spreadsheet (version 2003). An Excel spreadsheet is a very flexible and simple programme for data capture and processing. I had large amounts of data with different variables, frequently run calculations (regression analysis), comparisons on our data, and in order to keep track of items in a simple list for personal or shared use we have chosen this convenient spreadsheet program. All numerical variables (either continuous or district) were entered as they had been reported by the parents of students (e.g. birth weight, number of portions of meat in diet). Responses to categorical variables were coded and labelled. Binary categorical variables were coded with 0 and 1 for the ‘no’ and ‘yes’ statement respectively. Categorical variables with more than two answers were coded with integer numbers without using the 0 value. Ordinal variables were coded using the value of 0 to denote absence of a factor and increasing positive integers to denote gradual levels of intention of a factor. Visual record verification was performed by another investigator to ensure that every single questionnaire had been entered accurately. Although SPSS was used for data analysis, Excel was preferable for data entry, because the latter was easier to use. After checking the data from Excel were imported into SPSS.

The majority of the questionnaires were completed in full; however, small amounts of data were omitted by some of the respondents. As it was considered inappropriate to omit the entire case from analysis in this event, cases were only left out when the relevant variables made up part of the analysis. The entries were set as missing in SPSS.
3.5.3 Statistical analyses

Descriptive analysis was undertaken by calculating relative frequencies for categorical variables and means and standard deviations for continuous variables. To account for the two-stage sampling, Generalised Estimating Equations (GEE) (an extension of the generalised linear model) were used to fit random effects. Because of the two-stage nature of the sampling used in this part of the study, it was necessary to use a multilevel model that took account of possible variations at both school and child levels in analysing the data. This was achieved by applying GEE, which allows the estimation of parameters in the presence of clustering by assuming that observations on the individuals within clusters are not necessarily independent. This was done using the GENLIN procedure in SPSS.(187)

Logistic regression and Poisson regression models were used to calculate prevalence and prevalence ratios.(187) Prevalence estimates were initially calculated separately for boys and girls; an overall prevalence was later calculated to allow comparisons of our results with those of international studies.(188, 189) All analyses were performed with SPSS (version 16).

3.6 Results

3.6.1 Parental response rates

Out of the 6,053 questionnaires that were distributed to the parents of the selected children, 5,188 of them were completed and returned to the research team; this gave a response rate of 85.9%. The response rates by gender were: 86.2% for boys (3,585 questionnaires) and 84.6% for girls (1,603 questionnaires). Missing values did not exceed 10.0% for any of the questions. The parents of 865 students either declined to participate in the study or failed to respond (refusal rate: 14.3%), giving an overall participation rate of 85.7%. The refusal rate was found to be identical in the two genders. Table 3.1

Table 3.1: Response rates in the cross-sectional survey

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of questionnaires sent to the parents</th>
<th>Refused to participate, n (%)</th>
<th>Participated in the study (response rate %)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>4159</td>
<td>574(13.8%)</td>
<td>3585(86.2%)</td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>1894</td>
<td>291(15.3%)</td>
<td>1603(84.6%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6053</td>
<td>865(14.3%)</td>
<td>5188(85.7%)</td>
<td>5188</td>
</tr>
</tbody>
</table>
3.6.2 Characteristics of the participating children and their parents

Table 3.2 summarises the socio-demographic and lifestyle characteristics of the recruited children and of their parents.

Table 3.2: Socio-demographic and lifestyle characteristics of the participating children and their parents

<table>
<thead>
<tr>
<th>Variable</th>
<th>Boys (n=3585)</th>
<th>Girls (n=1603)</th>
<th>Total (n=5188)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father’s age (years) mean (SD)</td>
<td>43.6 (8.6)</td>
<td>44.4 (8.4)</td>
<td>43.8 (8.6)</td>
</tr>
<tr>
<td>Mother’s age (years) mean (SD)</td>
<td>35.2 (6.2)</td>
<td>36.2 (6.0)</td>
<td>35.5 (6.1)</td>
</tr>
<tr>
<td>Father’s education n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>260 (7.3%)</td>
<td>153 (9.5%)</td>
<td>413 (8.0%)</td>
</tr>
<tr>
<td>General education</td>
<td>1966 (54.8%)</td>
<td>922 (57.5%)</td>
<td>2888 (55.7%)</td>
</tr>
<tr>
<td>Higher education</td>
<td>1200 (33.4%)</td>
<td>459 (28.6%)</td>
<td>1659 (31.9%)</td>
</tr>
<tr>
<td>Missing</td>
<td>159 (4.4%)</td>
<td>69 (4.3%)</td>
<td>228 (4.4%)</td>
</tr>
<tr>
<td>Mother’s education (highest qualification) n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>381 (10.6%)</td>
<td>208 (13.0%)</td>
<td>589 (11.3%)</td>
</tr>
<tr>
<td>General education</td>
<td>2035 (56.8%)</td>
<td>963 (60.1%)</td>
<td>2998 (57.8%)</td>
</tr>
<tr>
<td>Higher education</td>
<td>1057 (29.5%)</td>
<td>364 (22.7%)</td>
<td>1421 (27.4%)</td>
</tr>
<tr>
<td>Missing</td>
<td>112 (3.1%)</td>
<td>68 (4.2%)</td>
<td>180 (3.5%)</td>
</tr>
<tr>
<td>Exposure of mother to farm animals during pregnancy in this child? n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>155 (4.3%)</td>
<td>63 (3.9%)</td>
<td>218 (4.2%)</td>
</tr>
<tr>
<td>No</td>
<td>3266 (91.1%)</td>
<td>1467 (91.5%)</td>
<td>4733 (91.2%)</td>
</tr>
<tr>
<td>Missing</td>
<td>164 (4.5%)</td>
<td>73 (4.6%)</td>
<td>237 (4.6%)</td>
</tr>
<tr>
<td>Was the child born in Madinah? n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2999 (83.7%)</td>
<td>1318 (82.2%)</td>
<td>4317 (83.2%)</td>
</tr>
<tr>
<td>No</td>
<td>521 (14.5%)</td>
<td>257 (16.0%)</td>
<td>778 (15.0%)</td>
</tr>
<tr>
<td>Missing</td>
<td>65 (1.8%)</td>
<td>28 (1.7%)</td>
<td>93 (1.8%)</td>
</tr>
<tr>
<td>Child’s birth weight (kg); mean (SD)</td>
<td>2.94 (0.64)</td>
<td>2.91 (0.66)</td>
<td>2.93 (0.64)</td>
</tr>
<tr>
<td>Did the mother breastfeed? n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2935 (81.9%)</td>
<td>1319 (82.3%)</td>
<td>4254 (82.0%)</td>
</tr>
<tr>
<td>No</td>
<td>567 (15.8%)</td>
<td>240 (15.0%)</td>
<td>807 (15.6%)</td>
</tr>
<tr>
<td>Missing</td>
<td>83 (2.3%)</td>
<td>44 (2.7%)</td>
<td>127 (2.4%)</td>
</tr>
<tr>
<td>Birth order n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First child</td>
<td>626 (17.5%)</td>
<td>226 (14.1%)</td>
<td>852 (16.4%)</td>
</tr>
<tr>
<td>Second child</td>
<td>587 (16.4%)</td>
<td>292 (18.2%)</td>
<td>879 (17.0%)</td>
</tr>
<tr>
<td>Third or greater</td>
<td>2296 (64.0%)</td>
<td>1034 (64.5%)</td>
<td>3330 (64.2%)</td>
</tr>
<tr>
<td>Missing</td>
<td>76 (2.1%)</td>
<td>51 (3.2%)</td>
<td>127 (2.4%)</td>
</tr>
<tr>
<td>How many years has the child lived in Madinah? n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than one year</td>
<td>3354 (93.6%)</td>
<td>1487 (92.8%)</td>
<td>4841 (93.3%)</td>
</tr>
<tr>
<td>One year or less</td>
<td>47 (1.3%)</td>
<td>19 (1.2%)</td>
<td>66 (1.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>184 (5.1%)</td>
<td>97 (6.0%)</td>
<td>281 (5.4%)</td>
</tr>
<tr>
<td>Does the father smoke? n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>828 (23.1%)</td>
<td>405 (25.3%)</td>
<td>1233 (23.8%)</td>
</tr>
<tr>
<td>No</td>
<td>2695 (75.2%)</td>
<td>1164 (72.6%)</td>
<td>3859 (74.4%)</td>
</tr>
<tr>
<td>Question</td>
<td>Yes</td>
<td>No</td>
<td>Missing</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>Does the mother smoke?</td>
<td>30 (0.8%)</td>
<td>13 (0.8%)</td>
<td>43 (0.8%)</td>
</tr>
<tr>
<td>Did the mother smoke during the 1st year of child’s life?</td>
<td>24 (0.6%)</td>
<td>14 (0.9%)</td>
<td>38 (0.7%)</td>
</tr>
<tr>
<td>Number of smokers in the household?</td>
<td>2675 (74.6%)</td>
<td>1156 (72.1%)</td>
<td>3831 (73.8%)</td>
</tr>
<tr>
<td>Was there a cat at home during the 1st year of child’s life?</td>
<td>160 (4.5%)</td>
<td>67 (4.2%)</td>
<td>227 (4.4%)</td>
</tr>
<tr>
<td>Did the child receive antibiotics in the 1st year of life?</td>
<td>2002 (55.8%)</td>
<td>926 (57.8%)</td>
<td>2928 (56.4%)</td>
</tr>
<tr>
<td>Did the child receive paracetamol during the first year of life?</td>
<td>3011 (84%)</td>
<td>1232 (76.8%)</td>
<td>4243 (81.7%)</td>
</tr>
<tr>
<td>On average, how many times has the child been administered paracetamol in last 12 months?</td>
<td>634 (17.7%)</td>
<td>373 (23.3%)</td>
<td>1007 (19.4%)</td>
</tr>
<tr>
<td>How many hours a day does the child watch TV?</td>
<td>2167 (60.4%)</td>
<td>960 (59.8%)</td>
<td>3127 (60.3%)</td>
</tr>
<tr>
<td>How many times a week does the child take exercise?</td>
<td>2262 (63.1%)</td>
<td>1253 (78.2%)</td>
<td>3515 (67.8%)</td>
</tr>
<tr>
<td>Type of air conditioning at home</td>
<td>219 (6.1%)</td>
<td>516 (32.2%)</td>
<td>735 (14.2%)</td>
</tr>
<tr>
<td>How many times on average does a truck pass the street adjacent to your home?</td>
<td>28 (0.8%)</td>
<td>24 (1.5%)</td>
<td>52 (1.0%)</td>
</tr>
</tbody>
</table>
Which cooking fuel is normally used in your household? n (%)  
<table>
<thead>
<tr>
<th></th>
<th>Rarely</th>
<th>Frequently</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electricity only</td>
<td>154 (4.3%)</td>
<td>49 (3.1%)</td>
<td>203 (3.9%)</td>
</tr>
<tr>
<td>Gas only</td>
<td>3270 (91.2%)</td>
<td>1484 (92.6%)</td>
<td>4754 (91.6%)</td>
</tr>
<tr>
<td>Wood fire or coal</td>
<td>3 (0.1%)</td>
<td>7 (0.4%)</td>
<td>10 (0.2%)</td>
</tr>
<tr>
<td>Both electricity &amp; gas</td>
<td>48 (1.3%)</td>
<td>20 (1.2%)</td>
<td>68 (1.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>110 (3.1%)</td>
<td>43 (2.7%)</td>
<td>153 (2.9%)</td>
</tr>
</tbody>
</table>

Diet – how frequent does the child eat the following?  

**Meat n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>244 (6.8%)</td>
<td>135 (8.4%)</td>
<td>379 (7.3%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1169 (32.6%)</td>
<td>553 (34.5%)</td>
<td>1722 (33.2%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>2052 (57.2%)</td>
<td>859 (53.6%)</td>
<td>2911 (56.1%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>120 (3.3%)</td>
<td>76 (4.7%)</td>
<td>247 (4.8%)</td>
<td></td>
</tr>
</tbody>
</table>

**Fish n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1631 (45.5%)</td>
<td>744 (46.4%)</td>
<td>2375 (45.8%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1606 (44.8%)</td>
<td>689 (43.0%)</td>
<td>2295 (44.2%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>171 (4.8%)</td>
<td>76 (4.7%)</td>
<td>247 (4.8%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>177 (4.9%)</td>
<td>94 (5.8%)</td>
<td>271 (5.2%)</td>
<td></td>
</tr>
</tbody>
</table>

**Fruit n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>534 (14.9%)</td>
<td>173 (10.8%)</td>
<td>707 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1500 (41.8%)</td>
<td>686 (42.8%)</td>
<td>2186 (42.1%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>1431 (39.9%)</td>
<td>677 (42.2%)</td>
<td>2108 (40.6%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>120 (3.3%)</td>
<td>67 (4.2%)</td>
<td>187 (3.6%)</td>
<td></td>
</tr>
</tbody>
</table>

**Vegetables n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>444 (12.4%)</td>
<td>152 (9.5%)</td>
<td>596 (11.5%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1313 (36.6%)</td>
<td>580 (36.2%)</td>
<td>1893 (36.5%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>1623 (45.3%)</td>
<td>779 (48.6%)</td>
<td>2402 (46.3%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>205 (5.7%)</td>
<td>92 (5.7%)</td>
<td>297 (5.7%)</td>
<td></td>
</tr>
</tbody>
</table>

**Legumes n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1180 (32.9%)</td>
<td>483 (30.1%)</td>
<td>1663 (32.0%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1555 (43.4%)</td>
<td>680 (42.4%)</td>
<td>2235 (43.1%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>673 (18.8%)</td>
<td>347 (21.6%)</td>
<td>1020 (19.7%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>205 (5.7%)</td>
<td>93 (5.8%)</td>
<td>270 (5.2%)</td>
<td></td>
</tr>
</tbody>
</table>

**Cereal n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>97 (2.7%)</td>
<td>41 (2.6%)</td>
<td>138 (2.7%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>394 (11.0%)</td>
<td>181 (11.3%)</td>
<td>575 (11.1%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>2935 (81.9%)</td>
<td>1291 (80.5%)</td>
<td>4226 (81.4%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>159 (4.4%)</td>
<td>90 (5.6%)</td>
<td>249 (4.8%)</td>
<td></td>
</tr>
</tbody>
</table>

**Pasta n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>764 (21.3%)</td>
<td>338 (21.1%)</td>
<td>1102 (21.2%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>1915 (53.4%)</td>
<td>862 (53.8%)</td>
<td>2777 (53.5%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>755 (21.1%)</td>
<td>335 (20.9%)</td>
<td>1090 (21.0%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>151 (4.2%)</td>
<td>68 (4.2%)</td>
<td>219 (4.2%)</td>
<td></td>
</tr>
</tbody>
</table>

**Rice n (%)**  
<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Once or twice a week</th>
<th>Three or more a week</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>136 (3.8%)</td>
<td>50 (3.1%)</td>
<td>186 (3.6%)</td>
<td></td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>744 (20.8%)</td>
<td>336 (21.0%)</td>
<td>1080 (20.8%)</td>
<td></td>
</tr>
<tr>
<td>Three or more a week</td>
<td>2549 (71.1%)</td>
<td>1133 (70.7%)</td>
<td>3682 (71.0%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>156 (4.3%)</td>
<td>84 (5.2%)</td>
<td>240 (4.6%)</td>
<td></td>
</tr>
</tbody>
</table>
In 228 (i.e. 4.4% of the total of 5,188) questionnaires educational information was missing for both parents. Out of the remaining 4,960 questionnaires, there were recorded 2,888 (58.2%) fathers belonging to general education category; 1,659 (33.4%) fathers belonging to higher education category; and 413 (8.3%) fathers having no education at all. Among the fathers who belonged to the general education category, 1,966 (68.1%) of them were of boys and 922 (31.9%) of girls. In the category of fathers with higher education, 1,200 (72.3%) of them were of boys and 459 (27.7%) of girls. Finally, in the category of fathers with no education, 260 (63.0%) of them were of boys and 153 (37.0%) of girls.
For 180 (3.5%) children, the information about the education status of their mother was missing. A total of 2,998 (59.9%) children had their mothers belonging to the general education category; a total of 1421 (28.4%) children had their mothers belonging to the higher education category; and 589 (11.8%) children had their mothers belonging to the no education category. Among the 2,998 mothers belonging to the general education category, 2,035 (67.9%) of them were of boys and 963 (32.1%) of girls; among the 1,421 mothers belonging to the higher education category, 1,057 (74.4%) of them were of boys and 364 (25.6%) were of girls; among the mothers with no education, 381 (64.7%) of them were of boys and 208 (35.3%) were of girls.

From these data, it becomes evident that fathers were more educated than mothers as evidenced by the rates in the higher education category (31.9% vs. 27.4% respectively), and in the no education category (8.0% vs. 11.4% respectively).

3.6.3 Prevalence of symptoms suggestive of allergic disorders

Table 3.3 summarises the findings for the estimated prevalence of each of the allergic disorders studied. The overall prevalence of children having presented with asthma symptoms (i.e. ever having had wheeze or whistling in the chest) was 23.6% (95% CI: 21.3, 26.0); the respective prevalence in boys was 24.4% (95% CI: 22.0, 26.9) and in girls 21.9% (95% CI: 17.4, 27.1).

The prevalence of children ever having presented symptoms suggestive of allergic rhinitis was 24.2% (95% CI: 22.3, 26.2); the respective prevalence rate in boys was 26.7% (95% CI: 25.0, 28.5) and in girls 18.7% (95% CI: 16.9, 20.7). Overall, 10.4% (95% CI: 9.4, 11.4) of the children were reported with a history of a chronic (i.e. ≥6 months) itchy rash, which is a symptom suggestive of eczema; the respective prevalence rate in boys was 10.9% (95% CI: 9.8, 12.0) and in girls 9.2% (95% CI: 7.5, 11.3).

3.6.4 Prevalence of physician-diagnosed allergic disorders

The prevalence of children who had been formally diagnosed with asthma by a physician as reported by the parents, was 15.5% (95% CI: 14.1, 17.0). The respective prevalence in boys was 16.9% (95% CI: 15.5, 18.4) and in girls 12.2%. (95% CI: 10.1, 14.7). The overall
prevalence of children who had a clinical diagnosis of allergic rhinitis was 4.2% (95% CI 3.6, 4.7); the respective rate in boys was 4.6% (95% CI 4.0, 5.2) and in girls 3.2% (95% CI: 2.4, 4.4). The prevalence of children who were reported to have been clinically diagnosed with eczema was 14.0% (95% CI: 12.2, 15.9); the respective rate in boys was 15.1% (95% CI: 12.9, 17.5) and in girls 11.6% (95% CI: 9.8, 13.7).

3.6.5 Prevalence of symptoms of allergic disorders in the last 12 months

The prevalence of parental reports of symptoms of asthma in the last 12 months prior to the study was 10.2% (95% CI: 8.9, 11.7) in all of the children; the respective rate in boys was 11.6% (95% CI: 10.5, 12.9) and in girls 7.0% (95% CI: 5.0, 9.9).

The prevalence of allergic rhinitis symptoms in the last 12 months was 18.2% (95% CI: 16.6, 20.0) for all children; the respective rate in boys was 20.0% (95% CI: 18.3, 21.7) and in girls 14.3% (95% CI: 12.2, 16.7). The overall prevalence of symptoms of eczema within the last 12 months was 8.8% (95% CI: 7.8, 9.8); the respective rate in boys was 9.3% (95% CI: 8.2, 10.5) and in girls 7.6% (95% CI: 5.9, 9.8).
Table 3.3: Prevalence of parental reports of symptoms of diagnosed and current status of asthma, allergic rhinitis and eczema in the sample of 5,188 schoolchildren of Madinah

<table>
<thead>
<tr>
<th>Parental-reported outcomes</th>
<th>Boys Prevalence % (95%CI)</th>
<th>Girls Prevalence % (95%CI)</th>
<th>Total Prevalence % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever had symptoms of asthma</td>
<td>24.4 (22.0, 26.9)</td>
<td>21.9 (17.4, 27.1)</td>
<td>23.6 (21.3, 26.0)</td>
</tr>
<tr>
<td>Ever had symptoms of rhinitis</td>
<td>28.7 (25.0, 28.5)</td>
<td>18.7 (16.9, 20.7)</td>
<td>24.2 (22.3, 26.2)</td>
</tr>
<tr>
<td>Ever had symptoms of eczema</td>
<td>10.9 (9.8, 12.0)</td>
<td>9.2 (7.5, 11.3)</td>
<td>10.4 (9.4, 11.4)</td>
</tr>
<tr>
<td>Diagnosed asthma</td>
<td>17.9 (15.5, 18.4)</td>
<td>12.2 (10.1, 14.7)</td>
<td>15.5 (14.1, 17.0)</td>
</tr>
<tr>
<td>Diagnosed rhinitis</td>
<td>6.9 (4.0, 5.2)</td>
<td>3.2 (2.4, 4.4)</td>
<td>4.2 (3.6, 4.7)</td>
</tr>
<tr>
<td>Diagnosed eczema</td>
<td>17.1 (12.9, 17.5)</td>
<td>11.6 (9.8, 13.7)</td>
<td>14.0 (12.2, 15.9)</td>
</tr>
<tr>
<td>Asthma symptoms in the last 12 months</td>
<td>11.6 (10.5, 12.9)</td>
<td>7.0 (5.0, 9.9)</td>
<td>10.2 (8.9, 11.7)</td>
</tr>
<tr>
<td>Rhinitis symptoms in the last 12 months</td>
<td>20.0 (18.3, 21.7)</td>
<td>14.3 (12.2, 16.7)</td>
<td>18.2 (16.6, 20.0)</td>
</tr>
<tr>
<td>Eczema symptoms in the last 12 months</td>
<td>9.3 (8.2, 10.5)</td>
<td>7.6 (5.9, 9.8)</td>
<td>8.8 (7.8, 9.8)</td>
</tr>
</tbody>
</table>

3.6.6 Gender-related variations in the prevalence of asthma

In all the allergic disorders studied, the estimated prevalence was found to be higher in boys and girls (Table 3.3). This held both for the prevalence of the reported symptoms, as well as for the prevalence of clinically diagnosed disorders. However, none of the differences in the prevalence rates between boys and girls were statistically significant.

3.6.7 Co-morbid allergic disorders

Table 3.4 displays the prevalence rates of co-morbid allergic disorders, i.e. the rates of children who were reported to have presented symptoms of more than one of the studied allergies. 9.9% of children (95% CI: 8.7, 11.1) presented symptoms of both asthma and allergic rhinitis, while the overall prevalence of children who presented symptoms of both asthma and eczema was estimated at 4.4% (95% CI: 3.8, 5.1). The overall prevalence of children with symptoms of both allergic rhinitis and eczema was estimated at 4.8% (95% CI: 4.2, 5.4) and the overall prevalence of children who combined all three allergic disorders was 2.6% (95% CI: 2.2, 3.0). The respective prevalence rates by gender are displayed in Table 3.5. Similarly to the prevalence of each disorder separately; the prevalence rates of the co-morbid conditions were higher in boys than in girls; Figure 3.3 shows co-morbidities of allergic disorders in a Venn diagram.
Table 3.4: Prevalence of co-morbid allergic disorders (based on reported symptoms)

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>Boys Prevalence % (95% CI)</th>
<th>Girls Prevalence % (95% CI)</th>
<th>Total children Prevalence % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma and allergic rhinitis</td>
<td>11.1 (10.1, 12.2)</td>
<td>7.1 (5.4, 9.3)</td>
<td>9.9 (8.7, 11.1)</td>
</tr>
<tr>
<td>Asthma and eczema</td>
<td>4.6 (3.9, 5.4)</td>
<td>4.0 (3.1, 5.2)</td>
<td>4.4 (3.8, 5.1)</td>
</tr>
<tr>
<td>Allergic rhinitis and eczema</td>
<td>5.2 (4.6, 5.9)</td>
<td>3.8 (3.1, 4.7)</td>
<td>4.8 (4.2, 5.4)</td>
</tr>
<tr>
<td>All three disorders together</td>
<td>2.9 (2.5, 3.4)</td>
<td>1.9 (1.3, 2.6)</td>
<td>2.6 (2.2, 3.0)</td>
</tr>
</tbody>
</table>

Figure 3.3: Co-morbidities of allergic disorders based on ever had symptoms in a Venn diagram

3.6.8 Distribution of children according to the number of affecting allergic disorders

Table 3.5 shows the distribution of children per number of allergic disorders by which they are affected. 58.3% of the studied children (i.e. 3,023 children) did not present any symptoms of any allergic disorder under study (95% CI: 56.9, 59.6). 27.8% of the children were reported to have presented symptoms of only one allergic disorder (95% CI: 26.7, 29.1).
Eleven point three percent of children (95% CI: 10.4, 12.1) were found, according to parental reports, to have presented at some time in their life, symptoms of at least two of the studied disorders. Finally, a very small percentage of children 2.6% (95% CI: 2.2, 3.0) was found to have presented symptoms of all three of the studied disorders.

Table 3.5: Number of children affected by allergies

<table>
<thead>
<tr>
<th>Pattern of allergy in children of both genders</th>
<th>n (%)</th>
<th>95% CI for the rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergy at all</td>
<td>3023 (58.3%)</td>
<td>(56.9, 59.6)</td>
</tr>
<tr>
<td>Only one disorder</td>
<td>1446 (27.8%)</td>
<td>(26.7, 29.1)</td>
</tr>
<tr>
<td>Any two disorders together</td>
<td>584 (11.3%)</td>
<td>(10.4, 12.1)</td>
</tr>
<tr>
<td>All three disorders together</td>
<td>135 (2.6%)</td>
<td>(2.2, 3.0)</td>
</tr>
</tbody>
</table>

3.7 Discussion

3.7.1 Prevalence of allergic disorders in Saudi children

This cross-sectional survey is the largest study on the prevalence of allergic disorders among school-aged children ever undertaken in the Arab world. The findings indicate that the prevalence of allergies is very high among Saudi children; over 40% of children in the studied sample seem to have been affected by at least one allergic condition within the first eight years of their life. These findings raise important issues for public health and school authorities of Saudi Arabia, as well as to the general public.

Allergic rhinitis and asthma were found to be the most important problems, with each affecting almost 25% of the childhood population. Eczema was less prevalent, affecting about 10% of children. In any disorder studied, both in respect to symptoms reports as well as to previous clinical diagnoses, the measured prevalence rates were higher in boys than in girls.

3.7.2 Strengths and limitations

The main strengths of this work include the large sample size and the very high response rate; the latter is likely to be due to the combination of achieving good support from the participating schools and from the fact that we were undertaking work in a population that has not previously been investigated, hence research fatigue was not an issue.(190, 191)

Unlike the majority of previous studies, we did not confine ourselves to studying the
prevalence of asthma. (83, 145, 147, 178, 179, 192) Rather, we looked at other common allergic problems, namely eczema and rhinitis; we also studied the co-morbidity between these conditions. The use of a validated instrument was an additional strength, particularly since this offered the opportunity to compare prevalence estimates for children from Madinah with children of a similar age from across the world. (173)

The major limitation with this work is that it was conducted in only one city in Saudi Arabia in children of one age group; these findings may therefore not be generalisable to other sections of Saudi society. It is important that similar studies are now conducted in other urban and rural locations in Saudi Arabia in children of other age groups. There is also the need to build on this work and monitor allergic disease trends in Madinah. (52) Finally, as we had no data that allowed us to compare the characteristics of responders and non-responders, care must be taken in seeking to extrapolate data from this work across the entire Madinah region.

3.7.3 Comparison with other studies in Saudi Arabia

A high prevalence of childhood asthma has been observed in another study in Saudi Arabia which investigated the population of Jeddah and Riyadh regions in 1995; (145) this study estimated the prevalence of asthma at 23%, a figure that is similar to this study. Jeddah and Riyadh are characterised by marked geographical and environmental variations: Jeddah is a coastal city, while Riyadh is located in a very dry desert region, and Madinah is located more than 600 meters above the sea level which bears similarity to Riyadh and also has a hot desert climate. (141)

Another study in Saudi Arabia in 1993, (179) found that the prevalence of diagnosed asthma was 6.8% and the prevalence of history of wheeze was 10.6%. These figures are lower than the respective results found in this study, but they refer to a period 15 years prior to the data collection undertaken for this study. Therefore, our study offers some updated data about the prevalence of asthma in the country.

The prevalence of asthma in the last 12 months among school-aged children in Madinah (10.2%) is in agreement with that found in the Asir Region by Al-Ghamdi et al. (12.3%; 2008). (143, 180) Also, this study showed variations in the prevalence of asthma related to altitude: the prevalence in areas at sea level was 19.5%, while in other areas with higher
altitude the prevalence was estimated at 6.9%. The Asir Region includes several cities, but with highly homogenous populations. The populations in Asir are rural, including farmers who live in settled communities, largely organised in accordance with tribal and clan identities. The seaports of Asir and Madinah have also populations traditionally oriented towards the sea for trade or fishing, a characteristic that is also present in the population of the Eastern Province.

Another study in the Al-Khobar Region, Eastern Region of Saudi Arabia, found that the prevalence of diagnosed asthma,(144) was 9.5%; this figure is lower than the one recorded in our study which was 15.5%.(143)

The above-mentioned differences in the prevalence of asthma may be attributed to differences in income and environmental factors (climate and geographic influences) as shown in many studies.(178, 180, 193) The exposure to house dust mites and other allergens plays an important role in the development of wheezing and asthma.(144, 194) These locally operating environmental factors may also explain the high rate of asthma in this current study.

A study conducted in Jeddah-Riyadh-Gizan in 1986 found that the prevalence of eczema was 12%; this rate had increased to 13% by 1995. The 1995 rate is very close to the figure determined in Madinah in the current study. This similarity could be attributed to the similar ethnicity in Saudi people (90% Arab and 10% Afro-Asian),(195) and the environmental factors.(143, 145)

In 1998 a study was conducted in rural and urban regions in Jeddah.(178) The high prevalence of asthma and allergic diseases amongst urban inhabitants compare to rural in Saudi Arabia is likely to be associated with the increased affluence and resulting modern lifestyle.(178) In turn, this is consistent with the hypothesis, that the environment, possibly through lifestyle changes and patterns of infection has an impact on the manifestation of allergic diseases.(178) The study also found a significantly higher prevalence of allergic symptoms in Saudi children than in non-Saudi children.

A recently conducted study of children aged 6-14 years in Saudi Arabia estimated the prevalence of eczema at 5.6%.(196) There was a big difference in this figure compared with the figure of eczema in our present study. The current study showed that the prevalence of ever having allergic rhinitis was 24.2%. This figure is very close to the figures recorded in a
study in Jeddah and Riyadh, where the prevalence of allergic rhinitis was 20% and 25% in 1986 and 1995 respectively. (145)

3.7.4 Gender differences

The present study highlights that the prevalence of asthma and other allergic disorders is higher in boys than girls. The findings about asthma prevalence are comparable with those of a study conducted in Qatar between 2003-2004, (83) which suggests that there are significant differences in the prevalence of asthma between boys and girls. For allergic rhinitis, no significant differences between the two genders were found in the above study.

The differences in the prevalence of allergies between boys and girls may be socio-behavioural. It is believed that boys may be more prone to exposure to allergens and to respiratory infections, since they spend more time outdoors than girls. (197) On the other hand, it may be speculated that girls who spend more time indoors, are more likely to be exposed to indoor allergens. In both cases, potential exposures of children to allergens need to be further investigated through other analytical studies.

As mentioned in Section 3.7.3 in addition to socio-behavioural, exposure to allergens and infections, the differences in the prevalence of asthma or allergies between boys and girls may be explained by hormonal effects in both genders. For example, oestrogen is a predominantly female hormone found in adipose tissue which plays an important role in Th1 type of immune responses, and in turn it may be associated with underlying immunological mechanisms of development of asthma in children. (198)

3.8 Conclusions

This large study of allergic disease prevalence in primary school-aged children in Madinah, Saudi Arabia, has found that over 40% of children manifest symptoms indicative of allergic disease prevalence within the first eight years of life, these figures rank amongst the highest in the world. More work is now needed on assessing the prevalence of allergic problems in other parts of Saudi Arabia, other age groups, and in monitoring disease trends. Given these very high figures, the Saudi Government needs to give careful consideration to developing
health and educational policies that ensure the effective treatment and management of these children. There is furthermore a need to understand better what is driving this epidemic in Saudi children and prioritise the search for effective primary prevention strategies.

3.9 Chapter summary

There are reports that the prevalence of asthma in Saudi Arabia follows the increasing international trends. The main aim of this study was to determine the prevalence of asthma, eczema, and allergic rhinitis in Madinah, Saudi Arabia, amongst school-aged children. The study conducted was a two-stage cross-sectional survey of primary school students, aged 6–8 years, who were permanent residents of Madinah, one of the largest provinces in Saudi Arabia.

A total of 5,188 students (1,603 girls and 3,585 boys) participated in the study. The parents of the participating students completed the Arabic version of the ISAAC questionnaire. The prevalence of children ever having presented with asthma symptoms was 23.6% (95% CI: 21.3, 26.0); the respective prevalence in boys was 24.4% (95% CI: 22.0, 26.9) and in girls 21.9% (95% CI: 17.4, 27.1). The prevalence of children ever having presented symptoms of allergic rhinitis was 24.2% (95% CI: 22.3, 26.2); the respective prevalence rate in boys was 26.7% (95% CI: 25.0, 28.5) and in girls 18.7% (95% CI: 16.9, 20.7). The prevalence of children ever having presented an itchy rash (a symptom suggestive of eczema) was 10.4% (95% CI: 9.4, 11.4); the respective prevalence rate in boys was 10.9% (95% CI: 9.8, 12.0) and in girls 9.2% (95% CI: 7.5, 11.3).

There was a substantial percentage of children (13.9%) who reported co-morbid allergies (i.e. more than one allergic disorder), while 2.6% of children were reported to have presented the symptoms of all three conditions.

The findings indicate that the prevalence of allergies is at very high levels among Saudi children; over 40% of children in the studied sample seem to have been affected by at least one allergic condition within the first eight years of their life; and for any disorder studied, both in respect to symptoms reports as well as to previous clinical diagnoses, the measured prevalence rates were higher in boys than in girls.
The main strength of this study is the large sample size and the very high response rate. The major limitation is that it was conducted in only one city in Saudi Arabia and in children of only one age group; the findings may therefore not be generalised to other sections of Saudi society.

This survey identified asthma-affected children within primary schools, who could be used as cases for subsequent matched case-control studies.

Given the very high prevalence rates observed in Madinah, it is important that this work is now extended to other Saudi regions; it is also important that attempts are made to understand key potentially modifiable environmental risk factors.
Chapter 4: Matched case-control study of the association between obesity and asthma in 6-8 year-old children in Madinah, Saudi Arabia

4.1 Introduction

The substantial parallel increases in the prevalence of obesity(1, 2, 199-202) and asthma(52, 55, 66) observed over recent decades, have led to the suggestion that obesity may be causally implicated in the risk of developing asthma.(45, 203, 204)

The work by Camargo et al.(1999). has been important in this respect as they found that women who gained weight after the age of 18 years had an increased risk of developing asthma over the following four years.(30) Jose et al.(2006) subsequently reported that girls who became overweight or obese between 6-11 years of age were more likely to develop new asthmatic symptoms, but no association was observed in boys.(107) Also noteworthy is a large Norwegian longitudinal study in which 135,000 people aged 14-59 years were followed on average for 21 years; the authors found that increasing BMI was associated with increasing risk of developing asthma.(31) A clear positive association between obesity and asthma in children has also been reported in another two cohort studies.(30, 45)

Findings from these epidemiological studies have been synthesised in systematic reviews. For example, a systematic review of studies investigating the relationship between childhood BMI and risk of asthma in adolescence concluded that positive associations were evident in most of the studies (i.e. 8/10).(94) Furthermore, a systematic review and meta-analysis of 12 studies estimated that high body weight (either at birth or later in childhood) substantially increased the risk of developing childhood asthma (RR=1.5; 95% CI: 1.2, 1.8). The authors proposed a number of potential biological mechanisms, including dietary factors, gastro-oesophageal reflux, hormonal influences, the mechanical effects of obesity and an increased risk of atopy.(94)

This initial list of candidate mechanisms has subsequently been refined to five main causal theories attempting to explain the link between obesity and asthma; these theories are summarised as follows: 1) direct effects on functional respiratory mechanics; 2) changes in immune and inflammatory responses; 3) activation of common genes; 4) influence of
hormones and gender; and 5) interaction of diet, physical activity, and fetal programming. As discussed in Chapter 1, the most plausible amongst these are the latter two theories, namely a direct splinting effect on the diaphragm associated with increased abdominal girth and the pro-inflammatory effects of obesity resulting in immunological changes that increase the risk of allergic sensitisation.(94)

Despite the increasing epidemiological evidence of an association between obesity and asthma, it remains unclear whether this association that has been demonstrated mainly in European-origin populations is also found in other populations and, if so, what the most likely pathways are through which obesity may impact on the risk of developing asthma.

4.2 Aims and objectives

The aims of this study were to investigate the association between obesity and asthma in primary school boys and girls in Madinah, Saudi Arabia and to investigate if any associations identified could be explained by the potential mechanisms of impaired respiratory function and allergic sensitisation.

The objectives of the present study were to:

- Select from the previous large cross-sectional survey (Chapter 3) an appropriate sample of children with asthma (cases) and match them with a respective number of controls according to age and gender;
- Collect from the participating children data on their obesity status, lung function status, and their sensitisation to allergens;
- Investigate the role of impairments in lung function status and/or sensitisation to allergens in explaining any associations uncovered.
4.3 Methods

4.3.1 Design

The study presented in this chapter is an age- and gender-matched case-control study of 1,264 schoolchildren, aged 6-8 years with and without asthma. These children were selected from the initial sample of 5,188 children who were recruited for the cross-sectional study (Chapter 3) from the 37 randomly selected schools in Madinah. In the matched case-control study, 632 children with asthma (cases) were compared with 632 children without asthma (controls; matched for age and gender), in respect to their BMI, respiratory function measures, and sensitisation to allergens. Socio-demographic and lifestyle data were taken into account so that comparisons were, if necessary, adjusted for such factors. The methods were piloted in Madinah in 2008 and the data collection forms (including the signed parental consent forms for the cross-sectional study) used for this pilot were also used for the case-control study (boys and girls), with the exception of the information referring to the blood sample (see Appendices 15-18).

4.3.2 Recruitment of schools and students

The recruitment of schools and students was as described in Chapter 3 (Section 3.5.4) (Appendices 13 and 14). Eligible students for participation in Phase II of the research (i.e. the case-control study) were all the students of Phase I, whose parents gave their signed consent for participating in anthropometric measurements, lung function tests, and SPTs. Any cases identified had to be matched with controls from the same school. For this reason, one out of nine girls’ schools was rejected from Phase II, because scrutiny of the questionnaires revealed that the participating girls from this school were all asthma cases and, thus, no controls were available for matching.

Eligible children were those aged 6-8 years who had been residents in Madinah for at least one year prior to the start of the study. Because of high prevalence of asthma in children in Madinah the recruitment process went without any difficulties. All eligible subjects were invited to participate in the study via a letter and a consent form (Appendices 2-J, 2-K and 2-L), sent by the school to their parents. It was made clear to parents that students would be withdrawn from the study if at any point they expressed reluctance to participate or in the event of parental objections.
4.3.3 Identification of cases and matched controls

The parents of all recruited children had completed the ISAAC questionnaire (Chapter 2) administered in Phase I (Chapter 3) (Appendices 6-A and 6-B). ‘Cases’ were defined as those children who, according to parental reports, had “ever had wheeze” (83, 143, 205, 206) ‘Controls’ were defined as those children who, according to parental reports, had “never had wheeze”. Among the eligible controls, only those who matched in age and gender with the cases were selected for the case-control study.

4.3.4 Measures of obesity

The main measure of obesity was BMI,(207) but in addition we measured weight, TSFT(208) and WC.(208) Children were asked to wear normal light clothing during measurements and to take off their shoes.

Measurements of height to enable calculation of BMI (which was calculated as weight in kg divided by the square of height in metres (kg/m²)), weight, TSFT and WC were carried out in the schools by trained members of the healthcare team who were unaware of whether children had asthma or not. Height was measured on a portable stadiometer (SECA Leicester height measure) using the method described by Tanner et al.(209, 210) Measurements were made to the nearest 0.1cm. Children were weighed and measured separately from their classmates. Weight was measured by SECA Mechanical Column Scales to the nearest 0.1kg.

We used BMI percentiles for girls and boys per age as a measure of standardised weight. As there are no reference data available for Saudi children, we used the Centres for Disease Control and Prevention (CDC) BMI-for-age growth charts for girls and boys.(208) According to these charts, underweight was defined as a BMI less than the 5th centile; healthy weight was defined as a BMI between the 5th centile, but less than the 85th centile; overweight was defined as a BMI between the 85th and 94th centiles; and obese was defined as a BMI equal to or greater than the 95th centile.(211)

TSFT was measured thrice to the nearest millimetre with a Holtain Skinfold Calliper on the right arm. The triceps skin fold locus was defined as being halfway between the acromion and olecranon on the back of the arm measured with the elbow bent.(212, 213) TSFT was used mainly to determine relative obesity and the percentage of body fat.(212, 213)
WC was measured to the nearest centimetre with a Lufkin flexible steel tape measure, with children in the standing position after gentle expiration. The following anatomical landmarks were used: laterally midway, between the lowest portion of the rib cage and iliac crest; and anteriorly midway, between the xiphoid process of the sternum and the umbilicus (Appendices 7, 8, 9 and 21).(214)

4.3.5 Lung function tests

Lung function tests were performed to investigate whether restrictions in lung function were associated with the presence of asthma and whether such restrictions related to obesity which may potentially result in asthma.

Lung function testing was performed in the schools by trained members of the research team. All spirometric measurements were performed in the standing position (Appendices 10 and 21) using a Vitalograph Pneumotrac Spirometer. The best of at least three technically acceptable values for FEV1, FVC, FEV1%, and PEF were selected.(215-217)

4.3.6 Skin prick tests (SPT)

SPTs were performed in order to investigate whether atopy was associated with the presence of asthma and whether atopy potentiates in some way with obesity resulting in asthma.(218, 219)

SPT were undertaken using the volar aspect of the forearm; the skin having first been marked with a pen. Thereafter, one drop of each solution to be tested was put on the skin beside the respective mark. A panel of eight allergens (Table 4.1) was used. The cockroach allergen that had been tested in the pilot study could not be tested because it was out of stock in Saudi Arabia during the period of the study.

Histamine 10 mg/ml and 50% glycerine were used as positive and negative controls; respectively(220-222) The size of the wheal was recorded as the mean of the greatest diameter and the diameter perpendicular to its mid-point. Readings were made after 15 minutes and a mean diameter of 3mm or greater than the negative control was regarded as positive (Appendices 11 and 21).(161)
Table 4.1: Allergens tested with the skin prick tests

<table>
<thead>
<tr>
<th>Allergens tested and batch reference numbers</th>
<th>Batch No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(309 Cat) Batch No. U8003289-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(708 Dermatophagoides farina) Batch No. U800222-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(725 Dermatophagoides pteronyssinus) Batch No. U8002886-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(006 Grass mix) Batch No. U8003378-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(158 Rye) Batch No. U7001666-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(012 Tree mix (early blossoming)) Batch No. U8002769-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(013 Tree mix (mid blossoming)) Batch No. U8002113-GB</td>
<td>GB</td>
</tr>
<tr>
<td>(007 Weed mix) Batch No. U8003379-GB</td>
<td>GB</td>
</tr>
</tbody>
</table>

4.3.7 Socio-demographic and lifestyle data

Information was selected on an array of socio-demographic and lifestyle factors, which could potentially act as confounders in the relationship between obesity and asthma. These factors are listed in (Table 4.2).

Table 4.2: Socio-demographic and lifestyle variables

<table>
<thead>
<tr>
<th>Socio-demographic and lifestyle variables</th>
<th>Variable type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father’s age</td>
<td>Continuous in years*</td>
</tr>
<tr>
<td>Mother’s age</td>
<td>Continuous in years*</td>
</tr>
<tr>
<td>Birth weight</td>
<td>Continuous in kg</td>
</tr>
<tr>
<td>Father’s education</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- None</td>
</tr>
<tr>
<td></td>
<td>- General</td>
</tr>
<tr>
<td></td>
<td>- Higher</td>
</tr>
<tr>
<td>Mother’s education</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- None</td>
</tr>
<tr>
<td></td>
<td>- General</td>
</tr>
<tr>
<td></td>
<td>- Higher</td>
</tr>
<tr>
<td>Smoking status of the father</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Smoking status of the mother</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Birth order of the child</td>
<td>Ordinal</td>
</tr>
<tr>
<td>Child born in Madinah</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Child breastfed</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Paracetamol given in the 1st year of child’s life</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Antibiotics given in the 1st year of child’s life</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Paracetamol given in the last 12 months</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Exposure of the mother to farm animal while pregnant</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Cat at home in the 1st year of child’s life</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Cat at home in the last 12 months</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>Exposure of the child to a farm animal in 1st year of life</td>
<td>Binary (yes/no)</td>
</tr>
<tr>
<td>----------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Frequency of physical exercise per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
<tr>
<td>Frequency of watching TV per week</td>
<td>Binary</td>
</tr>
<tr>
<td></td>
<td>- Less than 3h</td>
</tr>
<tr>
<td></td>
<td>- More than 3h</td>
</tr>
<tr>
<td>Type of cooking fuel at home</td>
<td>Nominal with 3 categories</td>
</tr>
<tr>
<td></td>
<td>- Gas only</td>
</tr>
<tr>
<td></td>
<td>- Electricity only</td>
</tr>
<tr>
<td></td>
<td>- Both</td>
</tr>
<tr>
<td>Type of air conditioning system at home</td>
<td>Nominal with 4 categories</td>
</tr>
<tr>
<td></td>
<td>- Electric fan</td>
</tr>
<tr>
<td></td>
<td>- Water system</td>
</tr>
<tr>
<td></td>
<td>- Freon system</td>
</tr>
<tr>
<td></td>
<td>- Both Freon &amp; Water systems</td>
</tr>
<tr>
<td>Frequency of trucks passing near child’s home</td>
<td>Binary</td>
</tr>
<tr>
<td></td>
<td>- Rarely</td>
</tr>
<tr>
<td></td>
<td>- Frequently</td>
</tr>
<tr>
<td>Frequency of eating meat per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
<tr>
<td>Frequency of eating fruits per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
<tr>
<td>Frequency of eating rice per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
<tr>
<td>Frequency of eating nuts per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
<tr>
<td>Frequency of eating fast food per week</td>
<td>Ordinal with 3 levels</td>
</tr>
<tr>
<td></td>
<td>- Never</td>
</tr>
<tr>
<td></td>
<td>- Once or Twice</td>
</tr>
<tr>
<td></td>
<td>- Three or More</td>
</tr>
</tbody>
</table>

* From a strict point of view, age is a quantitative discrete variable, rather than a continuous one. For the needs of the present analyses though, this variable was treated as continuous.
4.4 Statistical analyses

4.4.1 Sample size

As described in Section 2.7.4, we aimed to recruit around 600 cases and 600 controls. All calculations were performed using Epi Info™ software. This is a computer programme developed by the US Centres for Disease Control, which provides several tools for epidemiological analysis. The Epi Info functionality for sample size calculation was used to undertake estimates of sample size requirements.

4.4.2 Analysis of data

Analysis of data focused on investigating any potential association between obesity (as it was expressed by BMI) and the risk of asthma. Because the literature suggested that we might find differing degrees of association between obesity and asthma (91, 224) between the genders all analyses were undertaken separately for boys and girls.

Cases were compared with their matched controls using a paired t-test for continuous variables and using the Wilson's methods for all qualitative variables (i.e. nominal binary; nominal with more than two categories; and ordinal variables). In nominal variables with more than two categories and in ordinal variables, the rates in each of the distinct categories in cases were compared with the rates in the respective categories in controls. For example, the frequency of case students who consumed meat once or twice a week was compared with the rate of the respective control students who consumed meat once or twice a week; the rate of case students who consumed meat three or more times per week was compared with the rate of the respective control students who consumed meat three or more times a week.

Multiple conditional logistic regression (225-227) analysis was performed to investigate the relationship between obesity and asthma, adjusted for covariates. From the several lifestyle variables considered, only those variables that differed significantly between cases and controls (identified by the t-tests and the Wilson's tests) were included as covariates in the multiple regression models. Multiple conditional logistic regression was undertaken both using all these variables and using the backward stepwise regression method. Because the data from this part of the study were in the form of matched pairs, it was necessary to use...
multiple conditional logistic regression to investigate the relationship between obesity and asthma. This is a form of logistic regression in which comparisons of the covariates between cases and controls are only considered within each case-control pair;(225-227) this command was programmed in SPSS using the COXREG procedure.

A small amount of data was missing for some variables from some respondents although most respondents filled in their questionnaires fully. In place of the entire case being omitted from analysis, cases were only omitted when the relevant variables were part of the analysis. In SPSS, this was achieved automatically through setting these entries as missing.

All statistical analyses were carried out using SPSS version 16.0 for Windows, and Confidence Interval Analysis (CIA) software.(229)

4.5 Results

4.5.1 Characteristics of cases and controls

Scrutiny of the data collected for the cross-sectional study (Chapter 3) identified 388 boys and 244 girls who were reported by their parents as ever having had wheeze; those children were considered as cases for the matched case-control study.

Table 4.3 summarises the findings on the measurements of obesity, lung function, and sensitisation to allergens in cases and controls, separately for boys and girls. Although, the data were collected on a variety of obesity measures, we focused on the BMI as the measure of obesity in our population; this decision was based on the observation that this is the more standard measurement that has been employed in epidemiological studies.(230, 231) That said, all measures of obesity (i.e. BMI, weight, TSFT, and WC) were higher in cases than the controls in both boys and girls and the differences were statistically significant. All lung function measures demonstrated smaller values in cases than in controls in both boys and girls and the differences were statistically significant. Cases, in both boys and girls, demonstrated higher rates of sensitisation to allergens compared to controls for all of the allergens studied.

Table 4.4 summarises the main characteristics of cases and controls separately for boys and girls. Socio-demographic and lifestyle variables that differed between cases and controls in boys were: birth weight; rates of uneducated mothers; smoking habits of the father;
breastfeeding; taking of paracetamol, none educated mother and antibiotics during the first year of life; taking of paracetamol during 12 months before the study; and the frequency of trucks passing near the child’s home.

In girls, socio-demographic and lifestyle variables that differed between cases and controls were smoking habits of the father; breastfeeding; taking of paracetamol during 12 months before the study; exposure to a cat and to farm animals during the first year of life; exposure to a cat during 12 months before study; type of air conditioning system at home; meat consumption per week; and nut consumption per week.

Boys were characterised by slightly lower birth weight (by 0.1kg) than the respective controls and the difference was statistically significant (95% CI: -0.20, -0.01). There was a higher rate of uneducated mothers among control boys compared to case boys; but the rates of mothers with general education and the rates of mothers with higher education did not differ significantly between cases and controls. Also, the rate of breastfed boys in the control group was higher than the rate in the case group and the difference was statistically significant. The rate of girls who were breastfed did not differ significantly between cases and controls, but the rate of those who were not breastfed was higher in controls than in cases (the difference was statistically significant). Although we were interested in a positive response to breastfeeding, the fact that there was a difference in rates for no breastfeeding made it necessary to consider this variable as a categorical covariate in the multivariate analysis.

There was a statistically significant difference between cases and controls for indoor pollutants, higher rates of smoking fathers were a. Statistically significant differences were also found between cases and controls for girls whose father smoked for example the girls cases were lower than in the controls in the respective controls and the difference was statistically significant. In respect of indoor exposures, differences between cases and controls were observed in respect of the type of air conditioning system used at home. A higher rate of control girls lived in a home with a Freon air conditioning system compared to cases; the difference is statistically significant. However, the rate of girls who lived in a home with a mixed air conditioning system (i.e. both Freon and water) was higher in cases than in controls; the difference in rates is statistically significant. On the contrary, the rates of girl participants who lived in a home with a water air conditioning system or those who lived in a home with an electric fan do not differ significantly between cases and controls.
Concerning potential exposures to outdoor pollutants, a higher rate of boys lived in a neighbourhood with frequent truck-related traffic, compared to the respective controls.

The rate of girls who came into contact with a cat during the first year of their life was higher in cases than in controls and the difference was statistically significant. The rate of girls who came into contact with a cat during a period of 12 months prior to the study was higher in cases than in controls and the difference was statistically significant. Similarly, the rate of girls who came into contact with a farm animal, during the first year of their life, was higher in cases than in controls and the difference was statistically significant.

Additionally, statistically significant differences were observed between girl cases and controls regarding their dietary habits. The rate of girls who never ate meat was higher in the control group than in the case group. On the contrary, the rates for the other two categories of this variable (i.e. once or twice and three or more a week) did not differ significantly between cases and controls.

The rate of girls who never included nuts in their diet was higher in cases than in controls and the difference was statistically significant. On the contrary, the rate of girls who ate nuts once or twice a week was higher in controls than in cases and the difference was statistically significant.

A higher proportion of boy cases received paracetamol during the first year of life compared to the respective controls and the difference was statistically significant. Similarly, the rate of boys receiving antibiotics during the first year of life was higher in cases than in controls and the difference was statistically significant. The rate of boy cases who received paracetamol medication rarely during 12 months before the study (i.e. at least once a year) was higher than in the respective controls and the difference was statistically significant. On the contrary, the rates of boy participants who received paracetamol medication more frequently during the last year before the study (i.e. once a week or once a month) did not differ significantly between cases and controls.

The rate of girls who received paracetamol medication at least once during a period of 12 months prior to the study was higher in controls than in cases and the difference was statistically significant. On the contrary, the rate of girls who received paracetamol more frequently in the 12 months before the study did not differ significantly between cases and controls.
Table 4.3: Main findings on the measurements of obesity, lung function, and sensitisation to allergens in cases and controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases (n = 388)</th>
<th>Controls (n = 388)</th>
<th>Differences for the mean or for rates between cases and controls (95% CI)</th>
<th>Cases (n = 244)</th>
<th>Controls (n = 244)</th>
<th>Differences for the mean or for rates between cases and controls (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measures of obesity</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Primary measures mean (sd)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.0 (3.8)</td>
<td>15.8 (2.5)</td>
<td>1.2 (+0.7, +1.7)*</td>
<td>19.0 (4.4)</td>
<td>15.9 (2.1)</td>
<td>3.1 (+2.5, +3.7)*</td>
</tr>
<tr>
<td><strong>Secondary measures mean (sd)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSFT (mm)</td>
<td>10.5 (4.2)</td>
<td>9.2 (3.3)</td>
<td>1.3 (+0.8, +1.8)*</td>
<td>13.8 (5.3)</td>
<td>10.5 (3.2)</td>
<td>3.3 (+2.6, +4.1)*</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>56.6 (8.8)</td>
<td>53.6 (6.4)</td>
<td>3 (+1.9, +4.0)*</td>
<td>61.0 (10.1)</td>
<td>53.9 (5.8)</td>
<td>7.1 (+5.6, +8.4)*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>26.1 (8.0)</td>
<td>23.9 (5.7)</td>
<td>2.2 (+1.2, +3.2)*</td>
<td>30.4 (9.6)</td>
<td>24.1 (5.4)</td>
<td>6.3 (+4.92, +7.69)*</td>
</tr>
<tr>
<td><strong>Lung function measures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC (Lt) mean (sd)</td>
<td>1.35 (0.36)</td>
<td>1.46 (0.37)</td>
<td>-0.11 (-0.16, -0.06)*</td>
<td>1.17 (0.31)</td>
<td>1.22 (0.30)</td>
<td>-0.05 (-0.10, +0.00)</td>
</tr>
<tr>
<td>FEVI (Lt) mean (sd)</td>
<td>1.15 (0.30)</td>
<td>1.31 (0.34)</td>
<td>-0.16 (-0.21, -0.12)*</td>
<td>0.96 (0.27)</td>
<td>1.08 (0.28)</td>
<td>-0.12 (-0.17, -0.08)*</td>
</tr>
<tr>
<td>PEF (Lt) mean (sd)</td>
<td>2.40 (0.64)</td>
<td>2.72 (0.56)</td>
<td>-0.32 (-0.41, -0.24)*</td>
<td>1.77 (0.76)</td>
<td>2.36 (0.57)</td>
<td>-0.59 (-0.70, -0.47)*</td>
</tr>
<tr>
<td><strong>Sensitisation to allergens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cat</td>
<td>216 (56%)</td>
<td>55 (14%)</td>
<td>42 (+36.0, +48.0)*</td>
<td>166 (68%)</td>
<td>35 (14%)</td>
<td>54 (+46.7, +61.3)*</td>
</tr>
<tr>
<td>Dermatophagoides farinae</td>
<td>99 (25%)</td>
<td>21 (5%)</td>
<td>20 (+15.2, +24.8)*</td>
<td>79 (32%)</td>
<td>6 (2%)</td>
<td>30 (+23.9, +36.1)*</td>
</tr>
<tr>
<td>Dermatophagoides pteronyssinus</td>
<td>99 (25%)</td>
<td>11 (3%)</td>
<td>22 (+17.4, +26.6)*</td>
<td>91 (37%)</td>
<td>16 (6%)</td>
<td>31 (+24.3, +37.8)*</td>
</tr>
<tr>
<td>Grass mix</td>
<td>66 (17%)</td>
<td>14 (4%)</td>
<td>13 (+8.8, +17.2)*</td>
<td>51 (21%)</td>
<td>5 (2%)</td>
<td>19 (+13.6, +24.4)*</td>
</tr>
<tr>
<td>Rye</td>
<td>55 (14%)</td>
<td>15 (4%)</td>
<td>10 (+6.0, +14.0)*</td>
<td>83 (34%)</td>
<td>2 (1%)</td>
<td>33 (+26.9, +39.1)*</td>
</tr>
<tr>
<td>Tree mix (early blossoming)</td>
<td>70 (18%)</td>
<td>13 (3%)</td>
<td>15 (+10.8, +19.2)*</td>
<td>89 (36%)</td>
<td>4 (2%)</td>
<td>32 (+27.7, +40.3)*</td>
</tr>
<tr>
<td>Tree mix (mid blossoming)</td>
<td>80 (21%)</td>
<td>18 (5%)</td>
<td>16 (+11.4, +20.6)*</td>
<td>81 (33%)</td>
<td>3 (1%)</td>
<td>30 (+26.0, +38.0)*</td>
</tr>
<tr>
<td>Weed mix</td>
<td>62 (16%)</td>
<td>10 (3%)</td>
<td>13 (+9.0, +17.0)*</td>
<td>66 (27%)</td>
<td>7 (2%)</td>
<td>20 (+19.2, +30.8)*</td>
</tr>
<tr>
<td>Sensitisation to 1 ≥ allergen</td>
<td>325 (84%)</td>
<td>107 (27%)</td>
<td>57 (+51.3, +62.7)*</td>
<td>234 (96%)</td>
<td>54 (22%)</td>
<td>74 (+68.2, +79.8)*</td>
</tr>
</tbody>
</table>

* Statistically significant difference; namely the null value of zero is not included in the 95% confidence interval
### Table 4.4: Socio-demographic and lifestyle characteristics of cases and controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Boys Cases (n = 388)</th>
<th>Boys Controls (n = 388)</th>
<th>Differences for the mean or for rates between cases and controls (95% CI)</th>
<th>Girls Cases (n = 244)</th>
<th>Girls Controls (n = 244)</th>
<th>Differences for the mean or for rates between cases and controls (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father’s age (years) mean (sd)</td>
<td>43.3 (8.4)</td>
<td>42.1 (7.8)</td>
<td>1.12 (-0.04, +2.28)</td>
<td>44.1 (9.0)</td>
<td>44.8 (8.9)</td>
<td>0.1 (-5.0, +5.2)</td>
</tr>
<tr>
<td>Mother’s age (years) mean (sd)</td>
<td>35 (6.1)</td>
<td>34.6 (6.2)</td>
<td>0.36 (-0.51, +1.23)</td>
<td>36.2 (6.0)</td>
<td>36.1 (6.1)</td>
<td>-0.1 (-4.3, +4.1)</td>
</tr>
<tr>
<td>Birth weight (Kg) mean (sd)</td>
<td>2.90 (0.66)</td>
<td>3.00 (0.58)</td>
<td>-0.10 (-0.20, -0.01)*</td>
<td>2.94 (0.67)</td>
<td>2.83 (0.62)</td>
<td>0.11 (-0.02, +0.24)</td>
</tr>
<tr>
<td>Father’s education (highest qualification) n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>14 (3.7%)</td>
<td>21 (5.6%)</td>
<td>-1.9 (-4.9, +1.1)</td>
<td>22 (9.4%)</td>
<td>14 (5.9%)</td>
<td>3.5 (-1.2, +8.2)</td>
</tr>
<tr>
<td>General education</td>
<td>192 (50.8%)</td>
<td>198 (53.2%)</td>
<td>-2.4 (-1.0, +4.0)</td>
<td>132 (56.2%)</td>
<td>156 (65.3%)</td>
<td>-9.1 (-8.9, +8.7)</td>
</tr>
<tr>
<td>Higher education</td>
<td>172 (45.5%)</td>
<td>153 (41.1%)</td>
<td>4.4 (-3.0, +11.0)</td>
<td>81 (34.5%)</td>
<td>69 (28.9%)</td>
<td>5.6 (-2.6, +13.6)</td>
</tr>
<tr>
<td>Mother’s education (highest qualification) n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>14 (3.7%)</td>
<td>32 (8.3%)</td>
<td>-4.6 (-7.9, -1.3)*</td>
<td>26 (10.9%)</td>
<td>29 (12.0%)</td>
<td>-1.1 (-6.7, +4.5)</td>
</tr>
<tr>
<td>General education</td>
<td>208 (54.5%)</td>
<td>205 (53.4%)</td>
<td>1.1 (-5.9, +8.1)</td>
<td>141 (59.0%)</td>
<td>144 (59.8%)</td>
<td>-0.8 (-9.5, +7.9)</td>
</tr>
<tr>
<td>Higher education</td>
<td>160 (41.9%)</td>
<td>147 (38.3%)</td>
<td>3.6 (-3.3, +10.5)</td>
<td>72 (30.1%)</td>
<td>68 (28.2%)</td>
<td>1.9 (-6.2, +10)</td>
</tr>
<tr>
<td>Father smoker n (%)</td>
<td>129 (33.3%)</td>
<td>96 (24.8%)</td>
<td>8.5 (+2.1, +14.9)*</td>
<td>56 (23.1%)</td>
<td>77 (31.8%)</td>
<td>-8.7 (-16.6, -0.8)</td>
</tr>
<tr>
<td>No</td>
<td>258 (66.7%)</td>
<td>291 (75.2%)</td>
<td>-8.5 (-14.9, -2.1)*</td>
<td>186 (76.9%)</td>
<td>168 (68.2%)</td>
<td>8.7 (+0.8, +16.6)*</td>
</tr>
<tr>
<td>Mother smoker n (%)</td>
<td>5 (1.3%)</td>
<td>1 (0.3%)</td>
<td>1.0 (-0.25, +2.25)</td>
<td>4 (1.7%)</td>
<td>2 (0.8%)</td>
<td>0.9 (-1.1, +2.9)</td>
</tr>
<tr>
<td>No</td>
<td>382 (98.7%)</td>
<td>385 (99.7%)</td>
<td>-1.0 (-2.3, +0.3)</td>
<td>236 (98.3%)</td>
<td>241 (99.2%)</td>
<td>-0.9 (-2.9, +1.1)</td>
</tr>
<tr>
<td>Birth order n (%)</td>
<td>206 (53.4%)</td>
<td>206 (53.1%)</td>
<td>0.3 (-6.7, +7.3)</td>
<td>43 (17.8%)</td>
<td>47 (19.5%)</td>
<td>-1.7 (-8.6, +5.2)</td>
</tr>
<tr>
<td>First child</td>
<td>125 (32.4%)</td>
<td>123 (31.7%)</td>
<td>0.7 (-5.9, +7.3)</td>
<td>189 (78.1%)</td>
<td>180 (74.7%)</td>
<td>3.4 (-4.1, +10.9)</td>
</tr>
<tr>
<td>Second child</td>
<td>55 (14.2%)</td>
<td>56 (15.2%)</td>
<td>-1.0 (-6.0, +4.0)</td>
<td>10 (4.1%)</td>
<td>14 (5.8%)</td>
<td>-1.7 (-5.5, +2.1)</td>
</tr>
<tr>
<td>Third or greater</td>
<td></td>
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</tr>
<tr>
<td>Was the child born in Madinah? n (%)</td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>332 (85.8%)</td>
<td>328 (85.4%)</td>
<td>0.4 (-4.5, +5.3)</td>
<td>202 (84.5%)</td>
<td>200 (82.6%)</td>
<td>1.9 (-4.7, +8.5)</td>
</tr>
<tr>
<td>No</td>
<td>55 (14.2%)</td>
<td>56 (14.6%)</td>
<td>-0.4 (-5.3, +4.5)</td>
<td>37 (15.5%)</td>
<td>42 (17.4%)</td>
<td>-1.9 (-8.5, +4.7)</td>
</tr>
<tr>
<td>Did the mother breastfeed? n (%)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>290 (74.4%)</td>
<td>330 (85.1%)</td>
<td>-9.6 (-15.1, -4.1)*</td>
<td>208 (86.7%)</td>
<td>193 (80.1%)</td>
<td>6.6 (0.0, +13.0)</td>
</tr>
<tr>
<td>No</td>
<td>92 (23.7%)</td>
<td>56 (14.4%)</td>
<td>8.5 (+2.1, +14.9)*</td>
<td>32 (13.3%)</td>
<td>48 (19.9%)</td>
<td>-8.7 (-16.6, -0.8)*</td>
</tr>
<tr>
<td>Paracetamol in the 1st year of child’s life n (%)</td>
<td>367 (95.6%)</td>
<td>329 (88.4%)</td>
<td>7.2 (+3.4, +11.0)*</td>
<td>213 (89.9%)</td>
<td>209 (87.4%)</td>
<td>2.5 (-3.1, +8.1)</td>
</tr>
<tr>
<td>Antibiotics in the 1st year of child’s life n (%)</td>
<td>311 (80.2%)</td>
<td>213 (54.9%)</td>
<td>24.4 (+18.2, +30.6)*</td>
<td>164 (69.5%)</td>
<td>148 (61.7%)</td>
<td>7.8 (-0.6, +16.2)</td>
</tr>
<tr>
<td>Paracetamol administration in the last 12 months n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Once a week at least</td>
<td>87 (22.9%)</td>
<td>70 (18.9%)</td>
<td>4.0 (-1.7, +9.7)</td>
<td>54 (22.9%)</td>
<td>39 (16.9%)</td>
<td>6.0 (-1.1, +13.1)</td>
</tr>
<tr>
<td>Once a month at least</td>
<td>220 (57.9%)</td>
<td>195 (52.7%)</td>
<td>5.2 (-1.8, +12.2)</td>
<td>135 (57.2%)</td>
<td>125 (54.1%)</td>
<td>3.1 (-5.7, +11.9)</td>
</tr>
<tr>
<td>Once a year at least</td>
<td>73 (19.2%)</td>
<td>105 (28.4%)</td>
<td>-9.2 (-15.2, -3.2)*</td>
<td>47 (19.9%)</td>
<td>67 (29.0%)</td>
<td>-9.1 (-16.7, -1.5)*</td>
</tr>
<tr>
<td>Exposure to animals n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure of mother to a farm animal while pregnant</td>
<td>11 (2.9%)</td>
<td>11 (2.9%)</td>
<td>0.0 (-2.4, +2.4)</td>
<td>14 (6.1%)</td>
<td>8 (3.4%)</td>
<td>2.7 (-1.1, +6.5)</td>
</tr>
<tr>
<td>Cat at home at 1st year of child’s life</td>
<td>15 (3.9%)</td>
<td>15 (3.9%)</td>
<td>0.0 (-2.7, +2.7)</td>
<td>19 (7.9%)</td>
<td>6 (2.5%)</td>
<td>5.4 (+1.5, +9.3)*</td>
</tr>
<tr>
<td>Cat at home in the last 12 months</td>
<td>29 (7.5%)</td>
<td>25 (6.5%)</td>
<td>1.0 (-2.6, +4.6)</td>
<td>18 (7.5%)</td>
<td>12 (5.0%)</td>
<td>2.5 (+1.2, +8.8)*</td>
</tr>
<tr>
<td>Farm animal at 1st year of child’s life</td>
<td>24 (6.2%)</td>
<td>16 (4.2%)</td>
<td>2.0 (-1.1, +5.1)</td>
<td>16 (6.8%)</td>
<td>5 (2.1%)</td>
<td>4.7 (+1.1, +8.3)*</td>
</tr>
<tr>
<td>Taking exercise per week n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>241 (64.3%)</td>
<td>254 (68.8%)</td>
<td>-4.5 (-11.1, +2.1)</td>
<td>201 (85.5%)</td>
<td>200 (86.2%)</td>
<td>-0.7 (-6.9, +5.5)</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>101 (26.9%)</td>
<td>86 (23.3%)</td>
<td>3.6 (-2.5, +9.7)</td>
<td>31 (13.2%)</td>
<td>25 (10.8%)</td>
<td>2.4 (-3.4, +8.2)</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>33 (8.8%)</td>
<td>29 (7.9%)</td>
<td>0.9 (-3.0, +4.8)</td>
<td>3 (1.3%)</td>
<td>7 (3.0%)</td>
<td>-1.7 (-4.3, +0.9)</td>
</tr>
<tr>
<td>Watching TV n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 hours per day</td>
<td>228 (60.0%)</td>
<td>241 (64.6%)</td>
<td>-4.6 (-11.4, +2.2)</td>
<td>137 (56.8%)</td>
<td>128 (54.9%)</td>
<td>1.9 (-6.9, +10.7)</td>
</tr>
<tr>
<td>&gt; 3 hours per day</td>
<td>152 (40.0%)</td>
<td>132 (35.4%)</td>
<td>4.6 (-2.2, +11.4)</td>
<td>104 (43.2%)</td>
<td>105 (45.1%)</td>
<td>-1.9 (-10.7, +6.9)</td>
</tr>
<tr>
<td>What is the fuel normally used in cooking in your household? n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electricity only</td>
<td>20 (5.2%)</td>
<td>20 (5.2%)</td>
<td>0 (-3.1, +3.1)</td>
<td>9 (3.8%)</td>
<td>15 (6.3%)</td>
<td>-2.5 (-6.4, +1.4)</td>
</tr>
<tr>
<td>Gas only</td>
<td>351 (90.9%)</td>
<td>349 (90.4%)</td>
<td>0.5 (-3.6, +4.6)</td>
<td>223 (92.9%)</td>
<td>220 (92.4%)</td>
<td>0.5 (-4.1, +5.1)</td>
</tr>
<tr>
<td>Both electricity &amp; gas</td>
<td>15 (3.9%)</td>
<td>17 (4.4%)</td>
<td>-0.5 (-3.3, +2.3)</td>
<td>8 (3.3%)</td>
<td>3 (1.3%)</td>
<td>2.0 (-0.7, +4.7)</td>
</tr>
<tr>
<td>Air conditioning type n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electric fan only</td>
<td>3 (0.8%)</td>
<td>1 (0.3%)</td>
<td>0.5 (-0.54, +1.54)</td>
<td>1 (0.4%)</td>
<td>2 (0.8%)</td>
<td>-0.4 (-1.77, +0.97)</td>
</tr>
<tr>
<td>Water system only</td>
<td>4 (1.0%)</td>
<td>5 (1.3%)</td>
<td>-0.3 (-1.8, +1.2)</td>
<td>4 (1.7%)</td>
<td>10 (4.1%)</td>
<td>-2.4 (-5.4, +0.6)</td>
</tr>
<tr>
<td>Freon system only</td>
<td>365 (94.3%)</td>
<td>372 (96.6%)</td>
<td>-2.3 (-5.2, +0.6)</td>
<td>194 (82.2%)</td>
<td>223 (92.5%)</td>
<td>-10.3 (-16.1, -4.5)*</td>
</tr>
</tbody>
</table>
## Freon & water systems

<table>
<thead>
<tr>
<th></th>
<th>15 (3.9%)</th>
<th>7 (1.8%)</th>
<th>2.1 (-0.2, +4.4)</th>
<th>37 (15.7%)</th>
<th>6 (2.5%)</th>
<th>13.2 (+8.2, +18.2)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rarely</td>
<td>237 (61.6%)</td>
<td>268 (70.9%)</td>
<td>-9.3 (-15.9, -2.7)*</td>
<td>168 (70.3%)</td>
<td>169 (70.7%)</td>
<td>-0.4 (-8.5, +7.7)</td>
</tr>
<tr>
<td>Frequently</td>
<td>148 (38.4%)</td>
<td>110 (29.1%)</td>
<td>9.3 (+2.7, +15.9)*</td>
<td>71 (29.7%)</td>
<td>70 (29.3%)</td>
<td>0.4 (-7.7, +8.5)</td>
</tr>
</tbody>
</table>

## How often does a truck pass through the street adjacent to your home? n (%)

- **Rarely**: 237 (61.6%) - 268 (70.9%) -9.3 (-15.9, -2.7)*
- **Frequently**: 148 (38.4%) - 110 (29.1%) 9.3 (+2.7, +15.9)*

## Diet - How many times a week does your child eat the following? n (%)

### Meats

<table>
<thead>
<tr>
<th></th>
<th>20 (5.2%)</th>
<th>16 (4.2%)</th>
<th>1.0 (-4.0, +2.0)</th>
<th>9 (3.7%)</th>
<th>26 (10.9%)</th>
<th>-7.2 (-11.8, -2.6)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>207 (54.4%)</td>
<td>227 (60.7%)</td>
<td>-1.3 (-8.2, +5.6)</td>
<td>186 (78.2%)</td>
<td>182 (76.2%)</td>
<td>2.0 (-5.4, +9.4)</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>134 (35.5%)</td>
<td>118 (31.6%)</td>
<td>3.9 (-2.7, +10.5)</td>
<td>73 (30.4%)</td>
<td>93 (40.1%)</td>
<td>-9.7 (-18.1, +1.3)*</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>19 (5.0%)</td>
<td>29 (7.8%)</td>
<td>-2.8 (-6.2, +0.6)</td>
<td>16 (6.7%)</td>
<td>23 (9.9%)</td>
<td>-3.2 (-8.1, +1.7)</td>
</tr>
</tbody>
</table>

### Fruits

<table>
<thead>
<tr>
<th></th>
<th>68 (17.7%)</th>
<th>44 (11.5%)</th>
<th>6.2 (-6.9, +19.3)</th>
<th>29 (12.0%)</th>
<th>24 (10.0%)</th>
<th>2.0 (-3.5, +7.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>207 (54.4%)</td>
<td>227 (60.7%)</td>
<td>-1.3 (-8.2, +5.6)</td>
<td>186 (78.2%)</td>
<td>182 (76.2%)</td>
<td>2.0 (-5.4, +9.4)</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>134 (35.5%)</td>
<td>118 (31.6%)</td>
<td>3.9 (-2.7, +10.5)</td>
<td>73 (30.4%)</td>
<td>93 (40.1%)</td>
<td>-9.7 (-18.1, +1.3)*</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>19 (5.0%)</td>
<td>29 (7.8%)</td>
<td>-2.8 (-6.2, +0.6)</td>
<td>16 (6.7%)</td>
<td>23 (9.9%)</td>
<td>-3.2 (-8.1, +1.7)</td>
</tr>
</tbody>
</table>

### Rice

<table>
<thead>
<tr>
<th></th>
<th>20 (5.2%)</th>
<th>16 (4.2%)</th>
<th>1.0 (-4.0, +2.0)</th>
<th>9 (3.7%)</th>
<th>26 (10.9%)</th>
<th>-7.2 (-11.8, -2.6)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>207 (54.4%)</td>
<td>227 (60.7%)</td>
<td>-1.3 (-8.2, +5.6)</td>
<td>186 (78.2%)</td>
<td>182 (76.2%)</td>
<td>2.0 (-5.4, +9.4)</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>134 (35.5%)</td>
<td>118 (31.6%)</td>
<td>3.9 (-2.7, +10.5)</td>
<td>73 (30.4%)</td>
<td>93 (40.1%)</td>
<td>-9.7 (-18.1, +1.3)*</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>19 (5.0%)</td>
<td>29 (7.8%)</td>
<td>-2.8 (-6.2, +0.6)</td>
<td>16 (6.7%)</td>
<td>23 (9.9%)</td>
<td>-3.2 (-8.1, +1.7)</td>
</tr>
</tbody>
</table>

### Nuts

<table>
<thead>
<tr>
<th></th>
<th>224 (59.4%)</th>
<th>227 (60.7%)</th>
<th>-1.3 (-8.2, +5.6)</th>
<th>151 (62.9%)</th>
<th>116 (50.0%)</th>
<th>12.9 (+4.2, +21.6)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>207 (54.4%)</td>
<td>227 (60.7%)</td>
<td>-1.3 (-8.2, +5.6)</td>
<td>151 (62.9%)</td>
<td>116 (50.0%)</td>
<td>12.9 (+4.2, +21.6)*</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>134 (35.5%)</td>
<td>118 (31.6%)</td>
<td>3.9 (-2.7, +10.5)</td>
<td>73 (30.4%)</td>
<td>93 (40.1%)</td>
<td>-9.7 (-18.1, +1.3)*</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>19 (5.0%)</td>
<td>29 (7.8%)</td>
<td>-2.8 (-6.2, +0.6)</td>
<td>16 (6.7%)</td>
<td>23 (9.9%)</td>
<td>-3.2 (-8.1, +1.7)</td>
</tr>
</tbody>
</table>

### Fast food

<table>
<thead>
<tr>
<th></th>
<th>217 (56.7%)</th>
<th>225 (59.2%)</th>
<th>-2.5 (-9.4, +4.4)</th>
<th>160 (67.5%)</th>
<th>164 (69.8%)</th>
<th>-2.3 (-10.5, +5.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>207 (54.4%)</td>
<td>227 (60.7%)</td>
<td>-1.3 (-8.2, +5.6)</td>
<td>186 (78.2%)</td>
<td>182 (76.2%)</td>
<td>2.0 (-5.4, +9.4)</td>
</tr>
<tr>
<td>Once or twice a week</td>
<td>134 (35.5%)</td>
<td>118 (31.6%)</td>
<td>3.9 (-2.7, +10.5)</td>
<td>73 (30.4%)</td>
<td>93 (40.1%)</td>
<td>-9.7 (-18.1, +1.3)*</td>
</tr>
<tr>
<td>Three or more a week</td>
<td>19 (5.0%)</td>
<td>29 (7.8%)</td>
<td>-2.8 (-6.2, +0.6)</td>
<td>16 (6.7%)</td>
<td>23 (9.9%)</td>
<td>-3.2 (-8.1, +1.7)</td>
</tr>
</tbody>
</table>

* Statistically significant difference; namely the null value of zero is not included in the 95% confidence interval
4.5.2 Univariate analysis

Table 4.5 shows the unadjusted effect of each of the obesity measures on the risk of having asthma in boys and in girls. All four obesity measures were found to be positively associated with asthma in both boys and girls. The ORs in girls were higher than those in boys.

Table 4.5: Univariate association of obesity measures with the risk of having asthma

<table>
<thead>
<tr>
<th>Measures of obesity</th>
<th>Multiplicative increase in odds of having asthma (95% CI) per unit increase of the independent variable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
</tr>
<tr>
<td>Primary measure</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.14 (1.08, 1.20)</td>
</tr>
<tr>
<td>Secondary measures</td>
<td></td>
</tr>
<tr>
<td>TSFT (mm)</td>
<td>1.10 (1.06, 1.15)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>1.06 (1.04, 1.08)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>1.06 (1.03, 1.08)</td>
</tr>
</tbody>
</table>

The OR of BMI in boys is 1.14 (95% CI: 1.08, 1.20). This means that an increase in BMI by 1kg/m² was associated with an increase in the risk for asthma by 1.14 times on average. The OR of BMI in girls is 1.37 (95% CI: 1.26, 1.50). This means that an increase in BMI by 1kg/m² was associated with an increase in the risk of asthma by 1.37 times on average.

4.5.3 Multivariate analysis

Table 4.6 shows the effect of BMI on the risk of asthma, in boys and girls, adjusted for socio-demographic and lifestyle variables, based on a multiple conditional logistic regression analysis by using variables which showed univariate association with asthma; such variables were included in each model and are displayed on the table. After adjustment for covariates, BMI still remained a positive predictor of asthma, both in boys and in girls. The adjusted OR of BMI was found to be higher in girls than in boys.

The adjusted OR of BMI in boys was 1.11 (95% CI: 1.03, 1.19). This means that an increase in BMI by 1kg/m² was associated with an increase in the odds of having asthma by 1.11
times on average. This result was adjusted for all those factors in (Table 4.6) that differed significantly between cases and controls in boys (denoted with an asterisk in Table 4.4).

Among the above factors, the ones which seemed to have an effect on the risk of asthma in boys (i.e. those which remained in the final model after a stepwise elimination process and those that gave statistically significant results) are: administration of antibiotics during the first of year of life; and administration of paracetamol during 12 months prior the study.

Boys who were given antibiotics in the first year of their life were 2.45 times at greater odds to be reported with asthma than those who were not. Likewise, boys who had been given paracetamol medication during 12 months prior to the study were 1.90 times at greater odds to be reported with asthma than those who had not.

The adjusted OR of BMI in girls was 1.38 (95% CI: 1.23, 1.56). This means that an increase in BMI by one kg/m^2 was associated with an increase in the odds of having asthma by 1.38 times on average. Once again, this result was adjusted for all those factors in Table 4.4 (denoted with an asterisk) that differed significantly between cases and controls in girls.

Among the above factors, those that seem to have an effect on the risk of asthma in girls are: father being a smoker; being breastfed; paracetamol administered during 12 months prior to the study; air conditioning type used at home; and frequency of meat consumption per week.

Girls whose fathers smoked were less likely to be reported with asthma compared to those whose fathers did not smoke (OR = 0.45; 95% CI: 0.22, 0.93).

Girls who were breastfed were found to be more likely to be reported with asthma by 3.62 times on average (95% CI: 1.42, 9.25). However this relationship in boys was non-significant (OR = 0.74, 95% CI: 0.44, 1.26). Our data supports the findings from a study where 4 weeks or longer of breastfeeding reduced the number of wheezing episodes and shortness of breath in boys by 19% and 15% respectively, but not in girls.(232) The research team suggested that gender is an effect modifier in the relationship between breastfeeding and asthma-like symptoms.(232)

Girls who were administered paracetamol medication once a week within the last 12 months prior to the study were found more likely to be reported with asthma than those who were administered rarely, by 7.09 times on average (95% CI: 2.48, 20.80). Likewise, girls who were administered paracetamol once a month, within the last 12 months prior to the study,
were found more likely to be reported with asthma than those who were administered rarely, by 2.23 times on average (95% CI: 1.05, 4.72). From both of the above results, paracetamol intake is associated with a positive risk of having asthma and the more frequent the dose, the higher the risk. Recent studies investigating the relationship between paracetamol intake in pregnancy and wheezing or asthma in early childhood also suggest that frequent use of paracetamol in late pregnancy may increase the risk of wheezing in infants.(233-235)

Girls who lived in a home with a mixed Freon-water air conditioning system, were found more likely to be reported with asthma, compared to those living in a home with a pure Freon system, by 19.4 times on average (95% CI: 3.56, 106).

Girls who included meat meals in their diet once or twice a week compared with those who never ate meat, were more likely to be reported with asthma, by 10.2 times on average (95% CI: 2.03, 51.20). Likewise, girls who included meat meals in their diet three or more times a week were more likely to be reported with asthma than those who never ate meat by 8.68 times on average (95% CI: 1.83, 41.00). The above results suggest that meat consumption is associated with the risk of having asthma, but a dose-response relationship may be suggested.
Table 4.6: Adjusted association of BMI with the risk of having asthma based on a multiple conditional logistic regression analysis

<table>
<thead>
<tr>
<th>Independent (X) variables in the multiple conditional logistic regression model#</th>
<th>ORs of developing asthma (95% CI) adjusted for other factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
</tr>
<tr>
<td>BMI</td>
<td>1.11 (1.03, 1.19)</td>
</tr>
<tr>
<td>Birth-weight</td>
<td>0.71 (0.49, 1.02)</td>
</tr>
<tr>
<td>Mother education (none compared to higher)</td>
<td>0.48 (0.16, 1.44)</td>
</tr>
<tr>
<td>Mother education (general compared to higher)</td>
<td>0.82 (0.51, 1.32)</td>
</tr>
<tr>
<td>Father smoking</td>
<td></td>
</tr>
<tr>
<td>Breastfed</td>
<td>1.17 (0.76, 1.80)</td>
</tr>
<tr>
<td>Paracetamol given in the 1st year of child’s life</td>
<td>0.74 (0.44, 1.26)</td>
</tr>
<tr>
<td>Antibiotics given in the 1st year of child’s life</td>
<td>1.66 (0.67, 4.09)</td>
</tr>
<tr>
<td>Paracetamol given to the child in the last 12 months (once a week compared to yearly)</td>
<td>2.45 (1.54, 3.91)</td>
</tr>
<tr>
<td>Paracetamol given to the child in the last 12 months (once a month compared to yearly)</td>
<td>1.94 (1.00, 3.80)</td>
</tr>
<tr>
<td>Cat at home 1st year of child’s life</td>
<td>1.90 (1.14, 3.14)</td>
</tr>
<tr>
<td>Cat at home in the last 12 months</td>
<td>*</td>
</tr>
<tr>
<td>Farm animal 1st year of child’s life</td>
<td>*</td>
</tr>
<tr>
<td>Air conditioning type used at home (Electric fan compared to Freon system)</td>
<td>*</td>
</tr>
<tr>
<td>Air conditioning type used at home (Water system compared to Freon system)</td>
<td>*</td>
</tr>
<tr>
<td>Air conditioning type used at home (Both Freon and water system compared to Freon system)</td>
<td>*</td>
</tr>
<tr>
<td>How frequently trucks pass near child’s house (frequently compared to rarely)</td>
<td>19.4 (3.56, 10.60)</td>
</tr>
<tr>
<td>Eating meat (once or twice a week compared to never)</td>
<td>*</td>
</tr>
<tr>
<td>Eating meat (three times a week or more compared to never)</td>
<td>*</td>
</tr>
<tr>
<td>Eating nuts (once or twice a week compared to never)</td>
<td>*</td>
</tr>
<tr>
<td>Eating nuts (three times a week or more compared to never)</td>
<td>*</td>
</tr>
</tbody>
</table>

# Only those variables which remained into the model in the last step of the backward stepwise regression process are displayed in table

* Not in the model for boys  ** Not in the model for girls
4.5.4 Investigating possible causal pathways in association between obesity and asthma

Table 4.7 shows the impact of factoring measures of respiratory obstruction and this reveals a possible impact on the associations between BMI and asthma in boys and girls. Table 4.7 also reveals the impact of factoring the presence of allergic sensitisation into the analysis and this in contrast shows a more marked reduction in the associations in girls, although a much more modest impact in boys.

The top row of Table 4.6 highlights the association between BMI and asthma after adjustment for other factors also found to be associated with obesity. This result is shown again as the top row of Table 4.7, and below this are shown the results for BMI when the analysis also adjusts for selected lung function and/or sensitisation measurements in addition to the other potential risk factors. The aim of these analyses was to investigate how much the coefficient of BMI changed when these measurements were taken into account, and Table 4.7 shows that adjusting for FEV1 or FVC made little difference to the coefficient of BMI, whereas adjusting for sensitisation reduced this coefficient, especially in girls, to a point where it was no longer significant. Thus at least some of the association between obesity and asthma may be explained by an increased risk of allergic sensitisation lying on the causal pathway, whereas this does not appear to be the case with impairment of lung function.

There was – in both genders – strong evidence, that children with asthma had greater respiratory obstruction and were more sensitised to aeroallergens in comparison to those with no history of asthma.

Thus, obesity may lead to sensitisation or obstructive lung impairments; however, both sensitisation and obstruction may lead to asthma. These predictors cannot be treated as confounders as the association between sensitisation or impaired lung function and asthma may be possible causal pathways in this complex relationship.

Overall, the association between impaired lung function and asthma in boys and girls in our cohort persists and it suggests that this link is unlikely to be on the possible causal pathway. However, the effect of obesity on asthma was attenuated – and indeed almost disappeared – when allergic sensitisation was considered in the analysis, suggesting allergic sensitisation is a much stronger predictor of asthma than obesity.
Table 4.7: Estimates (95% CIs) for the coefficient of BMI in conditional logistic regression analysis adjusted for selected lung function and sensitisation and also for other factors found to be associated with obesity in Table 4.3

<table>
<thead>
<tr>
<th>Lung and sensitisation factors</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.11 (1.03, 1.19)</td>
<td>1.38 (1.23, 1.56)</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.10 (1.02, 1.18)</td>
<td>1.37 (1.22, 1.54)</td>
</tr>
<tr>
<td>FVC</td>
<td>1.11 (1.03, 1.19)</td>
<td>1.40 (1.24, 1.57)</td>
</tr>
<tr>
<td>Sensitisation to more than one allergen</td>
<td>1.09 (0.99, 1.19)</td>
<td>1.25 (0.96, 1.60)</td>
</tr>
<tr>
<td>FEV1 + sensitisation to more than one allergen</td>
<td>1.09 (0.98, 1.19)</td>
<td>1.28 (0.96, 1.69)</td>
</tr>
<tr>
<td>FVC + sensitisation to more than one allergen</td>
<td>1.09 (0.99, 1.19)</td>
<td>1.25 (0.97, 1.61)</td>
</tr>
</tbody>
</table>
4.6 Discussion

4.6.1 Main findings

This large matched case-control study has demonstrated associations between measures of obesity and asthma in both boys and girls. This association is clearly stronger in girls than in boys; it is also maintained, after adjusting for a range of lifestyle and socio-demographic confounders. Incorporating lung function into the regression models had a very modest impact, virtually no difference, and leading to the notion that respiratory obstruction is unlikely to be an important factor in the cause-effect relationship.

Incorporating allergic sensitisation to one or more allergen in the logistic regression attenuated the association and resulted in a loss of significance of the association between BMI and asthma in both boys and girls suggesting that sensitisation may be on the causal pathway and a partial predictor factor in the obesity-asthma causal relationship in both boys and girls.

Overall, this study therefore adds to the increasing body of evidence implicating obesity as a risk factor for the development of asthma showing that this relationship also holds true in a Middle Eastern-origin population and provides important pointers into how this relationship may or may not be mediated in this population.

4.6.2 Strengths and limitations of this work

Key strengths of this study include the large and adequately powered study; the use of a validated and extensively used questionnaire to identify cases and controls; careful measurements of a range of measures of obesity by trained personnel who were blinded to case status; the measurement of and adjustment for a range of potential confounders; and the a priori decision to undertake separate analyses in boys and girls. We in addition sought to extend previous work by shedding light on the possible role of key causal mechanisms.(16)

The main limitations of this work were those inherent to case control studies, especially those with prevalent cases and controls, namely the risk of residual confounding, recall bias, and an inability to establish a temporal relationship between the onset of obesity and the subsequent development of asthma; reverse causality therefore remains a possibility.(236, 237)
Moreover, the identification of cases was based only on parental symptoms reports according to a questionnaire and not to full medical diagnosis; thus, although a validated culturally appropriate questionnaire was used, there remains the possibility of misclassification errors. If present, these are however likely to have operated non-differentially, which would have, if anything, been prone to attenuate the relationship between obesity rather than introduce spurious associations.(238)

In the Arabic language, there are a number of words that describe the meaning of wheezy chest. Among these words are humming, roar and whizz as stated by the Department of Arabic Language in Madinah, Ministry of Education, who revised the Arabic-translated version of the ISAAC questionnaire. This questionnaire has been previously used in an Arabic country ‘Oman’. (239) These terms were discussed with the members of the research teams who suggested that the term ‘wheeze’ would be easily understood by parents. This is because in the Arabic language, we have also the exact word “wheeze”, and it is widely understood by general public, so parents should not have any problems in recognising and reporting of “wheezing” symptoms in children. Again, this has been confirmed by parents during the pilot study. We have the word “wheeze”, so parents will not have any problems in the recognitions and reporting of “wheeze” in children.

Recall bias and misclassification errors may however be a limitation of the ISAAC questionnaires and the choice of question I relied upon in order to establish case status. Thus, some children with transient viral associated wheeze (VAW) phenotype may have been identified. Accurate differentiation between these phenotypes was however difficult to achieve within the constraints of the study.(240) In subsequent work, I hope to investigate this issue further by undertaking a sensitivity analysis on the subset of ‘cases’ who also had corresponding lung function test results indicating a picture of asthma.

Another result that may have been affected by recall bias is that girls whose fathers smoked were less likely to be reported with asthma compared to those whose fathers did not smoke. These findings could be explained by recall bias or chance or confounding. Another study from the Kingdom of Saudi Arabia found significant associations between paternal smoking and asthma (P < 0.001) and these data are therefore more consistent with the existing literature.(241)
Finally, there are substantial shortcomings in the handling of bias, confounding and effect modification in case-control, cross-sectional and other observational studies investigating associations between other risk factors and the development of asthma in children. Some of the questions in the questionnaire included the aspect of subjectivity in the answers; for example, in the question about the frequency of trucks passing by near home (aiming to estimate environmental exposure to airborne particles) the possible answers were rarely and frequently.

4.6.3 Considering the findings from this study in the context of the wider literature

Our study is consistent with an increasing number of epidemiological studies that have reported a positive association between obesity and the risk of developing childhood asthma.(29-31, 138) However, the observed association refers to reported symptoms indicative of asthma and not to a clinically diagnosed disease. Wheeze and cough are non-specific symptoms, which may be attributed to a number of different causes, including asthma. A similar study in Australian children reported an association between obesity and symptoms of wheeze and cough, but not with diagnosed asthma.(242)

We have found that the association between obesity and asthma was stronger in girls than in boys. This has been observed in other studies as well,(138, 224) although some review studies conclude that evidence is conflicting as to whether gender affects the development of asthma in obese children.(243) It is suggested that obesity is generally found to be more consistently associated with asthma in women than men and this may be explained by a possible influence of sex hormones.(26, 244, 245) It is not clear whether the effect of sex hormones – if any – also plays a role in younger girls. Whether the gender difference observed in the present study is simply due to the higher levels of obesity found in girls (Table 4.3) or is due to differences in body fat distribution and/or associated biochemical responses is unclear.(224, 236)

A cross-sectional study of children aged 6-7 years in Spain reported a small protective effect of Mediterranean diet, seafood, and cereals for current severe asthma and that fast food intake is a risk factor for current severe asthma.(243) In the present study meat intake in girls was found to increase the odds of asthma by 8-10 times. If diet is indeed a risk factor for asthma
in children, the association found between obesity and asthma in our study is adjusted for this factor due to use of multiple regression analysis.

A wide number of studies suggest that atopic sensitisation is a strong risk factor for asthma,(26, 161, 244, 246, 247) something which is confirmed from the findings of the present study. Whether obesity is involved in the association between atopic sensitisation on asthma now needs to be further explored. Some studies report a positive association between obesity and atopy.(242, 246) If obesity is a causal factor of atopy and, in turn, atopy is a causal factor of asthma, then any association between obesity and asthma may be explained by this chain of events. On the other hand, some studies conclude that the association between obesity and asthma is stronger in non-atopic than in atopic individuals,(248, 249) which suggests that in the association between obesity and asthma, atopy may not be involved so extensively. Our investigation of key causal pathways provides some evidence to suggest that this relationship may indeed be causal, this being partially mediated through increased allergic sensitisation.

4.6.4 Implications for policy, practice and future research

The findings of the present study may be valuable for public health authorities of Saudi Arabia as it provides additional evidence of the considerable adverse risks associated with obesity. Although causality cannot be proven by this or indeed any other epidemiological investigation, the findings from this work, when combined with an increasing number of studies worldwide, provide increasing evidence of a causal relationship between obesity and asthma.

4.7 Conclusions

In conclusion, our large matched case-control study provides the first evidence demonstrating a modest association between obesity and asthma in Saudi boys and girls. Our investigation of key causal pathways suggests that this relationship may indeed be causal, this being partially mediated through increased allergic sensitisation. The study has also demonstrated a potential implication of frequent use of paracetamol in the risk of symptoms suggestive of asthma in both boys and girls, as well as a potential implication of antibiotics intake during
the first year of life. The use of certain drugs as risk factors of childhood asthma is outwith the scope of this thesis and it is not further discussed; however, the results in the present study may generate hypotheses for further epidemiological studies.

### 4.8 Chapter summary

Previous studies have demonstrated a positive association between obesity and asthma; however, it still remains unclear whether this association is causal. The available theory has suggested five main possible patho-physiological mechanisms, which may explain the association between obesity and asthma. Among these mechanisms, a direct effect on respiratory mechanics and immunological changes - due to allergic sensitisation – were particularly plausible.

This chapter has described a matched case-control study investigating the relationship between childhood obesity and asthma in a sample of 1264 school-aged children in Madinah, Saudi Arabia. A sample of 632 children, aged 6-8 years, with a history of symptoms of asthma as detected by the validated ISAAC questionnaire were matched with age- and sex-matched controls (i.e. with no reports of previous symptoms of asthma). Data on socio-demographic characteristics and lifestyle factors were collected through the ISAAC questionnaire, appropriately modified for Arabic populations. All children had their BMIs measured, and spirometry and SPTs were undertaken.

Multiple conditional logistic regression analysis was performed to investigate the relationship between obesity and asthma, as well as between asthma and lung function measures and between asthma and sensitisation to allergens, adjusted for covariates. Univariate analysis showed that all obesity measures considered (i.e. BMI, weight, WC, and TSFT) were found to be positively associated with asthma in both boys and girls. The ORs found for girls were higher than those for boys.

After adjusting for a number of lifestyle variables – as possible confounders in a multivariate analysis – BMI still remained a significant predictor of the occurrence of asthma both in boys and girls. Again, higher ORs were found for girls.

BMI remained a significant positive predictor of asthma when measures of lung function were incorporated into the final model. There was however a modest attenuation in the OR
(particularly in girls) when allergic sensitisation was added to the model, this also resulted in a loss of the association between BMI and asthma in both boys and girls.

Overall, this study has shown that obesity appears to be a risk factor for the development of symptoms suggestive of asthma – more so in girls than boys – and that this may in part be due to obesity increasing the risk of allergic sensitisation. The chapter which follows provides the conclusions found to this study.
Chapter 5: Discussion and conclusions

5.1 Main findings

This thesis has described a large epidemiological study which firstly aimed to investigate the prevalence of asthma and other allergic disorders (143) and then secondly to study the association between obesity and asthma in Saudi primary school-aged children. To the best of my knowledge, the cross-sectional survey is the largest study of its type on this topic in the Arab world. The subsequent matched case-control study is also one of the largest matched case-control studies on this topic ever undertaken. Prior to the two studies, a comprehensive pilot study was undertaken to investigate the feasibility of undertaking these studies and to investigate any challenges that may be encountered.

The pilot study revealed that asthma, allergic rhinitis, and atopic eczema are very common among schoolchildren in Madinah and, therefore, any further investigation of their prevalence in larger samples of the population could be justified. The prevalence of asthma was estimated, from the pilot study (Phase I), at 12.9% (95% CI: 10.0, 16.0) among girls and at 19.8% (95% CI: 17.1, 22.5) in boys. The prevalence of allergic rhinitis was estimated at 16.8% (95% CI: 13.4, 20.2) among girls and at 26.7% (95% CI: 24.0, 30.0) in boys. The prevalence of atopic eczema was estimated at 8.5% (95% CI: 6.0, 11.0) for girls and at 10.4% (95% CI: 8.3, 12.5) among boys.

An important conclusion inferred from Phase I of the pilot investigation was that this study would be acceptable to schools, parents and children. The participation rate in the pilot study was 77.9%; and more than 1300 families answered the questionnaire showing their interest to provide information about the lifestyle characteristics and health status of their children, through the ISAAC questionnaire.

The second part of the pilot study (Phase II) revealed the challenges of conducting an extensive matched case-control study, which would investigate any association between obesity and asthma in schoolchildren in Madinah. It was concluded that conducting such a matched case-control study was meaningful and feasible. The only aspect in the research design that was found to be very difficult to carry out was blood testing. Performing phlebotomy on children aged 6-8 years proved to be a difficult task, 31% of the parents were not willing to give consent and most of the children were scared of being punctured.
Moreover, blood tests would greatly increase the cost of the study as most of the required parameters needed more specialised analyses, and consequently very expensive reagents and consumables, as well as highly skilled personnel. Due to the highly specialised nature of some blood tests, the latter had to be performed in a laboratory outside Saudi Arabia, something which would further increase the cost of the study and would expand the time schedule for data collection. Consequently, it was decided that blood tests on allergic parameters would be excluded from the matched case-control study.

The findings of the cross-sectional survey confirmed the findings of the pilot study, namely that the prevalence of the three studied conditions (asthma, allergic rhinitis, and atopic eczema) was very high among Saudi children; over 40% of children in the studied sample (n = 5188) were found to have been affected by at least one condition within the first eight years of life. Allergic rhinitis and asthma were the most important problems, with each of them affecting almost 25% of the children population. Atopic eczema was found at lower prevalence, affecting about 10% of children. The survey also revealed that asthma and the other allergic disorders are more prevalent in boys than in girls.

The matched case-control study demonstrated an association between obesity and asthma in both boys and girls. This association was clearly stronger in girls than in boys and it remained significant after adjusting for a range of lifestyle and socio-demographic variables, which could act as confounders. Incorporating lung function measures into the regression models was of little consequence and the positive association between BMI and asthma persisted in both boys and girls.

Allergic sensitisation was found to be a very strong predictor of asthma; its inclusion in the multiple regression models attenuated the association between BMI and asthma, thereby suggesting that the effect of obesity on asthma may at least partially be mediated through increasing the risk of allergic sensitisation.

In conclusion, the matched case-control study supports the increasing body of evidence implicating obesity as a risk factor for the development of asthma showing that this relationship also holds true in Asian-origin populations and provides important pointers into how this relationship may be mediated.
5.2 Considering the findings in the context of the general literature

There is limited previous literature reporting the prevalence of asthma in the Middle East countries compared with the Western countries; (83, 145, 147, 178, 192), however they report comparable prevalence estimates, this finding is challenged by the results of the cross-sectional study in this thesis which has shown that childhood asthma, as well as allergies, are to be found at high levels among Saudi children.

Comparing the findings of the cross-sectional study in this thesis with the results from other countries from the ISAAC study, (173) it is shown that Saudi Arabia is internationally a very high prevalent region of childhood asthma and allergies.

The discrepancy between symptoms suggestive of and diagnosed disease, revealed from the cross-sectional study in highlighting the possible problem of under-diagnosis of allergic rhinitis, and possibly also asthma, which echoes the findings from previous studies. (250, 251)

The results of the matched case-control study in this thesis are consistent with an increasing number of epidemiological studies that have reported a positive association between obesity and the risk of developing childhood asthma. (29-31, 138)

However, the observed association refers to reported symptoms indicative of asthma and not necessarily to clinically diagnosed disease. Wheeze and cough are non-specific symptoms which may be attributed to a number of different causes, including asthma.

We have found that the association between obesity and asthma was stronger in girls than in boys. This has also been observed in other studies, (26, 138) although some review studies conclude that evidence is conflicting as to whether gender affects the development of asthma in obese children. (243) It is suggested that obesity is generally found to be more consistently associated with asthma in women than in men and this may be explained by a possible influence of sex hormones. (26) It is not clear whether the effect of sex hormones – if any – plays a role in young or pre-pubescent girls as well. Whether the gender difference observed in the matched case-control study in this thesis is simply due to the higher levels of obesity found in girls (Table 4.3) or is due to differences in body fat distribution (boys tend to be more muscular than girls and increased weight in boys may reflect increased muscle mass rather than increased adiposity) and/or associated biochemical responses is unclear. For
example, the role of leptin, which is produced by adipose tissue and may promote asthma via effects on lung growth or via effects on immune and inflammatory cells.(224, 236)

A wide number of studies suggest that atopic sensitisation is a strong risk factor for asthma,(26, 161, 246, 247) something which is confirmed from the findings of the present study as well. Whether obesity is involved in the association between atopic sensitisation on asthma remains to be clarified. Some studies report a positive association between obesity and atopy.(242, 246) If obesity is a causal factor of atopy and atopy, in turn, is a causal factor of asthma, then any association between obesity and asthma may be explained by this chain of events. On the other hand, some studies conclude that the association between obesity and asthma is stronger in non-atopic than in atopic individuals,(248, 249) which suggests, that in the association between obesity and asthma, atopy may not be involved so extensively.

5.3 Is there a causal relationship between obesity and asthma?

Asthma is a disease characterised by airflow obstruction, which varies markedly, both spontaneously and with treatment. Patients with asthma have inflammation in the airways, which makes them more responsive than their non-asthmatic counterparts to a wide range of triggers, leading to excessive narrowing with consequent reduced airflow and symptomatic wheezing and dyspnoea.(42, 108)

Obesity has been thought to be an independent risk factor for asthma, particularly amongst women.(245) In an attempt to further understand whether this is indeed likely to be a causal relationship, it is useful to consider Bradford-Hill’s criteria of causation (discussed in Section 1.7.3).(122)

Figures 5.1 – 5.3 summarise the possible causal pathway which may link obesity with asthma, according to the two patho-physiological mechanisms, functional respiratory mechanics and immune and inflammatory responses, and are supported by the findings of the research presented in this thesis.
Figure 5.1: Possible chain of causal events linking obesity with asthma (Adapted from reference. (117))

Figure 5.2: Diagrammatic representation of two possible routes linking obesity with asthma in the pre-pubertal children that were investigated in this thesis
Figure 5.3: Possible mechanisms of how obesity leads to asthma through inducing atopic sensitisation

Obesity also increases the release of oestrogen, which may increase the risk of sensitisation – particularly in females – and thereby increase the risk of asthma.(198, 252)
5.3.1 Temporal sequence

Population surveys have shown that persons with asthma are disproportionately obese when compared to persons who have never had asthma. (253) However, although studies suggest that obesity increases the risk of asthma, the temporal relationship is still not properly established. (32, 244) This may be because it is almost, if not entirely, impossible to conduct controlled experimental studies in human subjects, partly due to ethical considerations. This limits the available studies to cross-sectional, case-control, or prospective study designs where the temporal sequence of disease events is difficult to be established accurately. (253) Moreover, obesity and asthma are considered chronic diseases and, therefore, the length of time involved is usually long, adding to the burden of proving their temporal relationship.

In the case-control study of this thesis, the temporal sequence between obesity and asthma cannot be specified. Because data on asthma are derived from participants’ responses on past events, it was not possible to determine when asthma symptoms started (the main question was: “has your child ever had wheeze”). Moreover, obesity estimation was based only on measurements of BMI conducted during the study; there was not any information available about the obesity status of participating children in the past (i.e. we were not able to know when an obese child started being obese).

5.3.2 Plausibility, experimental evidence, and coherence

The association of obesity and asthma is biologically plausible. Mouse models of asthma demonstrated that obesity and adipokines have the capacity to enhance airway hyper-responsiveness, airway inflammation, and allergic responses. (254) Similarly, in the study by Holguin and Fitzpatrick in 2010, it was proposed that obesity affects lung function of asthmatic patients by mediating oxidative stress. (113) This may explain the increase in airway inflammation and reduction of the effectiveness of inhaled corticosteroids seen in obese patients, which are in parallel to the observation made by Beuther. (255) According to Holguin and Fitzpatrick (2010) oxidative stress may become evident during exposure to an aggravating factor or during asthma exacerbation. (113) Many studies have demonstrated that atopy is a key mediating factor and it has been suggested that there are increases in atopy with obesity, (246, 256-258) although positive associations appear confined to female subjects and mostly to children. (224, 236, 242)
It is believed that adipocytes release a number of inflammatory mediators which trigger allergic response. (26)

Mai, Chen, and Krewski, (259) proposed that leptin could be associated in the pathogenesis of asthma. Leptin is a protein produced by adipose tissue and it is capable of stimulating the production of pro-inflammatory mediators, such as tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interferon-γ (IFN-γ). Increase in these pro-inflammatory mediators could result in increased airway inflammation and AHR. (259)

5.3.3 Consistency

Numerous, but not all, cross-sectional studies on obesity and asthma from different countries have shown that the prevalence of obesity among adults with asthma was higher compared to those without asthma. (16, 253, 260) Most of these studies used self-reported asthma, regardless of whether the condition was diagnosed by a physician or not, and used BMI as the principal anthropometric measure of obesity. In addition, a few studies also suggested that the association between obesity and asthma is stronger among women compared to men. (245, 248, 261, 262) Generally, most of the studies show a consistent association between obesity and asthma.

5.3.4 Strength

In 2001, Schachter et al. (263) conducted a study to assess whether there is a parallel increase in the prevalence of obesity and asthma. After adjustment for age, gender, smoking history, and other confounding variables, obesity was found to be a significant risk factor for asthma with an OR equal to 2.04. Similarly, in a large cross-sectional study in Anqing, China, people with either very low or very high BMI were found to have a 2.5-fold increased risk of symptomatic airway responsiveness. (264)

Moreover, longitudinal data from the study of Litonjua et al. (265) showed that obesity is associated with airway hyper-responsiveness, with an OR of 7. In the case-control study of this thesis the ORs found for BMI were more modest (e.g. from 1.1 to almost 1.4; see Chapter 4); thus, the observed association between obesity and asthma should be considered of medium strength. However, it is not necessary for an association to be strong in order to be
causal(117) therefore, it cannot be excluded that the association between obesity and asthma found in this thesis is causal.

5.3.5 Dose-response relationship

In a meta-analysis of seven studies (n=333,102) by Beuther and Sutherland in 2007, a dose-response effect of elevated BMI on asthma has been observed.(27) The OR of having asthma, in subjects with normal weight versus those who were overweight, was found to be 1.38 (95% CI, 1.17, 1.62); a larger value of OR was found when normal weight individuals were compared with obese individuals, (OR=1.92; 95% CI, 1.43, 2.59). In the case-control study of this thesis, the logistic regression model applied assumed a dose-response relationship between obesity (as it is approximated by the calculation of BMI) and asthma.

5.3.6 Reversibility

Studies have shown that weight loss on the basis of behavioural change has led to significant improvements in the clinical manifestation of asthma in many obese patients.(253) Weight loss has also been associated with a decrease in the levels of leptin in blood, a protein capable of inducing inflammation in the airways, among obese children.(259) In the present thesis we were not able to investigate the existence of any reversibility in the observed associations, as we did not collect data about changes in the BMI of children by time.

5.3.7 Study design

Studies that have demonstrated association between obesity and asthma are mostly cross-sectional, case-control, and few were prospective studies.(16) In these studies, association of obesity and asthma was demonstrated among several populations.(253) However, a better designed study is still warranted in order to minimise the effects of confounders and bias, which would in turn strengthen the association and serve as a basis in proving causality.(266) The studies presented in this thesis employed cross-sectional and case-control designs. Consequently, the cross-sectional study does not investigate the association between obesity and asthma while the case-control study has weak ability to show causality.(117) Therefore,
their findings, particularly those of the case-control study, should be considered to add to the existing evidence of a causal relationship between obesity and asthma, but the latter still needs to be clarified through experimental studies.

5.3.8 Judging the evidence

For the past three decades, an epidemic of obesity and an epidemic in asthma in the western world have been observed.(266) A potential causal association between these two disorders has been investigated in a multitude of epidemiological studies and some investigators have already suggested possible patho-physiological mechanisms to explain the role of obesity in the development of asthma.(255, 259, 266) It has also been shown that weight reduction leads to improvements in asthma severity and disease manifestation.(255) Despite the available evidence from this and previous studies, it still remains unsettled whether this relationship of obesity and asthma is causal or confounded by residual factors, since mechanistic and physiological studies have produced heterogeneous and, at times, conflicting findings.(267) Therefore, it is still essential to conduct more and even better designed studies, to clarify the nature of the relationship between obesity and asthma. That said, the importance of weight regulation is in general an important consideration and this may have beneficial effects in relation to asthma prevention and management.(253)

5.4 Strengths and limitations

5.4.1 Two stage cross-sectional survey to determine the prevalence of asthma in 6-8 year-old children in Madinah, Saudi Arabia

The main strengths of the cross-sectional survey included the very high response rate (85.9%) and the large sample size (n=5,188); the former was likely to be due to the combination of achieving good support from the participating schools and from the fact that we were undertaking work in a population that had not previously been investigated. The use of a validated instrument was an additional strength, particularly since this offered the opportunity to compare prevalence estimates for children from Madinah with children of a similar age from across the world.(83, 173)
The major limitation with the cross-sectional survey was that it was conducted in only one city Madinah in Saudi Arabia, and in children of one age group only; these findings may therefore not be generalisable to other sections of Saudi society or to other age groups. It is important that similar studies are now conducted in other urban and rural locations in Saudi Arabia and among children of other age groups. There is also the need to build on this work and monitor allergic disease trends in Madinah.(268, 269) Another limitation that needs to be considered is related to the criterion applied for the identification of asthma cases (a positive response to the ‘ever had wheeze’ question). Future work needs to investigate the impact of changing the definition (e.g. to wheezing within the last 12 months prior to the study or parental reports of a clinically diagnosed asthma). Indeed, identification of asthma cases based on reports of formal clinical diagnoses in the past would be ideal, since it would be more objective and would minimise misclassification errors. However, the use of such a definition would limit the number of cases since some 6-8 year old children with asthma in Saudi Arabia will not have received a formal diagnosis of asthma (see Table 2.2). After all, one of the aims of this thesis was to estimate the burden of childhood asthma in Saudi Arabia by investigating the prevalence of symptoms suggestive of the disease. The high prevalence rates of wheeze found in this thesis justify the conduct of further studies in which a clinical screening for asthma could be applied. Finally, as we had no data that allowed us to compare the characteristics of responders and non-responders, due care must be taken in seeking to extrapolate data from this work across Madinah.

### 5.4.2 Matched case-control study of the association between obesity and asthma in 6-8 year-old children in Madinah, Saudi Arabia

Key strengths of the matched case-control study included the size of the study; the use of a validated and extensively used questionnaire to identify cases and controls; careful measurements of a range of measures of obesity by trained personnel who were blinded to case status; the measurement of and adjustment for, a range of potential confounders; and the a priori decision to undertake separate analyses in boys and girls.(270) We, in addition, sought to extend previous work by shedding light on the possible role of key causal mechanisms.

The main limitations of the matched case-control study were those inherent to case-control studies, especially those with prevalent cases and controls, namely an inability to establish a
temporal relationship between the onset of obesity and the subsequent development of asthma, and the risk of residual confounding, recall bias and reverse causation (discussed below). Moreover, since the identification of cases was based only on parental symptoms reports according to a questionnaire and not to full medical diagnosis; and beside the fact that a validated culturally appropriate questionnaire was used, there remains the possibility of misclassification errors. If such an error was present, it is likely that this would have been non-differential and this would therefore have likely attenuated the relationship between obesity rather than introduce spurious associations.(271-273)

The risk of recall bias is inherent in retrospective studies and particularly in studies based on self-responses. For example, ISAAC study part III found a positive association between paracetamol intake during the first year of life and development of childhood asthma.(274) However, it has been suggested that the results of the study may be confounded by recall bias, since parents of children with asthma may be more likely to report use of paracetamol.(274, 275) In the present thesis, parents whose children had probably experienced any serious episodes of wheezing would be more likely to report such symptoms, compared to those whose children had presented with more minor symptoms. Therefore, misclassification errors resulting from recall bias may be expected.

Usually, recall bias in case-control studies refers to errors occurring in the measurement of the exposure. Namely, we are supposed to have classified our participants into cases and controls (without any error) and we consider the possibility that recalling of past exposure events may be different between cases and controls.

In the case-control study of this thesis however, recall bias is likely to affect the classification of participating children in cases and controls; thus, recall bias may be a source of misclassification error in case status. Since the definition of a ‘case’ has been considered as a child that ‘ever had wheeze’ and since this piece of information was based on parental responses, there remains the possibility that some children had wheezed in the past, but their parents did not remember it. Therefore, recall bias, here, may have confounded the accuracy of the outcome and not the accuracy of the (potential) causes. The latter are not expected to be biased, since the studied exposures in the case-control study were quantified by objective measurements (BMI, spirometric tests, SPT), carried out by trained professionals who were blinded to the state of cases or controls.
5.5 Reverse causality

The inability to establish a temporal relationship between the onset of obesity and the development of asthma warrants particular consideration in a prevalent case-control study.

Reverse causality is the cause and effect in reverse, that is the “effect” actually precedes the “cause”, contrary to a common perception or to the initial hypotheses of a certain study.(276, 277)

With regard to obesity and asthma, the issue of reverse causation is possible as children might become overweight or obese as a result of a switch to less physical activities after the diagnosis of asthma or as a consequence of asthma therapy (particularly oral steroids).(278, 279)

Gennuso et al. in a review of medical records of children and adolescents of a health centre found significantly higher rates of obesity in children with asthma when compared with those without asthma.(278) The authors suggest that children with asthma have reduced physical activity since physical exercise regularly exacerbates asthma attacks by inducing bronchospasm and this may lead these children to become overweight or obese.(278)

On the other hand, Chinn (2003) considered the subject of temporality in her review paper which included a number of longitudinal studies in which it was possible to exclude the possibility of reverse causality.(267) Chinn concluded that the association between obesity and asthma is real, although it does not seem to have a simple explanation. Chinn considered the aspect of temporality by reviewing five longitudinal studies in which reverse causality was not likely to be present.(267) One of these studies followed up more than 80,000 nurses for five years and found statistically significant relative risks for asthma with BMI increase.(30) Three of these studies were in children and found significant associations between BMI increase and the occurrence of asthma in later life.(224, 237, 262) Another longitudinal study which followed a cohort of community-based young adults for 10 years also reported statistically significant associations between BMI change through time and risk for developing asthma.(245) The findings of these longitudinal studies are indicative of obesity preceding asthma and not vice-versa.

Since the available longitudinal evidence may suggest that obesity precedes asthma, it seems that reverse causation is unlikely to be an adequate explanation of the observed findings in this thesis.
5.6 Implications for public health policy, future research, and practice

The work in this thesis has identified a high prevalence of asthma and allergic disorders among schoolchildren in Madinah. Given the fact that these conditions are likely to continue to pose a significant burden to individuals and society over the life-course, this suggests that childhood asthma and allergic problems are likely to be an important public health issue in Saudi Arabia for the future. (169, 280, 281) Moreover, taking into account that children below the age of 15 represent about 50% of the total population of Saudi Arabia, childhood asthma and allergies emerge as a key issue for the health of the nation, as well as a challenge for the public health authorities of the country.

Given the very high prevalence rates observed in Madinah, it is important that this work is now extended to other Saudi regions, as well as to other age groups. By doing so, more information will be collected and a complete picture of the status of asthma and allergies in the country can be formed. It is furthermore important that this population-based work is repeated in due course to allow disease trends to be determined. (268, 269, 282) Moreover, further cross-sectional studies are required to investigate the distribution of asthma and allergies in respect of geographic areas, socioeconomic status, and lifestyle characteristics of the Saudi society. All the above will enable a more thorough understanding of the burden and nature of these health conditions, which is the first step in the process of planning the appropriate preventive strategies and management.

At a further stage, attempts need to be made to understand key, potentially modifiable, environmental and behavioural risk factors. After a descriptive analysis of the distribution of asthma and allergic conditions in the population, the identification of the most common risk factors which lead to morbidity of these conditions should constitute the next step in the preventive strategy. Thus, a number of case-control, cohort, and interventional studies are definitely required in the future. If key risk factors are identified, then public health authorities and environmental authorities should undertake action, by planning the appropriate health promotion programmes, so that exposure of the population to these factors is minimised.

A first step in this direction has been undertaken through the work described in this thesis. The findings of the matched case-control study may be valuable for public health authorities in Saudi Arabia as it provides additional evidence of the considerable adverse risks associated with obesity. Although causality cannot be proven by this (or indeed any other single
epidemiological investigation), the findings from this work, when combined with an increasing number of studies worldwide, provide increasing evidence of a causal relationship between obesity and asthma. This then adds weight to the argument to consider the role of interventions to prevent or at least tackle obesity early on in life and thereby possibly reduce the risk of developing asthma. Even if such causality has not been unequivocally proven, public health authorities of Saudi Arabia should consider applying the “precautionary principle” and undertake initiatives for reducing obesity among Saudi children. Reduction of obesity in children will offer benefits in general health status, since obesity is a well-established risk factor for several other diseases. Moreover, given the high prevalence of obesity and asthma, School Health Departments should consider focusing attention on establishing systems for monitoring obesity and asthma among schoolchildren. Moreover, in subsequent analysis, I hope to repeat these analyses using the other assessed measures of obesity.

Comparing the prevalence of the reported symptoms investigated in the cross-sectional study (Table 3.4), and clinician-diagnosed disease, it is suggested that there may be substantial under-diagnosis of allergic rhinitis and to a lesser extent asthma. There is now, therefore, a need for further work to be undertaken now to verify this and, if confirmed, to take steps to improve diagnostic capacity and accuracy, particularly in community-based clinical settings.

From the biomedical research point of view, a more thorough investigation of the mechanisms which might link obesity and asthma are needed. For example, the role of leptin certainly warrants further investigation.

Moreover, there is a need for related work investigating the quality of care provided to children with allergic problems, as this has been found to be wanting in other parts of the world.(250, 251)

As mentioned in Chapter 1 (Section 1.2.3) primary healthcare physicians typically have poor understanding of the national and international protocol/guidelines for management of asthma. In addition, poor knowledge, unstructured and non-integrated provision of asthma services in expensive secondary care lead to unnecessary morbidity of asthma in Saudi Arabia.(148) A review that evaluated the systems for the management of asthma and respiratory disease in primary care in the UK highlighted asthma services are prominently led by nurses and self-management strategies are poorly implemented in the UK.(283) There is a window of opportunity to improve asthma services through the provision of comprehensive
and integrated care in the community. In turn, this approach may reduce the inequalities in asthma services, improve quality of care and reduce the burden of asthma in children and adults.

There is a need for a more proactive, systematic approach to the diagnosis and management of children that is delivered through the schools infrastructure. There is a need for better communication channels between hospital physicians and schools, and the need for periodic assessment of the quality of asthma care compared with recommendations on asthma management in Saudi asthma guidelines.(148)

I have mentioned above all the issues and challenges around conducting my studies. However, the absence of formal research ethics committees and any ethical approval mechanisms for conducting research involving human data prompts the Saudi Arabia government to establish these official regulatory bodies as soon as possible.

Finally, taking into account that tackling any public health problem is associated with a considerable cost for the healthcare system, it is important that any epidemiological work is accompanied by a number of health economic studies. The aim would be to determine the costs of each of the suggested preventive strategies as well as those of treating asthma and allergies. Tackling all issues surrounding the blood tests – financial, unfulfilled expectations that I have encountered and explained in the study plays a pivotal role in designing future large-scale studies. These studies should include more objective definitions of asthma/atopic disorders, comprehensive data such as, anthropometric measurements, pulmonary function, skin prick, and blood tests. In turn, such studies will provide information which will be useful to the Saudi government for making the appropriate and the most optimum healthcare policy.

5.7 Primary prevention of obesity

The analysis in the previous section concluded that public health authorities of Saudi Arabia should undertake initiatives for reducing obesity among Saudi children; therefore, a national strategy of primary prevention needs to be implemented. Such a strategy could include the following steps.(284)

1) Regular measurements of children
2) Promotion of a healthy diet
3) Promotion of physical activity.

5.7.1 Regular measurements of obesity status in the population of children

It is important that the prevalence of childhood obesity is continuously monitored in the population. For this purpose, a permanent monitoring system could be established in the School Health Departments. Such a system could include a periodical (for example, yearly) assessment of obesity status of children in all the schools of the country. In this way, updated data on the prevalence of obesity will be acquired which can help public health authorities to continuously investigate the burden of the morbidity. Moreover, such a system could be useful to individual families as well, by providing an early warning to them about the health status of their children. The latter is particularly important since a study in the UK showed that a substantial portion of parents are not able to identify whether their children are obese or not.

5.7.2 Promotion of a healthy diet

The public health authorities should design and launch appropriate health promotion programmes encouraging a healthier diet with the aim of reducing obesity. Such programmes should focus on two different groups: the children and their parents. Some key points which should be communicated through a health promotion programme include:

- Limiting the consumption of high energy foods.
- Following appropriate dietary recommendations required for the growth of children.
- Avoiding snacks and junk food.
- Having breakfast every day.
- Having regular meals at certain times and to limit the number of meals outside home.
- Limiting portion sizes in each meal.
5.7.3 Promotion of physical activity

Physical activity for children can be promoted by increasing the hours of sports activities in the school syllabus. (285) This will enable children who do not take any physical activity during their free time at home, to get some physical exercise during school hours. (285)

Local authorities can also be involved in promoting physical activity by creating the appropriate infrastructures (e.g. stadiums, gyms) and by establishing sport organisations. For example, municipal authorities could establish amateur sports clubs in which training could be offered to children at a low cost. Moreover, organisation of sports events (e.g. local championships between amateur teams) could encourage children to participate in physical activities through competition.

Health promotion programmes explaining the benefits, as well as methods, of taking moderate daily physical activity need to be directed at parents, so that they not only introduce more physical activity into their own daily life, but actively encourage their children to do more.

5.7.4 The role of schools and educators in the primary prevention of obesity

Given the fact that school constitutes one of the first connections of a child to the wider society, schools are important places where population-based prevention programmes can be applied. (286) Schools are places where healthy habits can start, as long as the appropriate care for promoting such habits is taken. Taking into account that children and adolescents will spend several years in school for their compulsory education, there are a lot of opportunities offered for promoting healthy lifestyles through schools.

For this reason, the role for the School Health Departments and of educators in the primary prevention of obesity becomes particularly vital. Consequently, the Government should pay attention to the School Health Departments by funding them and enhancing their involvement in health promotion.

The vital role of school educators, not only in the dissemination of knowledge but also in the psychosocial development of children, is widely accepted. It is made clear that another vital role of health educators is their contribution in promoting a healthy life style among children. For this reason, school educators should be continuously trained in aspects of obesity and
other health issues, so that they are able to disseminate information on a healthy lifestyle to their students.

Finally, we need to work very hard in Saudi Arabia to reduce obesity among the children by promoting the benefits of physical activity and good eating behaviours. This has to be a multi-dimensional approach as weight is influenced by many sectors of society including families, community organisations, healthcare providers, mosques, the media, School Health Departments and schools. The involvement of all of these sectors will be needed to reverse the problem. Also, we need an insightful board member, educators, and legislators to step up to meet the challenge. Through their exemplary leadership, Ministry of Health, School Health Departments and communities are indicating that obstacles can be overcome.

5.8 Personal reflections on my experiences with undertaking this thesis

5.8.1 My experiences prior to embarking on my PhD

After graduating from King Saud University with a Bachelor Degree in Pharmaceutical Sciences in 1994 I started working as a pharmacist in the Ministry of Education’s clinic, which provided basic healthcare for all school students in Madinah. I was involved in many health awareness and promotion programmes in the clinic and it led to my promotion as a manager, which I held until 2005. Our work in the clinic included diverse activities such as, handling health-related emergency situations, participation in the management of acute and chronic illnesses and injuries in children from all demographic backgrounds. In turn, this rich experience gave me confidence in tackling different healthcare problems and challenges in Madinah. From these experiences, I began to appreciate how widespread a problem asthma was in children in Madinah and it was this observation that first ignited my interest in studying children with asthma,

In order to move in this direction and acquire the necessary methodological skills, I enrolled in a Masters in Public Health at Dundee University, Scotland, UK and in 2006 I received my degree from this University.

The search for expertise in community-based asthma research drew me to Edinburgh and I then applied to and was accepted onto a programme of PhD studies at The University of
Edinburgh, Scotland, UK. I intend to apply for a university post once I get my Ph.D. so I can continue with my research work in the field.

5.8.2 Challenges encountered and how these were overcome

Since I had no previous experience of conducting a large-scale epidemiological study that required, amongst other things, much field work, I encountered several challenges which can be grouped into two broad categories: challenges related to a variety of technical issues about how to perform several research tasks; and challenges related to human psychology, such as: administration and communication skills and dealing with cultural and political issues.

Prior the beginning of my research, there was very limited understanding of the importance of this study amongst my peers in my Service in Saudi Arabia. Thus, at the beginning, very few of the personnel at the Administration of Education were convinced about the importance and usefulness of the research, making it challenging for me to get support for this study. This position gradually changed, as I communicated the importance of this work to my colleagues and highlighted the potential benefits to the local community of developing a research culture.

In order to cope with difficulties in technical issues, I had to acquire new skills and competencies, which was a major challenge for me. For this purpose, I first identified and completed relevant training courses in the field of Education for Health in Warwick, England, UK, in Dundee University Hospital, Scotland, UK, and in The University of Edinburgh, Scotland, UK.

Because of the religious and cultural norms around gender segregation, it was made difficult at times to manage the female research team. This issue was solved by having a female Saudi investigator as a senior member of the research team. There was also a need for training the research team from the School Health Department, Ministry of Education in Madinah, who were appointed to carry out respiratory function measurements. Due to gender segregation in Saudi Arabia, I had to train two different research teams, one for boys’ and one for girls’ schools. The female research team, although they had participated successfully in the pilot study, they were unable to proceed to data collection for the case-control study, due to difficulties related to their scheduled work. I therefore had to find and train a second female
team, in a limited time, which resulted in delays in data collection in the girls’ schools and in a subsequent imbalance in the proportions of boys and girls recruited for the study.

Finally, obtaining and analysing blood tests was another major challenge. Several children were scared to accept venesection and this concern was expressed by their parents, which could lead to a reduction of the sample size for the case control study. Moreover, blood sample analysis was related to financial difficulties, since the required tests were quite expensive, due to the specialised analyses that had to be performed; apart from that, the cost of the whole procedure increased, because blood samples had to be sent to Egypt for analyses, as some specialised laboratory equipment was not available in Saudi Arabia. Due to these difficulties, the inclusion of blood measurements in the study was considered not feasible and was abandoned. This was a valuable lesson from the pilot phase of work.

5.8.3 Key areas in which I have developed and areas for future training and development

I have, during the course of undertaking this thesis, developed a range of skills and experiences, which I’m sure, will be of immense value in my future academic career. I highlight a few key areas below.

First and foremost, I have developed a deep appreciation of the importance of rigour in undertaking research in order to be able to draw valid conclusions. In this respect, I now appreciate the importance of considering previous scholarship and then carefully building on this work through the formulation of carefully constructed research hypothesis and then selecting appropriate research designs to investigate this hypothesis. The second key lesson I have learnt is that there are a range of research approaches available to investigators and that a key task is to select, as far as is possible, the optimal research design. Thirdly, I now realise the importance of pilot work to assess the feasibility of undertaking larger, more definitive studies. I thus made some important modifications in the light of the insights obtained from my pilot work. A fourth key lesson has been the importance of planning, managing teams and actively taking steps to ensure the quality of the work. The fifth and final key lesson that I would like to note here is the importance of communicating the results of findings to participants, colleagues who have been part of the research endeavour and of course the academic community through presentations and peer-reviewed publications. In this way, it is
possible to contribute to creating a virtuous cycle in which research findings can have an impact and a research culture is created and actively promoted. The importance of this latter point to Madinah, Saudi Arabia and the Arab world in general cannot be overstated and in this respect it is heartening that I have received a number of approaches from colleagues throughout the Arab world who now wish to build on this work.

5.9 General conclusions

This work has revealed the very high prevalence of asthma, allergic rhinitis, and atopic eczema among the schoolchildren of Madinah. Over 40% of children are expected to manifest symptoms indicative of one or more allergic diseases within the first eight years of life; these figures rank Saudi Arabia amongst the countries with the highest prevalence rates in the world. In all three of these disorders, prevalence rates are higher in pre-pubertal boys than in girls.

The large matched case-control study conducted in this thesis provides the first evidence demonstrating an association between obesity and asthma in Saudi boys and girls. Our investigation of key causal pathways suggests that this relationship may indeed be causal, this being partially mediated through increased allergic sensitisation.

5.10 Further research

Based on the high prevalence of childhood asthma and allergies in the age group of 6-8 year-old schoolchildren in Madinah, more epidemiological work is needed on assessing the prevalence of these conditions in other parts of Saudi Arabia, within different age groups, as well as for monitoring disease trends. Therefore, more cross-sectional studies like the one presented in Chapter 3 are suggested, so that the prevalence of asthma and allergies is determined and monitored in more detail.

Since the association between obesity and asthma may be mediated through increasing the risk of allergic sensitisation this is a field of enquiry that particularly warrants further study. Firstly, it is important that these findings are replicated, preferably using a prospective design. Secondly, mechanistic studies are also needed to investigate if obesity results in
raised oestrogen and/or leptin levels as these may be key links in promoting Th-cell switching and allergic sensitisation. Thirdly, accompanying immunological investigations would also be very welcome (Figure 5.3).

From an epidemiological perspective, it is important that any future epidemiological studies should focus on children with clinically confirmed asthma and not only reports of asthma symptoms. This is because, in the case-control study presented in this thesis, asthma cases were identified based on parental reports of symptoms; therefore, misclassification bias may be an issue. A study on a population consisting of clinically diagnosed cases will help in minimising such bias and inferring more accurate conclusions about the role of obesity on the causation of asthma.

When key risk factors for obesity, asthma, and allergies are identified, research should focus on planning the appropriate health promotion programmes to promote a healthier lifestyle and avoiding exposures to factors triggering allergic reactions. Health promotion programmes for reducing obesity in children, as well as in the general population, are a priority since obesity is an already recognised risk factor for several morbidities. Its minimisation is therefore vital, even if a clear association with asthma is not yet determined.

Finally, there is a need for related research investigating the quality of care provided to children with allergic problems as this also plays a part in the entire chain of measures to be taken for fighting asthma.
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Appleton SL, Adams RJ, Wilson DH, Taylor AW, Ruffin RE, North West Adelaide Health Study T. Central obesity is associated with nonatopic but not atopic asthma in a representative population


<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Actomyosin</td>
<td>A protein complex of actin and myosin occurring in muscle; the essential contractile substance of muscle.</td>
</tr>
<tr>
<td>Adiposity</td>
<td>Synonym: obesity, excessive accumulation of lipids in a site or organ.</td>
</tr>
<tr>
<td>Adipocytes</td>
<td>An animal connective tissue cell for the synthesis and storage of fat. Such cells are bloated with globules of triglycerides, the nucleus being displaced to one side and the cytoplasm seen as a thin line around the fat droplet.</td>
</tr>
<tr>
<td>Adenosine Triphosphate (ATP)</td>
<td>A nucleotide present in all living cells which serves as an energy source for many metabolic processes and is required for ribonucleic acid synthesis.</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index - One of the anthropometric measures of body mass; it has the highest correlation with skin-fold thickness or body density.</td>
</tr>
<tr>
<td>Brown adipose tissue</td>
<td>Brown fat is one of the two types of adipose tissue that is present in many new-born or hibernating mammals. Its primary purpose is to generate body heat. In contrast to white adipocytes (fat cells), which contain a single, large fat vacuole, brown adipocytes contain several smaller vacuoles and a much higher number of mitochondria. Brown fat also contains more capillaries since it has a greater need for oxygen than most tissues.</td>
</tr>
<tr>
<td>β2-adrenergic receptor gene ADRB2</td>
<td>The β2-adrenergic receptor (B2AR or ADRB2) is the target of β2-agonist drugs used for bronchodilation in asthma and other respiratory diseases. The gene for this receptor (ADRB2) contains numerous single nucleotide polymorphisms (SNPs) some of which may be of pharmacogenetic relevance, although a consistent picture of genotype-phenotype relationships has yet to emerge.</td>
</tr>
<tr>
<td>Case-control study</td>
<td>(Case comparison study, case-compeer study, case history study, case referent study, retrospective study). The observational epidemiologic study of persons with the disease (or other outcome variable) of interest and a suitable control (comparison, reference) group of persons without the disease.</td>
</tr>
<tr>
<td>Causality</td>
<td>The relation of causes to the effects they produce. Most of epidemiology concerns causality and several types of causes can be distinguished. It must be emphasized, however, that epidemiologic evidence by itself is insufficient to establish causality, although it can provide powerful circumstantial evidence.</td>
</tr>
<tr>
<td>Chi-square (χ²) test</td>
<td>Any statistical test based on comparison of test statistic to a chi-square distribution. The oldest and most common chi-square tests are for detecting whether two or more population distributions differ from one another. These tests usually involve counts of data, and many involve comparison of samples from the distribution. The person chi-square test is probably the best known; another is the Mantel-Haenszel test.</td>
</tr>
<tr>
<td>Cohort</td>
<td>Any designated group of persons who are followed or traced over a period of time, as in cohort study (prospective study).</td>
</tr>
<tr>
<td>Confounding</td>
<td>(from the Latin confounder, to mix together)</td>
</tr>
<tr>
<td></td>
<td>It is a situation in which the effects of two processes are not separated. The distortion of the apparent effect of an exposure on risk brought about by the association with other factors that can affect an outcome.</td>
</tr>
<tr>
<td>C-reactive protein (CRP)</td>
<td>Blood test is used as an indicator of acute inflammation. C-reactive protein is of the pentraxin family, produced by the liver during periods of inflammation and detectable in serum in various disease conditions</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
<td>C-reactive protein</td>
<td>Particularly during the acute phase of immune response. Normally it should be negative in the bloodstream.</td>
</tr>
<tr>
<td>Cross-sectional study</td>
<td>(Disease frequency survey, prevalence study) a study that examines the relationship between diseases (or other health-related characteristics) and other variables of interest as they exist in a defined population at a particular time.</td>
</tr>
<tr>
<td>Cycling rate</td>
<td>A property of smooth muscle, an intrinsic rate of excitation and contraction.</td>
</tr>
<tr>
<td>db/db mice</td>
<td>Mice that are leptin resistant due to a defective leptin receptor.</td>
</tr>
<tr>
<td>Dendritic cells (DCs)</td>
<td>Immune cells which form part of the mammalian immune system. Their main function is to process antigen material and present it on the surface to other cells of the immune system, thus functioning as antigen-presenting cells.</td>
</tr>
<tr>
<td>Dizygotic twin</td>
<td>Two offspring produced in the same pregnancy from separate ova fertilised at the same time.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Observation over a period of time of an individual, group, or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.</td>
</tr>
<tr>
<td>Forced Capacity (FVC)</td>
<td>The total volume of air exhaled with maximal forced expiratory effort after full inspiration.</td>
</tr>
<tr>
<td>Forced Expiratory Volume in 1 second (FEV1)</td>
<td>Measure of the maximum amount of air during a forced vital capacity determination that can be expelled in a given number of seconds. It is usually given as FEV followed by a subscript indicating the number of seconds over which the measurement is made, although it is sometimes given as a percentage of forced vital capacity.</td>
</tr>
<tr>
<td>Functional Residual Capacity (FRC)</td>
<td>The volume of air remaining in the lungs at the end of a normal, quiet expiration. It is the sum of the residual volume and the expiratory reserve volume.</td>
</tr>
<tr>
<td>Gastro-oesophageal sphincter</td>
<td>The terminal few centimetres of the oesophagus, this preventing reflux of gastric contents into the oesophagus.</td>
</tr>
<tr>
<td>Gene</td>
<td>A sequence of DNA that codes a particular protein product or that which regulates other genes. Genes are the biological basis of heredity and occupy precisely defined locations on chromosomes.</td>
</tr>
<tr>
<td>Genome</td>
<td>The array of genes carried by an individual.</td>
</tr>
<tr>
<td>Genotype</td>
<td>The genetic constitution inherited by an organism or a person, as distinct from physical characteristics and appearance that emerge with development, i.e. Phenotype.</td>
</tr>
<tr>
<td>Glucocorticoid receptor gene NR3C1</td>
<td>The glucocorticoid receptor (GR) or nuclear receptor subfamily 3, group C, member 1 is a ligand-activated transcription factor that binds to cortisol and other glucocorticoids with high affinity.</td>
</tr>
<tr>
<td>Heterogeneity</td>
<td>In systematic reviews heterogeneity refers to variability or differences between studies in the estimates of effects.</td>
</tr>
<tr>
<td>Hyper-responsiveness (BHR)</td>
<td>Airway hyper-responsiveness is a characteristic feature of asthma and consists of increased sensitivity of the airway to an inhaled constrictor agonist, a steeper slope of the dose-response curve, and a greater maximal response to the agonist. Measurements of airway responsiveness are useful in making a diagnosis of asthma, particularly in patients who have symptoms that are consistent with asthma and who have no evidence of airflow obstruction.</td>
</tr>
<tr>
<td>IL-4</td>
<td>A soluble cytokine factor produced by activated T-lymphocytes that promotes antibody production by causing proliferation and differentiation of B-cells. Interleukin-4 induces the expression of class II major histo-compatibility complex and fce receptors on B-cells. It also acts on T-lymphocytes, mast cell lines and several other haematopoietic...</td>
</tr>
<tr>
<td><strong>IL-6</strong></td>
<td>A cytokine that stimulates the growth and differentiation of human B-cells and also a growth factor for hybridomas and plasmacytomas. It is produced by many different cells including T-cells, monocytes, and fibroblasts. A single chain 25 kD cytokine originally described as a pre B-cell growth factor, now known to have effects on a number of other cells including T-cells which are also stimulated to proliferate. An inducer of acute phase proteins and colony-stimulating factor acting on mouse bone marrow.</td>
</tr>
<tr>
<td><strong>IL-10</strong></td>
<td>A factor produced by Th2 helper T-cells, some B-cells and LPS activated monocytes. It is a co-regulator of mast cell growth. It is produced by T-cells and B-cells. Shows extensive homology with the Epstein-Barr virus bcrfi gene.</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>The number of instances of illness commencing, or of persons falling ill, during a given period in a specified population. More generally, the number of new events, e.g. new cases of disease in a defined population, within a specified period of time.</td>
</tr>
<tr>
<td><strong>Infancy</strong></td>
<td>Babyhood; the earliest period of extra-uterine life.</td>
</tr>
<tr>
<td><strong>Leptin</strong></td>
<td>A hormone released by adipose cells in concentrations proportional to body fat levels.</td>
</tr>
<tr>
<td><strong>Lipopolysaccharide (LPS)</strong></td>
<td>The major constituents of the cell walls of gram-negative bacteria. Highly immunogenic and stimulates the production of endogenous pyrogen interleukin-1 and tumour necrosis factor.</td>
</tr>
<tr>
<td><strong>Meta-analysis</strong></td>
<td>A statistical synthesis of the data from separate but similar, i.e. comparable studies, leading to a quantitative summary of the pooled results. In the biomedical sciences, the systematic, organised and structured evaluation of a problem of interest, using information (commonly in the form of statistical tables or other data) from a number of independent studies.</td>
</tr>
<tr>
<td><strong>Methacholine</strong></td>
<td>A slowly hydrolyzed muscarinic agonist. It is used as a parasympathomimeticbrachconstrictor agent and as a diagnostic aid for bronchial asthma. It has also been used in the treatment of glaucoma and in the treatment of Raynaud's syndrome and other vasospastic conditions.</td>
</tr>
<tr>
<td><strong>Methacholine challenge</strong></td>
<td>A screening test for airways reactivity.</td>
</tr>
<tr>
<td><strong>Methodology</strong></td>
<td>The scientific study of methods, not be confused with methods.</td>
</tr>
<tr>
<td><strong>Monozygotic twin</strong></td>
<td>Two offspring developed from one fertilised ovum.</td>
</tr>
<tr>
<td><strong>Null hypothesis</strong></td>
<td>The statistical hypothesis that one variable has no association with another variable or set of variables, or that two or more population distributions do not differ from one another. In simplest terms, the null hypothesis states that the results observed in a study, experiment, or test are no different from what might have occurred as a result of the operation of chance alone.</td>
</tr>
<tr>
<td><strong>Ob/Ob mice</strong></td>
<td>The ob/ob mice are a mutant strain of mice characterized by morbid obesity and hyperphagia. They are deficient in the ob gene. They arose at random in a colony of mice in the 1950s and have proved invaluable in the study of obesity. The ob gene was identified in 1994 and is now called leptin, a circulating adiposity signal.</td>
</tr>
<tr>
<td><strong>Odds</strong></td>
<td>The ratio of the probability of occurrence of an event to non-occurrence, or the ratio of the probability that something is so, to the probability that is not so.</td>
</tr>
<tr>
<td><strong>Odds ratio</strong></td>
<td>The ratio of two odds. The term odds is defined according to the situation under discussion.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>All the possible results that may stem from exposure to a causal factor, or from prevention or therapeutic interventions; all identified changes in health status arising as a consequence of the handling of a health problem.</td>
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<tr>
<td>Oxidative Stress</td>
<td>Oxidative Stress (OS) is a general term used to describe the steady state level of oxidative damage in a cell, tissue, or organ, caused by the reactive oxygen species (ROS). This damage can affect a specific molecule or the entire organism. Reactive oxygen species, such as free radicals and peroxides, represent a class of molecules that are derived from the metabolism of oxygen and exist inherently in all aerobic organisms.</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>The origin and development of disease.</td>
</tr>
<tr>
<td>Population study</td>
<td>The group selected for investigation.</td>
</tr>
<tr>
<td>Prevalence</td>
<td>The number of events e.g. instances of given disease or other condition, in a given population at a designated time; sometimes used to mean Prevalence rate. Annual Prevalence is the total number of persons with the disease or attribute at any time during a year.</td>
</tr>
<tr>
<td>Prolinflammatory cytokine</td>
<td>Cytokines produced predominantly by activated immune cells such as microglia and are involved in the amplification of inflammatory reactions. These include IL-1, IL-6, TNF-α, and TGF-β.</td>
</tr>
<tr>
<td>P-value</td>
<td>The probability that a test statistic would be as extreme extreme than, observed if the null hypothesis were true. The letter P, followed by the abbreviation.</td>
</tr>
<tr>
<td>Questionnaire</td>
<td>A predetermined set of questions used to collect data– clinical data, social status, occupational group, etc. This term is often applied to a self-completed survey instrument, in contrast to with an interview schedule.</td>
</tr>
<tr>
<td>Random sample</td>
<td>A sample that is arrived at by selecting sample units so that each possible unit has a fixed and determinate probability of selection.</td>
</tr>
<tr>
<td>Rate</td>
<td>A measure of the frequency of occurrence of a phenomenon. In epidemiology and vital statistics, the rate is an expression of the frequency with which an event occurs in a specific population in a certain period of time.</td>
</tr>
<tr>
<td>Retrospective study</td>
<td>A research design that is used to test etiologic hypotheses in which inferences about exposure to the putative causal factor(s) are derived from data relating to characteristics of the persons under study or to events or experiences in their past.</td>
</tr>
<tr>
<td>Th1-type immune response</td>
<td>Th1 and Th2 type immune responses: describe a subset of T helper cell responses. T helper cells are a subset of T cells that secrete a variety of mediators (cytokines) playing a role in activation of other immune cells. A Th1 type immune response is usually induced by viral infection, or also by potent vaccination. A Th2 type immune response usually manifests an allergic reaction.</td>
</tr>
<tr>
<td>Tidal volume (TV)</td>
<td>The volume of air inspired or expired during each normal, quiet respiratory cycle. Common abbreviations are TV or v with subscript t.</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Tumour necrosis factor alpha is a cytokine produced primarily by monocytes and macrophages. It is found in synovial cells and macrophages in the tissues. It shares many properties with another cytokine – interleukin 1</td>
</tr>
<tr>
<td>Tumor Necrosis Factor TNF</td>
<td>Originally described as a tumour-inhibiting factor in the blood of animals exposed to bacterial lipopolysaccharide or Bacille Calmette-Guerin. Preferentially kills tumour cells in vivo and in vitro, causes necrosis of certain transplanted tumours in mice and inhibits experimental metastases. Human Tumour Necrosis factor alpha is a</td>
</tr>
<tr>
<td><strong>Sample</strong></td>
<td>A selected subset of a population. A sample may be random or non-random and may be representative or non-representative.</td>
</tr>
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<td>------------</td>
<td>------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Simple random sample</strong></td>
<td>In this elementary kind of sample each person has an equal chance of being selected out of the entire population. One way of carrying out this procedure is to assign each person a number, starting with 1, 2, and 3 and so on. Then numbers are selected at random, preferably from a table of random numbers, until the desired sample size is attained.</td>
</tr>
<tr>
<td><strong>Stratified random sample</strong></td>
<td>This involves dividing the population into distinct subgroups according to some important characteristic, such as age or socioeconomic status, and selecting a random sample out of each subgroup. If the proportion of the sample drawn from each of the subgroups, or strata, is the same as the proportion of the sample total population contained in each stratum (e.g. age group 10-29 constitutes 20% of the population, and 20% of the sample comes from this age stratum), then all strata will be fairly represented with regard to numbers of persons in the sample.</td>
</tr>
<tr>
<td><strong>Vagally mediated reflux</strong></td>
<td>Mechanisms of Oesophageal Reflux-Induced Bronchoconstriction. There are 2 proposed mechanisms whereby acid refluxing into the oesophagus induces or exacerbates airflow obstruction in asthmatics. These mechanisms include: 1. Vagally mediated reflex bronchospasm. 2. Microaspiration of gastric acid resulting in bronchoconstriction.</td>
</tr>
</tbody>
</table>
Appendices

Appendix 1: Search strategy for MEDLINE (Ovid SP)

1. Exp Asthma/
2. Asthma.mp.
4. Or/1-3
5. Exp Epidemiology/
7. 5 OR 6
8. Saudi Arabia.mp.
10. KSA.mp.
11. Or/8-10
12. 4 AND 7 AND 11
13. 12 not (animals/not humans)
14. Limit 13 to yr="1980-current"
15. advertisements/ or animation/ or architectural drawings/ or bibliography/
    or biography/ or book illustrations/ or bookplates/ or charts/ or comment/
    or letter/ or news/ or patient education handout/
    or published erratum/ or "retraction of publication"
16. 14 not 15
Appendix 2: Permissions, approvals and ethical considerations

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<th>To</th>
<th>Title of the letter</th>
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<tr>
<td>2-A</td>
<td>Researcher (MN)*</td>
<td>The General Directorate of Education (Boys)</td>
<td>Asking for permission</td>
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<tr>
<td>2-B</td>
<td>Researcher</td>
<td>The General Directorate of Education (Girls)</td>
<td>Asking for permission</td>
</tr>
<tr>
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<td>Researcher</td>
<td>Study protocol attached to the letters to General directorates</td>
<td>Study protocol</td>
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<td>2-D</td>
<td>General Directorate of Boys Department</td>
<td>Schools Head Teachers</td>
<td>Invitation letter</td>
</tr>
<tr>
<td>2-E</td>
<td>General Directorate of Girls Department</td>
<td>Schools Head Teachers</td>
<td>Invitation letter</td>
</tr>
<tr>
<td>2-F</td>
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<td>The General Directorate of Education (Boys)</td>
<td>Translation of the letter from Arabic-English</td>
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<td>The General Directorate of Education (Girls)</td>
<td>Translation of the letter from Arabic-English</td>
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<td>Researcher</td>
<td>Head Teachers</td>
<td>Information for the head teachers</td>
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<td>2-I</td>
<td>Researcher</td>
<td>Parents (sent to parents by head teachers)</td>
<td>Invitation letter</td>
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<td>2-J</td>
<td>Researcher</td>
<td>Parents</td>
<td>Parental information sheet</td>
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<td>2-K</td>
<td>Researcher</td>
<td>Parents</td>
<td>Parental consent form</td>
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<td>2-L</td>
<td>Researcher</td>
<td>Parents</td>
<td>Reminder letter</td>
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</table>

*Mahmoud Nahhas*
Appendix (2-A): Letter to the General Directorate of Education (Boys)

Allergy & Respiratory Research Group
Division of Community Health Sciences, The University of Edinburgh
20 West Richmond St
Edinburgh, EH8 9DX
Tel: +44 0131 650 3232
fax: +44 131 650 9119

Appendix
(2-A): Letter to the General Directorate of Education (Boys)

Page 184

Saudah / the doctor 
the head (of the) committee and public education directorate in the city of Jeddah .

willing be by , and peace

Salam on he and his family...

and students.

I congratulate you on the recent publication of the latest report on the education directorate. The report highlights the progress made in the field of education in the city of Jeddah, particularly in the field of primary education. The report also underscores the importance of investing in the education sector to ensure that all students have access to quality education.

The report emphasizes the need for continuous improvement in the education system to meet the changing needs of students and society. It also highlights the importance of involving all stakeholders in the education process, including parents, teachers, and the community.

I am confident that the education directorate will continue to work towards achieving the goals set out in the report and that it will continue to strive for excellence in the field of education.

I would like to thank you and your team for your efforts in ensuring the delivery of quality education to all students in the city of Jeddah.

Yours sincerely,

Researcher

Dr. Mohamed bin Abdul Fatah Nams
Appendix (2-B): Letter to the General Directorate of Education (Girls)

السلام عليكم ورحمة الله وبركاته ... وبعد...

يعلم مساعدكم أنني قد بدأت برنامج الدكتوراه في صحة المجتمع بجامعة أدنبرة بالملكة المتحدة ويفضل من الله وتوفيقه فقد أنهيت والله الحمد السنة الأولى في برنامج الدراسة للحصول على درجة الدكتوراه بعد اجتياز المناقشة الخاصة بالسنة الأولى بنجاح والتي اعتمدت تتيحه من قبل مجلس الكلية.

وحيط أن موضوع البحث العلمي الخاص ببرامجي للحصول على درجة الدكتوراه ينافس موضوعاً حيوياً وهما تشغيل الإجابة عليه كافة الأوضاع العلمية المهمة وتبذل فيه الجهود المستمرة فقد وافقت اللجنة المختصة بمناقشة لاعتماد موضوعي الذي يبحث العلاقة السببية بين الزواج الشعبي والوفيات بين الأطفال في السن المبكرة للمرحلة الابتدائية (6-8 سنوات) وإثبات صحة تلك العلاقة.

ومع ذلك يعد ساعدكم حريري الشديد في أن يتفق أبناء طبيباً الطبية على صلاة أمانة السلام من نتائج هذه الدراسة والمساعدة في تسجيلها عالمياً فقد حرصت أن تكون عملية البحث أبناء المدينة المنورة للمرحلة الابتدائية البنين والبنات ، سالما المولى جلت قدرته التوفر المستدام لنتي من حرص مساعدكم.

ودعكم لله وحوض بالبحث العلمي في مدينة المصطفى صلوات الله وسلامه عليه.

لذا أمل من ساعدكم التكرم بالموافقة على إجراء الدراسة في مدارس المنطقة للمرحلة الابتدائية والتوجيه لمن يلزم بتشريع الصناعات التي قد تكون في خلق دائرة للدراسة بما يناسب الأندية الدكتور / عزيز شيخ أستاذ الرعاية الصحية الأولية بكلية الطب جامعة أدنبرة، ومشارف الأكاديمي الأول على دراسي للحصول على درجة الدكتوراه بسومة المدينة المنورة خلال الفترة من (18-12-1429) إلى 7 - 1 - 1430 هـ للتوافق على سبيل العمل والوفر خلال الفترة المخصصة لإجراء الجزء العملي في الدراسة التجريبية، كما يسرني أن أرفق لمساعدكم من طي خطابي هذا مختصر البروتوكول الذي يشرح الخطوات العملية للدراسة.

بتقبلوا مساعدكم وافر التقدير والله يرعاكم... 

الباحث

د/ محمود بن عبد الفتاح نحاس
Appendix (2-C): Study protocol attached to the letters to General directorates translated into Arabic

يرتوكول الدراسة

عنوان الدراسة: التحقق من العلاقة السببية بين الربو الشعبي والسمنة بين أطفال المدارس بمنطقة المدينة المنورة للمرحلة الابتدائية (تعليم البنين والبنات).

مكان أجراء الدراسة: المدارس الابتدائية التعليم البنين والبنات بمنطقة المدينة المنورة.

موعد إجراء الدراسة: الفصل الدراسي الأول للعام 1429/1430 هـ

نطاق الدراسة: المرحلة الأولى/ دراسة مستعرضة a cross-sectional study

لكشف حالات الربو الشعبي بين أطفال المدارس (تحديدا الإصابة بالربو الشعبي) باستخدام استبيان التجري لحالات الربو الشعبي المعد من قبل (ISACA) الدراسات الدولية للربو والحساسية في سن الطفولة.

المرحلة الثانية/ دراسة الحالات والشواهد الصحية. بتحديد Case-control study عدد معينًا من الطلاب والطالبات المصاصبين بالربو الشعبي ومقارنتهم بمجموعة من الطلاب الأصحاء.

أهداف الدراسة: تهدف الدراسة في مرحلتها التجريبية لإيضاح العلاقة السببية بين السمنة والربو الشعبي وكذلك التركيز على مدى إمكانية تطبيق الدراسة على مستوى أكبر ونطاق أوسع بحيث يشمل عدد أكبر من الطلاب والطالبات في مدارس منطقة المدينة المنورة.

لاستفادة الموجبة من الدراسة: بشبكة الله تعالى ستعطي الدراسة مؤشرات واضحة في مسار العلاقة السببية بين السمنة والربو الشعبي لدى الأطفال واستمرار نتائجها بالنفع المباشر لكل طالب وطالبة حيث سيسلم تقرير طبي من الباحث يوضح الوضع الصحي الراهن له ويساعد هذا البحث على إيجاد الوسائل الممكنة لتغذير صحة الأجسام القاامة بإيجاد الطرق والوسائل المناسبة للحد من انتشار هذه المرضين في مملكتنا الحبيبة خاصة ومختلف دول العالم بشكل عام.

مراحل الدراسة: تتضمن المراحل العملية للدراسة إلى مرحلتين رئيستين كما هو موضح:
المرحلة الأولى: تنفيذ الدراسة التجريبية والتي تهدف إلى التحقق من الآلية المفترضة
لتنفيذ الدراسة وتتأكد من جميع المراحل وتشمل مرحلتين:
أ - مرحلة الدراسة المستعرضة للكشف حالات الربو الشبقي بين أطفال المدارس
(تحدي الإصابة بالربو الشبقي) وتوزيع الاستجابات من خلال المدارس وتعيينها من قبل أولياء الأمور والتوقيع عند قبولهم على نموذج شرح
الدراسة والموافقة على اشتراع ابنهم أو ابنتهم في الدراسة.
ب - المرحلة العملية (Case-control study) والتي ستتم داخل المدرسة من قبل الفريق الطبي وسيتم خلالها:
1- تحديد القياسات الحيوية للطفل (الطول، الوزن، سماكة الشحم لدى الأطفال).
2- تحديد كفاءة الرئة باستخدام جهاز قياس كفاءة الرئة
3- إجراء اختبار الحساسية (لعدد من المواد التي يعتقد أنها منتشرة في المملكة العربية السعودية من واقع البحوث السابقة)
4- سحب عينة من الدم (5 سم) لإجراء التحليل المخبري لهذه العينة للمجموعات
التالية: بعض من الهرمونات المشتركة بين السمنة والربو الشبقي، مهيجات الربو الشبقي، بعض أنواع الجينات الوراثية، بعض من أنواع الخلايا المضادة للحساسية في الجسم.

ج - مرحلة تحليل البيانات وتوزيع التقارير على الطلاب ونشر أول ورقة علمية.

المرحلة الثانية: إجراء الدراسة بالشكل الموسع بعد التأكد من حل جميع المعوقات التي
لوحظت في المرحلة الأولى (التجريبية).

هذا وبارك الله التوفيق ثم من سعادتك الدعم والتشجيع ... والله يرعاكم

مع تحيات الباحث

د/ محمود بن عبدالله نحاس
Appendix (2-D): Letter from General Directorate of Boys Department to schools Head teachers

FROM: M. S. H. U.
FAX NO.: 34 824277
Apr. 05 2009 02:32PM P1

للتعميم إلى جميع المدارس الإبتدائية
حسب البيان المرفق

وفق الله

الدكتور محمود بن عبد الفتاح

السلام عليك ورحمة الله ورخاءه...

إذاعة إلى الطلب المقدم من الباحث الدكتور محمود بن عبد الفتاح نحاس ومشغوله خطاب

جامعة أستراليا باستيغلال المتعددة ورغته في تطبيق بحثه بعنوان (بحث اللغة العربية بين مؤثرات كثرة الجمود والربيع الشعبي بين أطفال مدارس في منطقة المدينة المنورة) وذلك

الحصول على درجة الدكتوراه.

عليه نأمل تسهيل مهمة الباحث ورفقى البشري أثناء زيارة المدرسة وتعاون في توزيع

استمرار البحث على جميع الطلاب لتصور الدراسة (الأولى، الثاني والثالث) والمرافقة من طمه.

كم ترغب منكم ترشيح معلمي لديه الرغبة في الانخراط في البحوث كمساهمة بالدرجة للتعاون مع الباحث ويتبع ركائز البحث، علماً بأنه سوف يتم تزويدها في أي وقت من الأوقات من خلال

أيضاً الصحفية في حال مشاركتك في الدراسة بعد توظيفه على المادة الخاصة بالمشاركة ونحن

على رأى أصحابكم بأعمال البحث العلمي التي تساهم في صحة وسلامة أجيال المستقبل من أبناء

طيب الآلهة.

وكتم تحيتي.

د. محمود بن محمد سعيد

madinaedu@admin.madinaedu.gov.sa

هاتف: 012345678910
 Fax: 012345678910
 Email: info@madinaedu.gov.sa
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Appendix (2-E): Letters from General Directorate of Girls Department to schools Head teachers

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Appendix (2-F): Translation of the letter from General Directorate of Boys Department to schools Head teachers

To the head teacher of the (School Name) Primary School
May GOD please Him

Peace, mercy and blessings of God

This letter is in reference to the request from the researcher, Mr. Mahmoud Abdul-Fattah Nahhas, together with a letter from the University of Edinburgh, UK, regarding his research for his PhD entitled, (the causal relationship between indicators of body mass index and asthma among school children in the area of Madinah), and follows a phone call with the Director General of the School of Health at the Ministry of Education, who gave us his agreement to conduct the study. The study will be implemented in cooperation with the Department of Education in Madinah that represents the management of medical supervision of health units and schools for girls and boys.

This study of great international importance and your school has been selected for its excellence in management and its potential to help with the implementation of the study. We hope you will facilitate the research team and help them to complete the study. Please distribute this questionnaire to all students of primary classes (I, II and III) with the information sheet, which is attached with this letter.

Please note that the participation of the students is not mandatory and will not be done without the approval of the guardian who must sign a consent form to participate in this study. In order to facilitate this task, it is hoped you will nominate one of the school teachers, and they will act as a coordinator to communicate with the management of the medical supervision / health units for the preparation and processing of the study, under your supervision.

We will provide parents who have consented for their children to participate in this study with a detailed medical report of the findings by the research team. All data will be confidential.

Your interest in this scientific research will contribute to the health and safety of future generations of our city.

God bless,

General Director of Education in Madinah (Boys’ department)

Dr. Bahjat Mahmoud Junaid

[Attachment:.................]
Appendix (2-G): Translation of the letter from General Directorate of Girls Department to schools Head teachers

To the head teacher of the (School Name) Primary School
May GOD please her

Peace, mercy and blessings of God

This letter is in reference to the request from the researcher, Mr. Mahmoud Abdul-Fattah Nahhas, together with a letter from the University of Edinburgh, UK, regarding his research for his PhD entitled, (the causal relationship between indicators of body mass index and asthma among school children in the area of Madinah), and follows a phone call with the Director General of the School of Health at the Ministry of Education, who gave us his agreement to conduct the study. The study will be implemented in cooperation with the Department of Education in Madinah that represents the management of medical supervision of health units and schools for girls and boys.

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We will provide parents who have consented for their children to participate in this study with a detailed medical report of the findings by the research team. All data will be confidential.

Your interest in this scientific research will contribute to the health and safety of future generations of our city.

God bless,

General Director of Education in Madinah (Girls’ department)

Dr. Yousuf Ali Alfacee

Copy to: The Assistant to the School Affairs
Copy to: The Assistant for Academic Affairs
Copy to: Dr. Mahmoud Nahhas
Copy to: The Director of medical supervision
Copy to: The Director of school health polyclinic (1)
Copy to: The Director of school health polyclinic (2)
Copy to: Communications department
Appendix (2-H): Information for the head teachers

School letter for head teachers

[Head teachers]

Dear [head teacher/school name],

Re: Investigating the relationship between obesity and asthma among school aged children in Madinah Saudi Arabia: pilot study

I am writing to inform you that your school has been selected for the feasibility pilot study that I'm planning to conduct in October 2008. I'm looking for your help and support. I have enclosed a letter; questionnaire and patient information sheet which you need to photocopy and send to pupils parents and ask them to fill it in and return it to the school within three working days. Please do not hesitate to contact me if you require any further information.

Thank you

Yours sincerely

Mahmoud Nahhas

Enclosed: Parents letter, parental information sheet and questionnaires.
Appendix (2-I): Invitation for the parents

Letters of invitation for parents to give permission for their children to take part in the study

[Parents]

Dear [Parents pupils name],

Re: Investigating the relationship between obesity and asthma among school aged children in Madinah Saudi Arabia: pilot study

I am writing to invite you to give permission for your (son’s, daughter’s name) to take a part in the feasibility pilot study that I'm planning to conduct in October 2008. I have enclosed the questionnaire and patient information sheet which you need to complete carefully and send it back to the school within the next three days. Please do not hesitate to contact me if you require any further information.

I'm looking for your help and support.

Thank you

Yours sincerely

Mahmoud Nahhas

Enclosed: parental information sheet and questionnaires.
Appendix (2-J): Parental information sheet

Association between obesity and asthma in school children

PARENTAL INFORMATION SHEET

I am writing to invite you and your child to take part in a research study. Before you decide to participate, please take time to read these information sheets carefully which explain the study and why we are conducting it in greater detail. You may talk to others about the study if you wish.

Please ask the researcher if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

Did you know?

Obesity and asthma are both chronic conditions affecting millions worldwide. Over the last 20 years there has been a rapid increase in the prevalence of both of these conditions.

Globally, obesity has also increased, with an estimated 300 million obese adults worldwide in the year 2000 compared with 200 million in 1995.

Although traditionally thought of as a problem of westernised countries, an estimated 115 million obese adults reside in developing countries.

The prevalence of adult and child asthma is also increasing globally. In Saudi Arabia about two million people suffer from asthma.

What is the purpose of this study?

This study will determine the prevalence of asthma as well as investigating the relationship between adiposity and asthma among Saudi school children with a focus on assessing possible mechanical and immunological causal pathways.
Why has my child been invited to participate?

Your child is a student at Madinah primary school where this study is being conducted and as such is eligible to take part. In doing so, he/she will help us investigate the relationship between the two conditions.

Do I have to give permission for my child to take part?

You will need to give permission for your child to take part. It is up to you to decide. If you agree, we will discuss the study in greater detail and then ask you to sign a consent form that will give us permission to study your child. However, your child is able to withdraw from the study at any time without giving a reason. This would not affect the standard of care they receive from the School Health Department.

What will happen to my child if (he/she) takes part?

The study will be conducted at your child’s school by a well-trained and qualified team from the School Health Department and will consist of two phases:

Phase one:

Once you complete and return the reply form in this information pack to the School we will send you a questionnaire form to complete and return to the school. Based on your answers to the questionnaire the researcher, Mr Mahmoud Nahhas, will contact you to discuss the study and phase two with you and he is happy to answer any further questions.

Are any medicines or treatments involved in this study?

No, this is simply an examination study to tell us more about the causal relationship between adiposity and asthma.

What are the possible risks of taking part?

None.

What are the possible benefits of taking part?

We hope the knowledge gained will help to investigate the prevalence of asthma in Madinah.
Will my taking part in the study be kept confidential?
Yes. Answering the questionnaire will be kept strictly confidential and all emerging data will be anonymous.

What will happen if I don’t want my child to carry on with the study?
Your child is free to withdraw from the study at any time. If your child does withdraw, we will use the information already collected up to that point only with your consent. If you do not consent, we will destroy the letter received from you.

What if there is a problem?
Any complaint about the way you have been dealt with in the study will be addressed. If you wish to speak to someone about this you can contact: Professor Aziz Sheikh, General Practice section, Division of Community Health Sciences, The University of Edinburgh, 20 West Richmond Street, Edinburgh, EH8 9DX

Who is carrying out this study?
This study is being undertaken as part of a PhD research project by Mr Mahmoud Nahhas at The University of Edinburgh’s Division of Community Health Sciences. The aim of this study is to improve the delivery of care to patients with asthma. This study has been funded by the Ministry of Higher Education, Kingdom of Saudi Arabia under the supervision of the General Directorate of School Health Department In (Boys and Girls Department–Ministry of Education, Riyadh, Saudi Arabia).

What should I do now?
If you decide that you would like your child to take part in this study, please fill in the response form as well as the questionnaire and send it to the school in the envelope that has been provided.

I want to know more about the study before I decide.
If you would like more information about the study, you can speak to Mr. Mahmoud Nahhas who is the person responsible for the study, Division of Community Health Sciences: GP Section, The University of Edinburgh Levinson House 20 West Richmond Street Edinburgh EH8 9DX
Appendix (2-K): Consent forms

Association between obesity and asthma in school children

PARENTAL CONSENT FORM

Centre no:-----------------------------
Study no:-----------------------------
Participant identification number:--------------------------

Name of researcher: Mr. Mahmoud Nahhas

1. I confirm that I have read and understood the information sheet dated……..(Version ……..) for the above study .I have had the opportunity to answer all the questions in the questionnaires.

2. I understand that my child’s participation is voluntary and that he/she is free to withdraw at any time without giving any reason.

3. I agree with my child taking part in the above study.

____________________            _______________            _______________
Name of father            Date            Signature

____________________            _______________            _______________
Researcher            Date            Signature

When completed, 1 for Parent of child; 1 for researcher site file; 1 (original) to be kept in study file.

Thank you for taking the time to complete this consent form

Please give to Mahmoud Nahhas
Appendix (2-L): Reminder letter

Association between obesity and asthma in school children

Dear [Parents pupils name],

Re: Investigating the relationship between obesity and asthma among school aged children in Madinah Saudi Arabia: pilot study

I am writing to remind you about a letter sent to you on (Data) to give permission for your (Son, daughter name) to take a part in the feasibility pilot study that I am planning to conduct in October 2008 to investigate the relationship between obesity and asthma among the children. I have enclosed the questionnaire and parental information sheet which you have not yet sent back to school to inform whether you agree/ or not that your (son /daughter) is permitted to take part in the study or not. Could you please send me your reply within the next two working days and do not hesitate to contact me if you require any further information.

I am looking for your help and support.

Thank you

Yours sincerely

Mahmoud Nahhas
**Appendix 3: Pilot study GANTT Chart**

<p>| M/D | S | S | M | T | W | T | F | S | S | M | T | W | T | F | S | S | M | T | W | T | F | S | S | M |
| Oct | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |
|     |  28 | 29 | 30 | 31 |
| Nov | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
|     | 30 | 31 |
| Dec | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| Jan. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 |
|     | 27 | 28 | 29 | 30 | 31 |</p>
<table>
<thead>
<tr>
<th>No</th>
<th>Work to do</th>
<th>Starting date</th>
<th>Last date</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The total period of the pilot study</td>
<td>11 / 10 / 2008</td>
<td>23 / 1 / 2009</td>
<td>15 weeks</td>
</tr>
<tr>
<td>2</td>
<td>Training of the professionals and administrative activities</td>
<td>11 / 10 / 2008</td>
<td>12 / 10 / 2008</td>
<td>2 days</td>
</tr>
<tr>
<td>3</td>
<td>Presentation for head teachers (Boys Department)</td>
<td>13 / 10 / 2008</td>
<td>13 / 10 / 2008</td>
<td>1 day</td>
</tr>
<tr>
<td>4</td>
<td>Presentation for head teachers (Girls Department)</td>
<td>14 / 10 / 2008</td>
<td>14 / 10 / 2008</td>
<td>1 day</td>
</tr>
<tr>
<td>5</td>
<td>Sending the questionnaire to the schools</td>
<td>15 / 10 / 2008</td>
<td>15 / 10 / 2008</td>
<td>1 day</td>
</tr>
<tr>
<td>6</td>
<td>Collecting the result from schools</td>
<td>18 / 10 / 2008</td>
<td>31 / 10 / 2008</td>
<td>2 weeks</td>
</tr>
<tr>
<td>7</td>
<td>Starting the field work (visiting schools)</td>
<td>1 / 11 / 2008</td>
<td>5 / 12 / 2008</td>
<td>5 weeks</td>
</tr>
<tr>
<td>8</td>
<td>Receiving all the laboratory result (deadline)</td>
<td>6 / 12 / 2008</td>
<td>12 / 12 / 2008</td>
<td>1 week</td>
</tr>
<tr>
<td>9</td>
<td>Data analysis and interpretation</td>
<td>13 / 12 / 2008</td>
<td>9 / 1 / 2008</td>
<td>4 weeks</td>
</tr>
<tr>
<td>10</td>
<td>Writing up the report</td>
<td>10 / 1 / 2009</td>
<td>23 / 1 / 2009</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>
Appendix 4: Two days course timetable of training program for research team

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30-9:00</td>
<td>Welcome and introduction to research in general</td>
<td>Asthma; definition, epidemiology, relationship with obesity</td>
</tr>
<tr>
<td>9:00-9:30</td>
<td>Orientation to the proposed research and highlighting the objectives and study population</td>
<td>Training on respiratory assessing questionnaire</td>
</tr>
<tr>
<td>9:30-10:00</td>
<td>Obesity; definition, epidemiology and measurement</td>
<td>Blood test</td>
</tr>
<tr>
<td>10:00-10:30</td>
<td>Coffee break</td>
<td>Coffee break</td>
</tr>
<tr>
<td>10:30-11:30</td>
<td>Practical training on anthropometric measurement</td>
<td>Practical training on pulmonary function measurements</td>
</tr>
<tr>
<td>11:30-12:30</td>
<td>Praying Dohor</td>
<td>Praying Dohor</td>
</tr>
<tr>
<td>12:30-1:30</td>
<td>Practical training on measuring weight and height</td>
<td>Procedures and training on sampling the study students</td>
</tr>
<tr>
<td>1:30-2:30</td>
<td>Practical training on skin fold measurements</td>
<td>Practical training on skin prick test</td>
</tr>
</tbody>
</table>
Appendix 5: Evaluation sheet

Appendix (5-A): Evaluation sheet for healthcare professional (research team) on the training course

1. Overall how would you rate the training course?  
   Do you have any general comments?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>😞</td>
<td>😞</td>
<td>😊</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

   Please circle one number

   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………

2. Did the training course meet your expectations? Yes/No – please explain:

   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………

3. Am I satisfied with the duration of the training course?  
   Yes/No – please explain:

   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………

4. Do you think the training course gave you some new ideas or skills that will help you in the future? Yes/No – please explain

   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………
   ……………………………………………………………………………………………………
5. Overall, how would you rate the anthropometric measurement technique?
Do you have any general comments?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>😞</td>
<td>😐</td>
<td>😊</td>
</tr>
</tbody>
</table>

| 1 | 2 | 3 | 4 | 5 | 6 |

Please circle one number

6. Overall, how would you rate the pulmonary function test technique?
Do you have any general comments?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>😞</td>
<td>😐</td>
<td>😊</td>
</tr>
</tbody>
</table>

| 1 | 2 | 3 | 4 | 5 | 6 |

Please circle one number

7. Overall, how would you rate the skin prick test technique?
Do you have any general or comments?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>😞</td>
<td>😐</td>
<td>😊</td>
</tr>
</tbody>
</table>

| 1 | 2 | 3 | 4 | 5 | 6 |

Please circle one number
8. Overall, how would you rate the blood sample technique?
Do you have any general or comments?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>😞</td>
<td>😐</td>
<td>😊</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Please circle one number

Thank you for taking the time to complete this questionnaire

Please give to Mahmoud Nahhas
Appendix (5-B): Evaluation sheet for healthcare professionals (research team) on ISAAC questionnaire and Phase I

1. Overall, how would you rate the questions asked in the questionnaire?

<table>
<thead>
<tr>
<th>Poor</th>
<th>Okay</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>☹</td>
<td>😊</td>
<td>☻</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Please circle one number

……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
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……………………………………………………………………………………………………
……………………………………………………………………………………………………

2. Do you think that the questions asked of the parents were straightforward and easy to be answered? Yes/No – please explain

……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………

3. Do you think there are some more questions which need to be added to the questionnaire? Yes/No – please write them:

……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
……………………………………………………………………………………………………
4. Do you have any general comments in this part of the study?

........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
........................................................................................................................................

Thank you for taking the time to complete this questionnaire

Please give to Mahmoud Nahhas
Appendix 6: ISAAC questions

Appendix (6-A): Core demo questions

<table>
<thead>
<tr>
<th>Core questionnaire wheezing module for 6–7 year olds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has your child ever had wheezing or whistling in the chest at any time in the past?</td>
</tr>
<tr>
<td>Yes [ ] No [ ]</td>
</tr>
<tr>
<td>IF YOU ANSWERED &quot;NO&quot; PLEASE SKIP TO QUESTION 6</td>
</tr>
</tbody>
</table>

| 2. Has your child had wheezing or whistling in the chest in the last 12 months? |
| Yes [ ] No [ ] |
| IF YOU ANSWERED "NO" PLEASE SKIP TO QUESTION 6 |

| 3. How many attacks of wheezing has your child had in the last 12 months? |
| None [ ] 1 to 3 [ ] 4 to 12 [ ] More than 12 [ ] |

| 4. In the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing? Never woken with wheezing [ ] Less than one night per week [ ] One or more nights per week [ ] |

| 5. In the last 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths? |
| Yes [ ] No [ ] |

| 6. Has your child ever had asthma? Yes [ ] No [ ] |

| 7. In the last 12 months, has your child's chest sounded wheezy during or after exercise? |
| Yes [ ] No [ ] |

| 8. In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or a chest infection? |
| Yes [ ] No [ ] |

<table>
<thead>
<tr>
<th>Core questionnaire rhinitis module for 6–7 year olds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has your child ever had a problem with sneezing, or a runny, or a blocked nose when he/she DID NOT have a cold or the flu?</td>
</tr>
<tr>
<td>Yes [ ] No [ ]</td>
</tr>
<tr>
<td>IF YOU ANSWERED &quot;NO&quot; PLEASE SKIP TO QUESTION 6</td>
</tr>
</tbody>
</table>

| 2. In the past 12 months, has your child had a problem with sneezing, or a runny, or a blocked nose when he/she DID NOT have a cold or the flu? |
| Yes [ ] No [ ] |
| IF YOU ANSWERED "NO" PLEASE SKIP TO QUESTION 6 |

| 3. In the past 12 months, has this nose problem been accompanied by itchy-watery eyes? |
| Yes [ ] No [ ] |

| 4. In which of the past 12 months did this nose problem occur? (please tick any which apply) |
| January [ ] February [ ] March [ ] April [ ] May [ ] June [ ] July [ ] August [ ] September [ ] October [ ] November [ ] December [ ] |

| 5. In the past 12 months, how much did this nose problem interfere with your child's daily activities? |
| Not at all [ ] A little [ ] A moderate amount [ ] A lot [ ] |

| 6. Has your child ever had hay fever? |
| Yes [ ] No [ ] |
### Core questionnaire eczema module for 6–7 year olds

1. Has your child ever had an itchy rash which was coming and going for at least 6 months?
   - Yes [ ] No [ ]

   **IF YOU ANSWERED "NO" PLEASE SKIP TO QUESTION 7**

2. Has your child had this itchy rash at any time in the last 12 months?
   - Yes [ ] No [ ]

   **IF YOU ANSWERED "NO" PLEASE SKIP TO QUESTION 7**

3. Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?
   - Yes [ ] No [ ]

4. At what age did this itchy rash first occur?
   - Under 2 years [ ] Age 2–4 [ ] Age 5 or more [ ]

5. Has this rash cleared completely at any time during the last 12 months?
   - Yes [ ] No [ ]

6. In the last 12 months, how often, on average, has your child been kept awake at night by this itchy rash?
   - Never in the last 12 months [ ] Less than one night per week [ ] One or more nights per week [ ]

7. Has your child ever had eczema?
   - Yes [ ] No [ ]
Appendix (6-B): ISAAC Core Questionnaire for 6-7 year olds

Core questionnaire for wheezing and asthma

1 Has your child ever had wheezing or whistling in the chest at any time in the past?
   Yes ☐
   No ☐

   IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

2 Has your child had wheezing or whistling in the chest in the past 12 months?
   Yes ☐
   No ☐

   IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

3 How many attacks of wheezing has your child had in the past 12 months?
   None ☐
   1 to 3 ☐
   4 to 12 ☐
   More than 12 ☐

4 In the past 12 months, how often, on average, has your child’s sleep been disturbed due to wheezing?
   Never woken with wheezing ☐
   Less than one night per week ☐
   One or more nights per week ☐

5 In the past 12 months, has wheezing ever been severe enough to limit your child’s speech to only one or two words at a time between breaths?
   Yes ☐
   No ☐

6 Has your child’s ever had asthma?
   Yes ☐
   No ☐

7 In the past 12 months, has your Child’s chest sounded wheezy during or after exercise?
   Yes ☐
   No ☐

8 In the past 12 months, has your Child’s had a dry cough at night, apart from a cough associated with a cold or chest infection?
   Yes ☐
   No ☐
Core questionnaire for rhinitis

All questions are about problems which occur when your child’s DO NOT have a cold or the flu.

1. Have your child ever had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?  
   - Yes  
   - No

IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

2. In the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she DID NOT have a cold or the flu?  
   - Yes  
   - No

IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

3. In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?  
   - Yes  
   - No

4. In which of the past 12 months did this nose problem occur? (Please tick any which apply)
   - January  
   - February  
   - March  
   - April  
   - May  
   - June  
   - July  
   - August  
   - September  
   - October  
   - November  
   - December

5. In the past 12 months, how much did this nose problem interfere with your child’s daily activities?  
   - Not at all  
   - A little  
   - A moderate amount  
   - A lot

6. Have your child ever had hay-fever?  
   - Yes  
   - No
Core questionnaire for eczema

1. Has your child ever had an itchy rash which was coming and going for at least six months?  
   - Yes  
   - No  

   IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

2. Has your child had this itchy rash at any time in the past 12 months?  
   - Yes  
   - No  

   IF YOU HAVE ANSWERED “NO” PLEASE SKIP TO QUESTION 6

3. Has this itchy rash at any time affected any of the following places:  
   - Yes  
   - No  

   the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?

4. At what age did this itchy rash first occur?  
   - Yes  
   - No  

5. Has this rash cleared completely at any time during the last 12 months?  
   - Yes  
   - No

6. In the last 12 months, how often, on average, has your child been kept awake at night by this itchy rash?  
   - Never in the last 12 months  
   - Less than one night per week  
   - One or more nights per week

7. Has your child ever had eczema?  
   - Yes  
   - No

Thank you for taking the time to complete this questionnaire

Please give it to Mahmoud Nahhas
Appendix (6-C): Environmental Questionnaire

1. How much does your child weigh?: [ ] kg / stone / pounds
   (please circle the measurement you used)

2. How tall is your child?: [ ] metres / centimetres / feet and inches
   (please circle the measurement you used)

3. In the past 12 months, how often, on average, did your child eat or drink the following?: (Please leave blank if you do not know what a food is)

<table>
<thead>
<tr>
<th>Food Description</th>
<th>Never or occasionally</th>
<th>Once or twice per week</th>
<th>Three or more times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat (e.g. beef, lamb, chicken, pork)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seafood (including fish)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables (green and root)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulses (peas, beans, lentils)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cereal (including bread)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pasta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rice</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Margarine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potatoes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fast food/burgers</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4. How many times a week does your child engage in vigorous physical activity long enough to make him/her breathe hard?:
   
   Never or occasionally
   Once or twice per week
   Three or more times a week

5. During a normal week, how many hours a day (24 hours) does your child watch television?:
   
   Less than 1 hour
   1 hour but less than 3 hours
   3 hours but less than 5 hours
   5 hours or more

6. In your house, what fuel is usually used for cooking?:
   
   Electricity
   Gas
   Open fires
   Other – Please specify

7. In your house, what fuel is usually used for heating?:
   
   Electricity
   Gas, kerosene, paraffin
   Wood, coal, oil
   Other – Please specify
8. In the first 12 months of your child’s life, did you usually give paracetamol (e.g. Panadol, Pamol) for fever?:
   Yes [ ]
   No [ ]

9. In the past 12 months, how often, on average, have you given your child paracetamol (e.g. Panadol, Pamol)?:
   Never [ ]
   At least once a year [ ]
   At least once per month [ ]

10. In the first 12 months of life, did your child have any antibiotics?:
    Yes [ ]
    No [ ]

11. How many older brothers and sisters does your child have?:
    [ ] brothers and sisters

12. How many younger brothers and sisters does your child have?:
    [ ] brothers and sisters

13. Was your child born in (NZ - See instructions)?:
    Yes [ ]
    No [ ]
14. How many years has your child lived in (NZ - see instructions)?: □ years

15. What level of education has the child’s mother received?: (local wording)
   Primary school
   Secondary school
   College, university or other form of tertiary education

16. How often do trucks pass through the street where you live, on weekdays?:
   Never
   Seldom
   Frequently through the day
   Almost the whole day

17. What was the weight of your child when he/she was born?: □ kg / stone / pounds
   (please circle the measurement you used)

18. Was your child breastfed?:
   Yes
   No
19. Did you have a cat in your home during the first year of your child’s life?:
   Yes
   No

20. In the past 12 months, have you had a cat in your home?:
   Yes
   No

21. Did you have a dog in your home during the first year of your child’s life?
   Yes
   No

22. In the past 12 months, have you had a dog in your home?:
   Yes
   No

23. In your child’s first year of life did he/she have regular (at least once a week) contact with farm animals (e.g. cattle, pigs, goats, sheep or poultry)*?:
   Yes
   No
24. Has this child’s Mother had regular (at least once a week) contact with farm animals (e.g. cattle, pigs, goats, sheep or poultry) while being pregnant with this child?

   Yes ☐
   No ☐

25. Does your child’s mother (or female guardian) smoke cigarettes?

   Yes ☐
   No ☐

   If YES, about how many cigarettes does the child’s mother (or female guardian) smoke each day? ☐ number of cigarettes

26. Does your child’s father (or male guardian) smoke cigarettes?

   Yes ☐
   No ☐

   If YES, about how many cigarettes does the child’s father (or male guardian) smoke each day? ☐ number of cigarettes

27. Did your child’s mother (or female guardian) smoke cigarettes during your child’s first year of life?

   Yes ☐
   No ☐

28. How many people living in the house smoke cigarettes, including parents? ☐ people

Thank you very much for your help with this questionnaire. We appreciate your assistance.
Appendix 7: Anthropometric measurements

What are Anthropometrics?

The term anthropometric refers to comparative measurements of the body. Anthropometrics are physical measurements like height, weight, length, and waist circumference. Once measured these values are plotted on the appropriate growth chart.

Equipment

For anthropometric measurements (weight, height, waist circumference and skinfold thickness) the following equipment is needed:

Calibration weights:
Double beam floor model scale or electronic digital scale
Portable scales:
Skinfold calipers:
Steel measuring tape:
Height adjustment ruler:

Weighing Children

Preparation

1. Balance the scale at zero before each use:

Many digital scales are self-zeroing. However, you may have to push a button to zero it.

For the beam balance, move both weights left to zero before each use. If the scale does not balance at the midpoint, adjust the counterweight until it does.

2. Weigh children and adults in light indoor clothing and without shoes
**Procedure**

Have the client stand in the centre of the scale.

For beam balance:

- Move the larger weight to the right until the indicator arrow drops below the centre.

- Move the larger weight back to the left one segment to move the indicator arrow slightly above the midpoint.

- Move the smaller weight to the right until the indicator arrow balances at the midpoint.

Read the measurement and record it to the nearest 0.1 Kg. (Be sure to read the indicator arrow on the beam scale at eye level. Avoid reading the indicator arrow at varying heights and distances.)
*Note: Make sure your digital scale is electronic, not a spring balance scale. Spring balance scales are not as accurate. You can tell if a digital scale is a spring balance scale by asking the manufacturer and/or checking to see if the scale moves or jiggles when pressure is applied. Spring balance scales will move or jiggle when pressure is applied.

**Guidelines for Maintaining Scales**

- Scales should be checked for accuracy and calibrated (adjusted) if necessary:
  - At time of purchase
  - Each time the scale is moved
  - At least annually.

Research staff should not try to adjust digital/electronic scales. If adjustment is necessary, please contact the manufacturer.

- Floor scales should be installed on a firm, level surface. Infant scales should be stationed on a solid table or counter that does not rock or vibrate.

- Scale should be kept free from debris and away from drafts or motors that create air currents or vibration.

- Be sure you know the capacity of the scale. Overloading an electronic scale may cause damage.

- Maintain scales in a ‘private’ location.
Measuring Height

Equipment

• Measuring board with tape and moveable headboard or a metal tape attached to a flat wall and a separate headboard. (The rod on the scales should not be used to measure height. It is not accurate.)

• The wall should not have cladding or baseboard and the floor should not have a plush carpet.

Who to Measure in Standing Position

• Adults

• Children who are 24 months and older who are able/willing to stand.

Note: Children 2 -3 years who cannot/will not stand and/or measure less than 76.2 Centimeter and/or weigh less than 9 Kilogram must be measured in the recumbent position and plotted on the 0 - 36 month growth chart. Children who are measured standing must be plotted on the 2-20 chart. (It does not matter if these children are weighed on the infant or the adult scale.)

Preparation

1. Disinfect the headboard surface. Wash your hands.

2. Children should have thick socks, shoes, and jackets or any bulky clothing removed. Adults should remove coats, jackets, and shoes. Remove any hair ornaments or braids on top of head.

Procedure

1. Have the child or adult stand with back against the measuring surface with feet together flat on the floor, arms at side and knees and back straight. When possible, head, heels, buttocks and shoulder blades should touch the measuring surface. (Some individuals may not be able to maintain all four contact points.)
2. With the person looking straight ahead, slide the headboard gently down to the head, compressing the hair. Be sure that the headboard is level and at right angles to the tape and that the heels are still flat against the floor.

3. With your eyes level with the indicator, read the height to the nearest 1/8 inch and jot this figure down. If necessary, use a footstool to read the tape at eye level.

4. Have the person step away, and then repeat the procedure again.

5. Compare the two measurements. If they agree within 1/4 inch, record the second reading. If they do not agree within 1/4 inch, repeat the procedure until two measurements agree.
Appendix 8: Waist Circumference measurement

**Equipment**

- Flexible, non-stretchable, narrow steel tape measure.

**Position of waist circumference measurement**

The subject is to stand comfortably with his or her weight evenly distributed between both feet and the feet about 25-30cm apart. The measurement is taken on the line of the umbilicus in a horizontal plane. The observer sits by the side of the subject and fits the measuring tape snugly but not so tightly as to compress underlying soft tissues. It is strongly recommended that a flexible but inelastic tape be used. The circumference is measured to the nearest 0.1cm at the end of normal expiration. Minimal clothing should be worn and preferably no clothing over the measurement site.

**Procedure**

1. Participants are asked to remove their clothes, except for light underwear. If this is not possible, for example due to cultural reasons, the alternative is to measure the circumference on the subject without heavy outer garments and record this fact in the data collection form. Tight clothing, including the belt, should be loosened and the pockets emptied.
2. The measurer should stand at the side of the participant in order to have a clear view of the mirror.
3. Participants should be standing with their feet fairly close together (about 12-15 cm) with their weight equally distributed to each leg. Participants are asked to breathe normally; the reading of the measurement should be taken at the end of gentle exhaling. This will prevent subjects from contracting their abdominal muscles or from holding their breath.
4. The measuring tape is held firmly, ensuring its horizontal position. Use the grid lines on the mirror to verify that the tape position is horizontal all around the waist. The tape should be loose enough to allow the observer to place one finger between the tape and the subject's body.
5. Measurements are recorded to the resolution of the tape (nearest millimetre/half centimetre).

Abdominal (waist) circumference mark

Measuring tape position for waist circumference
Quality control

During the survey

Quality control measures during the survey involve checking and re-calibrating of equipment and monitoring of the performance of the measurers.

The checking and re-calibrating of equipment should occur at regular device-dependent intervals. A log book of the checking and recalibrations need to be kept.

For monitoring the performance of the measurers the following information should be checked routinely for each measurer (if the data management allows this):

1. Distribution of terminal digit for
   I. weight measurement;
   II. height measurement;
   III. a waist circumference measurement;

2. Distribution of terminal digits for full kilograms for weight measurement.

3. Mean and standard deviation of
   I. weight measurement;
   II. height measurement;
   III. a waist circumference measurement;

4. Recording of reasons for measurements that were not performed.

5. Daily work load, to avoid fatigue.

If any problems are detected they need to be discussed with the individual measurer immediately. Just letting the measurer know that he/she has problems with the measurement procedures may correct the errors. If this does not produce results and errors persist, the measurer should be retrained or dismissed.
Supervisor should make surprise visits to the examination sites and observe the measurers, recording the compliance with the protocol in performance evaluation forms that can later be used to review the audit with the measurers. The auditors could also act as guest participants and take part in all anthropometric measurements.

**After the survey**

After the survey it is important to check the overall quality of anthropometric measurements. The retrospective quality assessment will discover problems that may have slipped through the control measures during the survey. It is also needed to ensure that results are accurate and comparable with other studies before they can be published.

The retrospective quality assessment is made on the pooled data of all measurers and should include:

1. Item response rates for
   - I. weight measurement;
   - II. height;
   - III. a waist circumference measurement;
2. Distribution of terminal digits for
   - I. weight measurement;
   - II. height measurement;
   - III. a waist circumference measurement;
3. Distribution of terminal digits for full kilograms for weight measurement.
Appendix 9: Triceps skinfold measures (TSFT)

The triceps skinfold is measured at the upper arm mid-point mark on the posterior surface of the right upper arm. The arm circumference is measured on the right arm at the level of the upper arm mid-point mark. The examiner makes this mark on the posterior surface of the arm immediately after measuring the upper arm length.

Equipment
Skin-fold Calliper

The procedures for making the mid-arm circumference mark:

1. **Position the child**: Ask the child to turn so that you stand facing his or her right side. Have the participant stand upright with the weight evenly distributed on both feet, the shoulders relaxed, and the right arm hanging loosely at the sides. Flexing or tightening the arm muscles will yield an inaccurate measurement.

2. **Take the measurement**: Continue to stand facing the right side of the child. Do not stand behind the child for this measurement. Wrap the measuring tape around the arm at the level of the upper arm mid-point mark. Position the tape perpendicular to the long axis of the upper arm. Pull the two ends of the overlapping tape together so that the zero-end sits below the measurement value and the result lies on the lateral aspect of the arm (not the posterior surface). Check that the tape fits snug around the arm but does not compress the skin. Take the measurement to the nearest 0.1 cm.
Procedure

1. **Position the child:** Ask the child to turn so that you stand behind his or her right side. Have the participant stand upright with the weight evenly distributed on both feet, the shoulders relaxed, and the arms hanging loosely at the sides. Flexing or tightening the arm muscles will yield an inaccurate measurement.

2. **Grasp the skin-fold:** Using your thumb and index finger, grasp a fold of skin and subcutaneous adipose tissue approximately 2.0 cm above the mid-arm circumference mark. If you have difficulty separating the skin-fold from the triceps muscle, start at the elbow where the tissue tends to be looser and work your way up to the mark. Ensure that the skin-fold consists of a double thickness and sits parallel to the long axis of the arm.

3. **Position the calliper:** Holding the skinfold 2.0 cm above the circumference mark, place the tips of the calliper jaws over the complete skin-fold. Ensure that the mark remains in the centre between the tips and that the jaws sit perpendicular to the length of the skinfold. The picture below shows the correct placement of the calliper for this measurement.

4. **Take the measurement:** Continue to hold the skin-fold in place and release the calliper handle to exert full tension on the skin-fold. Wait 3 seconds for the needle on the calliper dial to settle on an accurate measurement. Read the thickness to the nearest 0.1 mm.

5. **Record the result:** Record this result to the recording sheet Remove the calliper jaws then let go of the skin-fold. Proceed to the next measure.
Appendix 10: Pulmonary function test

Overview of spirometry

- Definition of Spirometry

Spirometry is a medical screening test that measures various aspects of breathing and lung function. It is performed by using a Spirometer, a special device that registers the amount of air a subject inhales or exhales and the rate at which the air is moved into or out of the lungs. Spirograms are tracings or recordings of the information obtained from the test. The most common spirometric tests require that the subject exhale as forcefully as possible after taking in a full, deep breath. The subject's effort is called the forced expiratory manoeuver.

- Types of Spirometers

There are two types of Spirometers: 1) those that record the amount of air exhaled or inhaled within a certain time (volume) and 2) those that measure how fast the air flows in or out as the volume of air inhaled or exhaled increases (flow). Both are used in screening for lung disease.

What we can measure by Spirometer?

The most common measurements used are:

- **FEV1 - Forced Expiratory Volume in one second.** This is the amount of air we can blow out within one second. With normal lungs and airways we can normally blow out most of the air from our lungs within one second.

- **FVC - Forced Vital Capacity.** The total amount of air that we blow out in one breath.

- **FEV1 divided by FVC (FEV1/FVC).** Of the total amount of air that we can blow out in one breath, this is the proportion that we can blow out in one second.
What these measurements can show

A Spirometry reading usually shows one of four main patterns:

- Normal
- An obstructive pattern

Normal

Normal readings vary, depending on age, size, and sex. The ranges of normal readings are published on a chart, and doctors and nurses refer to the chart when they check the Spirometry readings.

An obstructive pattern - typical of diseases that cause narrowed airways

If the airways are narrowed, then the amount of air that can blow out quickly is reduced. So, the FEV1 is reduced and the ratio FEV1/FVC is lower than normal. As a rule, that is likely to indicate a disease that causes narrowed airways if:

- FEV1 is less than 80% of the predicted value for the age, sex and size, or
- FEV1/FVC ratio is 0.7 or less.

However, with narrowed airways, the total capacity of the lungs is often normal or only mildly reduced. So, with an obstructive pattern the FVC is often normal or near normal. The main conditions that cause narrowing of the airways and an obstructive pattern of Spirometry are asthma and chronic obstructive pulmonary disease (COPD). So, Spirometry can help to diagnose these conditions. Spirometry can also help to assess if treatment (inhalers etc) help the airways as the readings will improve if the narrowed airways become wider. As a guide, the following values help to diagnose COPD and its severity:

- COPD unlikely - FEV1 is 80% or more of the predicted value for the age, size and sex
- Mild airflow obstruction - FEV1 is 50-80% of the predicted value
• Moderate airflow obstruction - FEV1 is 30-49% of the predicted value

• Severe airflow obstruction - FEV1 is 30% or less of the predicted value

**A restrictive pattern - typical of certain lung diseases**

With a restrictive Spirometry pattern the FVC is less than the predicted value for the age, sex and size. This is caused by various conditions that affect the lung tissue itself, or affect the capacity of the lungs to expand and hold a normal amount of air. For example, conditions that causes fibrosis or scarring of the lung such as pneumoconiosis. Or, any other physical deformity that may restricts the expansion of the lungs. The FEV1 is also reduced but this is in proportion to the reduced FVC. So, with a restrictive pattern the ratio of FEV1/FVC is normal.

**A combined obstructive / restrictive pattern**

With this it may indicate two conditions, for example, asthma plus another lung disorder. Also, some lung conditions have features of both an obstructive and restrictive pattern. For example, with cystic fibrosis there is a lot of mucus in the airways which causes narrowed airways, and damage to the lung tissue may also occur.

**Is preparation needed before having Spirometry?**

The instructions may include such things as not to use a bronchodilator inhaler for a set time before the test (several hours or more, depending on the inhaler).

Not to have:

• Alcohol

• A heavy meal before Spirometry testing.

• Vigorous exercise for a few hours before the test.

• Ideally, not smoke for 24 hours before the test.

• Empty the bladder right before testing.
What is the risk in having Spirometry?

Spirometry is a very low risk test. However, blowing out hard can increase the pressure in your chest, abdomen and eyes. So, you may be advised not to have Spirometry if you have:

- Unstable angina
- Had a recent pneumothorax (air trapped beneath the chest wall)
- Had a recent heart attack or stroke
- Had recent eye or abdominal surgery
- Coughed up blood recently and the cause is not known.

Lung function tests

Lung function tests are performed by respiratory physiologists within a dedicated lung function laboratory.

A lung function test aims to evaluate how well the lungs are working. The most commonly performed tests are used to measure lung volumes, airway functioning and the efficiency of gas exchange.

These tests allow us to take baseline measurements and monitor lung function over time. They will assist the medical team throughout the child’s care and can be performed from the age of around three to four years.

We aim to make lung function tests fun and enjoyable for the child by creating a comforting environment.

What happens before the test?

If the test is being performed as an outpatient you will receive an appointment letter in the post. If your child is having a lung function test as an inpatient, the ward will arrange it and let you know when the appointment will take place. The medical team who request the test will explain in detail the requirement of the test and answer any questions. When you arrive at the lung function lab, you and your child will be greeted by a clinical physiologist. The physiologist will explain the test and will be happy to answer any questions. Prior to the test we will measure your child’s height and weight.
What do the tests involve?

The lung function laboratory has a number of machines designed to test different aspects of your child’s lung function. Below is a brief description of some of the tests your child may perform:

**Spirometry**

This test looks at how fast you can blow air out through the airways. This allows us to measure the flow of air from your lungs. Your child will be asked to breathe in until their lungs are completely filled with air before blowing out as hard and as fast as they can through a mouthpiece into a measuring device.

**Lung volumes**

For this test your child will sit inside a cubicle that looks similar to a telephone box. During the time in the box your child will perform a range of breathing exercises, which will allow us to calculate the volume of air in the lungs.

**Gas transfer**

This test measures how easily oxygen is transferred across the lung and into the blood. Your child will be asked to breathe in one very big breath of a harmless gas, and hold it in their lungs for about ten seconds before blowing it out again. We also perform basic exercise tests and other, more specialised, tests when required. The tests rely on patient effort, so we will give your child plenty of encouragement to help them to achieve reliable results. We have a range of games and incentives built into the testing programmes to make the test enjoyable and easy for your child.

**How long does the test last?**

The testing can last from between 15 to 90 minutes, depending on the number of different tests that are required. Your appointment letter will give an approximate duration of the test. We try to maintain your child’s interest throughout testing by making the experience as enjoyable as possible and allowing time to rest between tests.
How long until we get the results?

If you have an appointment to see the doctor on the same day as the test, a copy of the results will be given to you. If you are not seeing the doctor on the day of your test, we will send a report so it is available for your next appointment. At this time the doctor will be able to explain the result to you.
Appendix 11: Skin prick test

Skin prick test to aeroallergens

Principle
An allergen is introduced superficially into the skin and the response after 15 minutes is recorded.

*Check that baby has not had anti-histamines for at least 24 hours

Materials
- Negative control
- Positive control (Histamine Dihydrochloride 10mg/ml)
- Allergen extracts (cat, pollen, cockroach, desert weeds and house dust mite) in solution
- Alcohol swabs
- Skin prick test station containing: sterile disposable lancets, transparent ruler, ballpoint pen
- Watch or clock
- Adrenaline injection 1 in 1000 (0.10mg/kg)
- Tissues
- Container for used lancets

Procedure
Skin prick tests may be performed on the internal (volar) aspect of the forearm (more than 5cm above the distal skin crease at the wrist), or, alternatively, on the back.

- If necessary, cleanse the forearm with an alcohol swab and allow it to dry
- Using a pen, mark and number 6 prospective skin test sites at least 2cm apart to prevent coalescence of positive reactions
- Place a drop of negative control solution adjacent to mark 1
- Place a drop of negative control solution adjacent to marks 2, 3, 4 and 5
- Place a drop of positive control solution adjacent to mark 6
- A sterile lancet is introduced through each droplet at an angle of approximately 90° and then withdrawn. There should be no bleeding. Use a new disposable lancet for each test
- The droplets may be gently blotted with a tissue immediately after the prick tests have been performed
- Observe test sites for the presence of erythema and weal formation after 15 minutes.
Result: Weal diameter

- Record the weal diameter in millimetres using a transparent ruler. Weal diameter of ≥3mm greater than the negative control constitutes a positive result; ≤3mm a negative result.

<table>
<thead>
<tr>
<th>Result</th>
<th>(*delete as appropriate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>House dust mite: <em>Dermatophagoides pteronyssinu</em></td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>House dust mite: <em>Dermatophagoides farinae</em></td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Pollen of <em>Cynodon dactylon</em> (Bermuda grass)</td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Tree pollen mix</td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Cockroach</td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Desert weeds</td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Cat</td>
<td>mm positive/negative</td>
</tr>
<tr>
<td>Positive (histamine)</td>
<td>mm</td>
</tr>
<tr>
<td>Negative (saline)</td>
<td>mm</td>
</tr>
</tbody>
</table>

Side effects

- Transient itching at the site of test may be encountered. It is harmless and will resolve spontaneously.
- Severe allergic reactions/ anaphylaxis are extremely unlikely. In the unlikely event of a severe allergic reaction occurring, administer adrenaline in the following dose and summon immediate medical assistance:
  - Infants (less than one year old) 0.05-0.1 mL adrenaline 1:1000 (1mg/ml) intramuscular
  - These doses may be repeated every 10 minutes according to pulse and blood pressure, until improvement occurs.

(4) For total and serum specific IgE test:

1ml blood taken………………………………………………………… Yes □ No □
To be filled in when results have been received from laboratory tests

Result: Serum specific IgE levels - greater than 0.35kU/l will be considered positive

**Result** (*delete as appropriate)*

- Food allergen mix....__________kU/l        positive/negative*
- Grass allergen mix…__________kU/l        positive/negative*
- House dust mite……__________kU/l        positive/negative*

Result: Total IgE levels - greater than 5KU/mL considered raised

**Result** (*delete as appropriate)*

- Result:__________kU/l        normal/raised*
Appendix 12: Blood sample
Step 1 - Assemble equipment

Collect all the equipment needed for the procedure and place it within safe and easy reach on a tray or trolley, ensuring that all the items are clearly visible. The equipment required includes:

- A supply of laboratory sample tubes, which should be stored dry and upright in a rack; blood can be collected in
  - sterile glass or plastic tubes with rubber caps (the choice of tube will depend on what is agreed with the laboratory);
  - vacuum-extraction blood tubes; or
  - glass tubes with screw caps;
- A sterile glass or bleeding pack (collapsible) if large quantities of blood are to be collected;
- Well-fitting, non-sterile gloves;
- An assortment of blood-sampling devices (safety-engineered devices or needles and syringes, see below), of different sizes;
- A tourniquet;
- Alcohol hand rub;
- 70% alcohol swabs for skin disinfection;
- Gauze or cotton-wool ball to be applied over puncture site;
- Laboratory specimen labels;
- Writing equipment;
- Laboratory forms;
- Leak-proof transportation bags and containers;
- A puncture-resistant sharps container.

Ensure that the rack containing the sample tubes is close to you, the health worker, but away from the patient, to avoid it being accidentally tipped over.
Step 2 - Identify and prepare the patient

Where the patient is adult and conscious follow the steps outlined below.

- Introduce yourself to the patient, and ask the patient to state their full name.

- Check that the laboratory form matches the patient’s identity (i.e. match the patient’s details with the laboratory form, to ensure accurate identification).

- Ask whether the patient has allergies, phobias or has ever fainted during previous injections or blood draws.

- If the patient is anxious or afraid, reassure the person and ask what would make them more comfortable.

- Make the patient comfortable in a supine position (if possible).

- Place a clean paper or towel under the patient’s arm.

- Discuss the test to be performed (see Annex F) and obtain verbal consent. The patient has a right to refuse a test at any time before the blood sampling, so it is important to ensure that the patient has understood the procedure.

Step 3 - Select the site

- Extend the patient’s arm and inspect the antecubital fossa or forearm.

- Locate a vein of a good size that is visible, straight and clear. The diagram in Section 2.3, shows common positions of the vessels, but many variations are possible. The median cubital vein lies between muscles and is usually the most easy to puncture. Under the basilica there is an artery and a nerve, so puncturing here runs the risk of damaging the nerve or artery and is usually more painful. DO NOT insert the needle where veins are diverting, because this increases the chance of a haematoma.

- The vein should be visible without applying the tourniquet. Locating the vein will help in determining the correct size of needle.

- Apply the tourniquet about 4–5 finger widths above the venepuncture site and re-examine the vein.

Step 4 - Perform hand hygiene and put on gloves

- Perform hand hygiene; that is

  - Wash hands with soap and water, and dry with single-use towels; or
- If hands are not visibly contaminated, clean with alcohol rub – use 3 ml of alcohol rub on the palm of the hand, and rub it into fingertips, back of hands and all over the hands until dry.

- After performing hand hygiene, put on well-fitting, non-sterile gloves.

**Step 5 - Disinfect the entry site**

- Unless drawing blood cultures, or prepping for a blood collection, clean the site with a 70% alcohol swab for 30 seconds and allow drying completely (30 seconds) (40–42).

- Note: alcohol is preferable to povidone iodine, because blood contaminated with povidone iodine may falsely increase levels of potassium, phosphorus or uric acid in laboratory test results (6, 7).

- Apply firm but gentle pressure. Start from the centre of the venipuncture site and work downward and outwards to cover an area of 2 cm or more.

- Allow the area to dry. Failure to allow enough contact time increases the risk of contamination.

- DO NOT touch the cleaned site; in particular, DO NOT place a finger over the vein to guide the shaft of the exposed needle. If the site is touched, repeat the disinfection.

**Step 6 - Take blood**

**Venepuncture**

Perform venepuncture as follows.

- Anchor the vein by holding the patient’s arm and placing a thumb BELOW the venipuncture site.

- Ask the patient to form a fist so the veins are more prominent.

- Enter the vein swiftly at a 30 degree angle or less, and continue to introduce the needle along the vein at the easiest angle of entry.

- Once sufficient blood has been collected, release the tourniquet BEFORE withdrawing the needle. Some guidelines suggest removing the tourniquet as soon as blood flow is established, and always before it has been in place for two minutes or more.

- Withdraw the needle gently and apply gentle pressure to the site with a clean gauze or dry cotton-wool ball. Ask the patient to hold the gauze or cotton wool in place, with the arm extended and raised up. Ask the patient NOT to bend the arm, because doing so causes a haematoma.
Step 7 - Fill the laboratory sample tubes

- When obtaining multiple tubes of blood, use evacuated tubes with a needle and tube holder. This system allows the tubes to be filled directly. If this system is not available, use a syringe or winged needle set instead.

- If a syringe or winged needle set is used, best practice is to place the tube into a rack before filling the tube. To prevent needle-sticks, use one hand to fill the tube or use a needle shield between the needle and the hand holding the tube.

- Pierce the stopper on the tube with the needle directly above the tube using slow, steady pressure. Do not press the syringe plunger because additional pressure increases the risk of haemolysis.

- Where possible, keep the tubes in a rack and move the rack towards you. Inject downwards into the appropriate coloured stopper. DO NOT remove the stopper because it will release the vacuum.

- If the sample tube does not have a rubber stopper, inject extremely slowly into the tube as minimizing the pressure and velocity used to transfer the specimen reduces the risk of haemolysis. DO NOT recap and remove the needle.

- Before dispatch, invert the tubes containing additives for the required number of times (as specified by the local laboratory).

Step 8 - Draw samples in the correct order

Draw blood collection tubes in the correct order, to avoid cross-contamination of additives between tubes. As colour coding and tube additives may vary, verify recommendations with local laboratories. For illustration purposes, Table 2.3 shows the revised, simplified recommended order of draw for vacuum tubes or syringe and needle, based on United States National Committee Clinical Laboratory Standards consensus in 2003 (43).
Appendix 13: School characteristic (Girls)

<table>
<thead>
<tr>
<th>School information</th>
</tr>
</thead>
<tbody>
<tr>
<td>School name</td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Study information feedback (Girls)

<table>
<thead>
<tr>
<th>Phase one</th>
<th>Phase two</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responded to invitation</td>
<td>Responded to invitation</td>
</tr>
<tr>
<td>Responded to reminder letter</td>
<td>Responded to reminder letter</td>
</tr>
<tr>
<td>Total number of questionnaires</td>
<td>Total number of participants</td>
</tr>
<tr>
<td>Number of parents signed consent form</td>
<td>Total number of participants</td>
</tr>
<tr>
<td>Responded to invitation</td>
<td>Responded to reminder letter</td>
</tr>
<tr>
<td>Total number of participants</td>
<td>Total number of participants</td>
</tr>
<tr>
<td>Responded to invitation</td>
<td>Responded to reminder letter</td>
</tr>
<tr>
<td>Total number of participants</td>
<td>Total number of participants</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Responded to invitation</th>
<th>Responded to reminder letter</th>
<th>Total number of questionnaires</th>
<th>Number of parents signed consent form</th>
<th>Responded to invitation</th>
<th>Responded to reminder letter</th>
<th>Total number of participants</th>
<th>Total number of participants</th>
</tr>
</thead>
<tbody>
<tr>
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<td>No</td>
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<td>Yes</td>
<td>No</td>
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<td>Yes</td>
</tr>
</tbody>
</table>
## Appendix 14: School characteristic (Boys)

### School information

<table>
<thead>
<tr>
<th>School name</th>
<th>Total number of students</th>
<th>Location</th>
<th>Governmental</th>
<th>Private</th>
<th>Governmental building</th>
<th>Rental building</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

### Study information feedback (Boys)

<table>
<thead>
<tr>
<th>Phase one</th>
<th>Phase two</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responded to invitation</td>
<td>Responded to invitation</td>
</tr>
<tr>
<td>Responded to reminder letter</td>
<td>Responded to reminder letter</td>
</tr>
<tr>
<td>Total number of questionnaires</td>
<td>Total number of questionnaires</td>
</tr>
<tr>
<td>Number of parents signed consent form</td>
<td>Number of parents signed consent form</td>
</tr>
<tr>
<td>Responded to invitation</td>
<td>Responded to invitation</td>
</tr>
<tr>
<td>Responded to reminder letter</td>
<td>Responded to reminder letter</td>
</tr>
<tr>
<td>Total number of participants</td>
<td>Total number of participants</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Responded to invitation</th>
<th>Responded to reminder letter</th>
<th>Total number of questionnaires</th>
<th>Number of parents signed consent form</th>
<th>Responded to invitation</th>
<th>Responded to reminder letter</th>
<th>Total number of participants</th>
<th>Total number of participants</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
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<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Appendix 15: Data collection form for Phase II Case-control study (Girls)

Data collection form (Female form)

Pilot study—phase two
Investigating the relationship between
adiposity and asthma among school-aged children in Saudi Arabia:
exploring the causal direction of relationship

Researcher
Mahmoud Nahhas

Supervised by
Professor Aziz Sheikh
Professor Raj Bhopal
Dr. Chantelle Anandan

Date: ……./……/ 2008

<table>
<thead>
<tr>
<th>Student name</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of birth</td>
<td>……./……./……. year</td>
</tr>
<tr>
<td>School name</td>
<td></td>
</tr>
<tr>
<td>Student number</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td></td>
</tr>
</tbody>
</table>

This page must be completed before phase two by Mahmoud Nahhas

Estimated time to complete this form is one hour/Child
### Part 1  Anthropometric measurement

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Height</td>
<td>........ cm</td>
</tr>
<tr>
<td>2</td>
<td>Weight</td>
<td>........ kg</td>
</tr>
<tr>
<td>3</td>
<td>Waist circumference</td>
<td>........ cm</td>
</tr>
<tr>
<td>4</td>
<td>Triceps skinfold thickness</td>
<td>........ mm</td>
</tr>
<tr>
<td>5</td>
<td>Comment</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes

Completed by the nurse name : .....................

### Part 2  Skin prick test

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>House dust mites</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Milk</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Tree pollen mix</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Positive (histamine)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Negative (saline)</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes

Completed by the nurse name : .....................
**Part 3  Pulmonary function test**

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FVC</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>FEV1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(FEV1%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PEFR</td>
<td>(L/min)</td>
</tr>
<tr>
<td>5</td>
<td>Nitrous Oxide, N₂O</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Comment</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes
Completed by the physician name ............

**Part 4  Immunology and blood sample**

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serum specific IgE</td>
<td>Grand 0-6</td>
</tr>
<tr>
<td>2</td>
<td>Total IgE</td>
<td>&lt; 100kU/L</td>
</tr>
<tr>
<td>5</td>
<td>Serum Leptin</td>
<td>(10–15 ng/ml)</td>
</tr>
<tr>
<td>6</td>
<td>Adiponectin</td>
<td>5.5±2.0 μg/ml</td>
</tr>
<tr>
<td>7</td>
<td>C-reactive protein</td>
<td>(&lt; 0.5 mg/dl)</td>
</tr>
<tr>
<td>8</td>
<td>Th1</td>
<td>1,000–2,000 Cells/mm³</td>
</tr>
<tr>
<td>9</td>
<td>Th2</td>
<td>1,000–2,000 Cells/mm³</td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes
Completed by the laboratory specialist name ............
Instructions to fill the form

1— The cover page (page 1) must be completed by Mahmoud Nahhas to make sure the consent form is signed.
2— Part 1 (page 2) completed by the nurse who is responsible for taking the measurement.
3— Part 2 (page 2) completed by the nurse who is responsible for doing the skin prick testing.
4— Part 3 (page 3) completed by the physician who is responsible for the pulmonary function test.
5— Part 4 (page 3) completed by laboratory specialist who is taking the blood sample.

Comments

........................................................................................................................................
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........................................................................................................................................
........................................................................................................................................
........................................................................................................................................
Appendix 16: Data collection form for Phase II Case-control study (Boys)

<table>
<thead>
<tr>
<th>Student name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of birth</td>
</tr>
<tr>
<td>School name</td>
</tr>
<tr>
<td>Student number</td>
</tr>
<tr>
<td>Code</td>
</tr>
</tbody>
</table>

This page must be completed before phase two by Mahmoud Nahhas

Estimated time to complete this form is one hour / Child
# Part 1 Anthropometric measurement

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Height</td>
<td>........... cm</td>
</tr>
<tr>
<td>2</td>
<td>Weight</td>
<td>........... kg</td>
</tr>
<tr>
<td>3</td>
<td>Waist circumference</td>
<td>........... cm</td>
</tr>
<tr>
<td>4</td>
<td>Triceps skinfold thickness</td>
<td>........... mm</td>
</tr>
<tr>
<td>5</td>
<td>Comment</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was ........ Minutes

Completed by the nurse name: ..................

# Part 2 Skin prick test

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>House dust mites</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Milk</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Tree pollen mix</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Positive (histamine)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Negative (saline)</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was ........ Minutes

Completed by the nurse name: ..................
### Part 3 Pulmonary function test

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FVC</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>FEV1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(FEV1%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PEFR</td>
<td>(L/min)</td>
</tr>
<tr>
<td>5</td>
<td>Nitrous Oxide, N2O</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Comment</td>
<td></td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes

Completed by the physician name ............

### Part 4 Immunology and blood sample

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serum specific IgE</td>
<td>Grand 0–6</td>
</tr>
<tr>
<td>2</td>
<td>Total IgE</td>
<td>&lt; 100kU/L</td>
</tr>
<tr>
<td>5</td>
<td>Serum Leptin</td>
<td>(10–15 ng/ml)</td>
</tr>
<tr>
<td>6</td>
<td>Adiponectin</td>
<td>5.5±2.0 μg/ml</td>
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<td>7</td>
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</tr>
<tr>
<td>8</td>
<td>Th1</td>
<td>1,000–2,000 Cells/mm³</td>
</tr>
<tr>
<td>9</td>
<td>Th2</td>
<td>1,000–2,000 Cells/mm³</td>
</tr>
</tbody>
</table>

Time needed for this part was .......... Minutes

Completed by the laboratory specialist name ............
Instructions to fill the form

1— The cover page (page 1) must be completed by Mahmoud Nahhas to make sure the consent form is signed.
2— Part 1 (page 2) completed by the nurse who is responsible for taking the measurement.
3— Part 2 (page 2) completed by the nurse who is responsible for doing the skin prick testing.
4— Part 3 (page 3) completed by the physician who is responsible for the pulmonary function test.
5— Part 4 (page 3) completed by laboratory specialist who is taking the blood sample.

Comments

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.................................................................................................................................
.................................................................................................................................
Appendix 17: Cross-sectional survey (Girls questionnaire and consent forms)
المحتويات

1. خطاب الدعوة للمشاركة
2. التعرف بالدراسة
3. الاستبانة
4. موافقة ولي الأمر
5. للتواصل والاستفسارات - الغلاف الخارجي

نشكر لكم تعاونكم وننتظر إمكشافكم في الدراسة

مع تحياتي
د. محمد بن عبد الله بن نايف

mahodnas@yahoo.com
حكاية
للمشاركة في الدراسة
المكرم ولي أمر الطالبة / فقه الله
السلام عليكم ورحمة الله وبركاته...
...
يسرني دعوكم للتفضل بالموافقة على مشاركتكم في الدراسة التي اعتزم القيام بها بالتعاون مع الإدارة العامة للتربية والتعليم بمنطقة المدينة المنورة (الصحة المدرسية) بعنوان (بحث العلاقة السببية بين مؤشرات سكتة الدماغ والربو الشعبي بين أطفال المدارس ومدينة المنورة) ولتحقيق من صحة هذه العلاقة وأسباب حدوثها بين الأطفال في منطقة المدينة المنورة من خلال مدارس البنين والبنات مختارة لأحد مناطق مملكتنا الحبيبة ومن ثم المساعدة في التخطيط لوضع الحلول المناسبة للفقرة من هذه المشكلة.
عليه فإنه يعدنا تعزيمك تتبعية المركبة وإعطاء المعلومات اللازمة التي تتعلق بابتكار الذي تم اختيارها للمشاركة في هذه الدراسة. علماً بأنه سيتم تزويدها بقرية مفصل عن الحالة الصحية لأبنائكم وقت إجراء الدراسة والتصاميم التي قد تحتاجها من واقع نتائج الدراسة مع الالتزام الكامل بالمحافظة على سرية هذه المعلومات والاستفادة على عدم استخدامها غير الدراسة الحالية، فيما أمل تفضيلكم بالتوخي على النموذج المرفق إذا بالموافقة أو عدم الموافقة بشكل واضح على اشتراك ابتكار في الدراسة ومن ثم التفضل بإعادتها إلى المدرسة وذلك خلال يومين من تسليمكم خطابي هذا.
شاكرًا ومق켜رًا لدعم جسر تعاونكم فيما قيم صالح أطفالنا.
والله الموفق...

الباحث
د/ محمود بن عبد الحكيم نجليس

mahodnas@yahoo.com

د/ محمود بن عبد الحكيم نجليس، جوال، 0505797737، البريد الإلكتروني، 173225772، 0505797737، 0505797737.
النشرة التعرفية الخاصة بالدراسة

المكم ولأمر الطالبة، وفقه الله

السلام عليكم ورحمة الله وبركاته

يسرنى دعوكم للتفضل بالموافقة على مشاركتكم في الدراسة التي نعزم القيام بها بالتعاون مع الإدارة العامة للتربية والتعليم ومنظمة المدينة المنورة (المدارس الإسلامية) بعنوان "بحث العلاقة السببية بين مؤشرات صحة الجسم والريو الشعبي بين طلاب المدارس في منطقة المدينة المنورة"، وسعتنا استعراض نتائج الدراسات المرتبطة التي حاولت جاهداً أن أجيب على الاستشارات التي قد تدور في ذهنكم وقد تحتاجون لمعرفتها.

وإذا كان القول "لا يوجد معلومات تمزج استقصاء عن أي معلومات قد تحتاجون لها أم لا" يتردد فلن تكون فإننا نستطيع الإجابة على مطالعكم أن استفساراتكم عبر وسائل التواصل مع الباحث المرقب.

هل تعلم أن زيادة الوزن والريو الشعبي من الأمراض المزمنة التي تصيب اللائي، فإن هذه الأمراض بدأت في الزيادة بشكل متدرّب في السنوات الأخيرة عالمياً ومحلياً مما جعلها تثير فتول العلماء والمحترمين. يوجد في المملكة العربية السعودية ما يزيد على مليوني مصاب بالريو الشعبي أعظمهم من الأطفال.

أهداف الدراسة:

1- تحديد معدل انتشار الريو الشعبي بين طلاب المدارس في منطقة المدينة المنورة.
2- دراسة العلاقة بين زيادة الوزن والريو الشعبي بين طلاب المدارس في منطقة المدينة المنورة.

لماذا تم اختيار أبينتي للمشاركة في الدراسة؟

تم اختيار أبينتي في الدراسة لأن الدراسة تشتمل أبناء مدينة المنورة الذين تتراوح أعمارهم بين 6-8 سنوات.

هل لا يدلى أي أوافق على مشاركتي أبينتي في الدراسة؟

ليس هناك أي إجبار على الاشتراك في الدراسة، وبدلاً من ذلك مناريكم على اشتراك أبينتي في الدراسة وعدم رغبتكم فيما بعد الاستمرار بها يمكن لابنكم الانسحاب من الدراسة أي وقت بدون إبداء الأسباب. وننصح بأن تكون على مستوى رعاية الطلاب للتسهيل.

ما الذي سيحدث لابنتي في حال موافقتي على المشاركة في البحث؟

سيتم إدراجه في الدراسة التي تنتمي إلى المدارس بواسطة فريق يحتوي مدقق على مستوى عال من الخبرة والمؤهلات وسيكون ذلك على مرحلتين.

المرحلة الأولى: تعربكم الالتسبيح المرفق بناءاً على الرعاية والموافقة على الاشتراك في الدراسة ومن ثم إرساله إلى المدرسة خلال.

ال_cm_ho@yahoo.com; جوال: 0505001678; هاتف: 050016781; الموقع الإلكتروني:
المرحلة الثانية: سيقوم فريق البحث العلمي بزيارة مدرسة لتبنيهم خلال الفترة الزمنية القادمة لإجراء الفحوصات الطبية المطلوبة للبحث.

هل سيتم تجربة أدوية أو سيتم إعطاء ابنتي أي أدوية؟
لا – أبدا. فقط تهدف الدراسة إلى تحديد العلاقة بين زيادة الوزن والرعب الشعبي فقط.

ما هي المضافات أو المخاطر الناطقة من مشاركتي في الدراسة؟
لا توجد أي مضافات مطلقة.

ما هي النتائج التي ستحصل عليها ابنتي من الممارسة في الدراسة؟
تعد مشاركتك بطلنا، مثل هذه الدراسات بمنافسة المساهمة في دراسات حقيقية علمية يسعى العديد من المختصين لإحداثها ويساعد ذلك أيضاً على دراسة مشكلة الرعب الشعبي ومشاركتك زيادة الوزن لدى الأطفال بعدم المضطربين صلى الله عليه وسلم.

هل سيتم استخدام المعلومات التي سيستفيد منها أي أشخاص آخر؟
لا. نستعمل المعلومات التي تجمعها هنا لأغراض لاحقة.

ماذا لو رفضت مشاركتي في الدراسة؟
إذا رفضت، يجب أن تشعر أنك لا تشعر بالمسؤولية في اختيارك. بالنسبة للمجتمع، ونتطلع إلى إزالة هذا الخطر عند وصولنا إليها، ونتطلع للمعلومات التي يمكننا أن نستفيد منها.

ماذا لو طلبتم التاليات التي أو رد فعلك أو جزء من الخيار؟
يمكن طرح أي شكاوى أو استفسارات ودعوة بالاتصال بالباحث الرئيسي (د. محمود بن عبدالفتاح تحاسم) – مرفق بيانات التواصل.

ما هو الطلب من المقابلة الآن؟
لا يوجد مواجهة على المتابعة، فالأمر يكون برمجة الاستبانس المرفق، وتتوفر على إجراء المشاركة على الاشتراك في الدراسة وأرسالها إلى الدراسة في موعود اقصائي يومين من استلامك لهذه النقطة.

إ hypothecation على بعض المعلومات الإضافية عن الدراسة؟
يمكنك التواصل مع الباحث الرئيسي (د. محمود بن عبدالفتاح تحاسم) – مرفق بيانات التواصل.
الاستياب

نأمل التكرم بتعبيتنه وإعادته إلى المدرسة

معلومات عن الطالبة

<table>
<thead>
<tr>
<th>اسم الطالبة:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>الصف:</td>
<td></td>
</tr>
<tr>
<td>المدرسة:</td>
<td></td>
</tr>
<tr>
<td>تاريخ الولد بالهجري:</td>
<td>موسم شعبان</td>
</tr>
<tr>
<td>تاريخ الولد بالميلادي:</td>
<td>موسم شعبان</td>
</tr>
</tbody>
</table>

العمر عند تعيين الاستياب: 

معلومات عن والدي الطالبة:

الرجاء الإجابة عن الأسئلة التالية بوضع علامة (✓) أمام الاختيار المناسب أو الكتابة في الأماكن المحددة لذلك:

1) الأب: 
   a) العمر: 
   b) مكان الميلاد: المملكة العربية السعودية 
   ج) أعلى شهادة حصل عليها: 

لا يوجد: ابتدائية | ثانوية | جامعية | شهادات دراسية عليها

2) الأم: 
   a) العمر: 
   b) مكان الميلاد: المملكة العربية السعودية 
   ج) أعلى شهادة حصلت عليها:

لا يوجد: ابتدائية | ثانوية | جامعية | شهادات دراسية عليها

3) من أجل تلقي هذا الاستياب؟ 
   الأب: 
   الأم: 
   شخص آخر:

4) تاريخ الإجابة على الاستياب: 
   1430 هـ

mahodnas@yahoo.com
استبيان عن حساسية الصدر

Core Questionnaire For Chest

الرجاء الإجابة عن الأسئلة التالية بوضع علامة ✓ (✓) أمام الاختيار المناسب:

1) هل أصيب طفلك من قبل بصرف في الصدر . في أي وقت مضى؟

نعم لا

إذا معتقدات الإجابة ب (لا) الرجاء الاتصال مباشرة للأجابة على الأسئلة.

2) خلال الأسبوع الماضي هل أصيب طفلك من قبل بصرف في الصدر؟

نعم لا

إذا معتقدات الإجابة ب (لا) الرجاء الاتصال مباشرة للأجابة على الأسئلة.

3) خلال الأسبوع الماضي، عمت مرة أصيب طفلك بصرف في الصدر؟

لم يصب 1-3 مرات

أكثر من 12 مرة

4) خلال الأسبوع الماضي، عمت مرة أصيب طفلك بصرف في الصدر من ليلة واحدة في الأسبوع؟

لم يصب

أكثر من 3 ليالي

5) خلال الأسبوع الماضي، هل شعر هذا الصغير الصدر layouts شديد لدرجة أنه لم يستطيع أن يتكلم إلا عقلًا أو

لم يصاب

6) هل أصيب طفلك أو عائلي من الرضيع أو الكبار في اليوم من اليوم بلغة؟

نعم لا

7) خلال الأسبوع الماضي، هل أصيب طفلك بصرف في الصدر أثناء أو بعد اللعب أو عمل أي مجهود؟

نعم لا

8) خلال الأسبوع الماضي، هل أصيب طفلك بصرف في الصدر بمكان بعيد عن صدره أو الأطراف أو التهابات الصدر؟

نعم لا

mahodnas@yahoo.com

المراجعات:

محمود بن عبد العال نحاس، جوال: 33876847، شعائر: 3386908887، الهوى: الفلكي

260
Core Questionnaire For Nose

1. هل أصيب طفلك من قبل بمشاعل مثل العطس أو نزل مخارج من الأنف أو انسداد الأنف، من غير المرات التي يكون فيها مصاباً بالرخاء أو البرد؟

   نعم  لا

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة إلى الإجابة على السؤال رقم 1

2. خلال الاثنين عشر شهراً الماضية، هل أصيب طفلك بمشاعل مثل العطس أو نزل مخارج من الأنف أو انسداد الأنف، من غير المرات التي يكون فيها مصاباً بالرخاء أو البرد؟

   نعم  لا

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة إلى الإجابة على السؤال رقم 1

3. خلال الاثنين عشر شهراً الماضية، هل طفح هذه المشاعل الأنفية مصحوبة بدموع أو حكة العينين؟

   نعم  لا

4. خلال الاثنين عشر شهراً الماضية، أي شهر من أشهر السنة أصيب طفلك بهذه المشاعل الأنفية؟

   نعم (لا) الأمام الأشهر التي أصيب فيها

   أكتوبر  نوفمبر  ديسمبر
   يناير  فبراير  مارس
   يوليو  أغسطس  سبتمبر

5. خلال الاثنين عشر شهراً الماضية، كيف اثرت هذه المشاعل الأنفية على نشاط طفلك اليوم؟

   لم تؤثر على الإطلاق
   اثرت بصورة متسطة
   اثرت بصورة شديدة

6. هل أصيب طفلك بما يسمى حمى القول و هي حساسية حادة لل الأنف والعيون؟

   نعم  لا

mahodnas@yahoo.com

المؤلف: محمود بن عبد沽اали ناصر، جوال: 0292930000، منزل: 0292930000، البريد الإلكتروني: mahodnas@yahoo.com

المستورد: 261
استبيان عن حساسية الجلد

Core Questionnaire For Skin

1 هل أصيب أو عانى طفح جلدي (حبيوب على الجلد) مع حكة بصورة مستمرة أو متقطعة استمرت لمدة سنة أطول على الأقل؟

نعم لا

إذا صحت الإجابة ب 1 لا الراجع الانتقال مباشرة للإجابة على السؤال رقم 7

2 خلال الاثنين عشر شهرا الماضية هل أصيب أو عانى طفح جلدي (حبيوب على الجلد) مع الحكة؟

نعم لا

إذا صحت الإجابة ب لا الراجع الانتقال مباشرة للإجابة على السؤال رقم 7

3 هل تكون هذا الطفح الجلدي (حبيوب على الجلد) مع الحكة يصعب أي من الوضع الناتجي ؟ ثبات مفصل الكوع النائيات الخلفية الرضحية مقدمة الكاحل أعلى الفخذ من الكتف حول الرقبة أو حول الأذن أو حول العينين?

نعم لا

4 في أي سن أصيب طفح جلدي لأول مرة بهذا الطفح الجلدي (حبيوب على الجلد) مع الحكة?

5 سنوات فأكثر

سناتين إلى 5 سنوات تحت سن السابعة

إذا صحت الإجابة ب لا الراجع الانتقال مباشرة للإجابة على السؤال رقم 7

5 خلال الاثنين عشر شهرا الماضية هل شعر هذا الطفح الجلدي (حبيوب على الجلد) مع الحكة تشفي (تعافي) بصورة مكتملة في أي وقت؟

نعم لا

إذا مثل الإجابة ب لا الراجع الانتقال مباشرة للإجابة على السؤال رقم 7

6 خلال الاثنين عشر شهرا الماضية، حسب مدة تقريبا استيقظ (قام) طفح جلدي من نوبة نتيجة هذا الطفح الجلدي (حبيوب على الجلد) مع الحكة بعدما واحدة خلال أسبوع

لا

7 هل أصيب أو عانى طفح جلدي من مرض الأسكتزيا (حساسية الجلد)؟

نعم لا

mahodnas@yahoo.com

© محمود بن عبد الفتاح عباس جوال: 0503505050 مكتبا 7173432828 البريد الإلكتروني:
استبيان عن البيئة المحيطة

Environmental Questionnaire

1) خلال النهار عشر شهور الماضية ، سكن مرة في المتوسط لنحاول طلبك الأسول أو المشروبات التالية؟

<table>
<thead>
<tr>
<th>النوع</th>
<th>مرارة أو مرة أو احيانا</th>
</tr>
</thead>
<tbody>
<tr>
<td>اللحوم (مثل غنم، دجاج)</td>
<td></td>
</tr>
<tr>
<td>المنتجات البحرية (بما فيها السمك)</td>
<td></td>
</tr>
<tr>
<td>الفواكه</td>
<td></td>
</tr>
<tr>
<td>الخضروات</td>
<td></td>
</tr>
<tr>
<td>البطولات (مثل الحمص والذيل)</td>
<td></td>
</tr>
<tr>
<td>الجبوب (بما فيها الخيا)</td>
<td></td>
</tr>
<tr>
<td>المكورات</td>
<td></td>
</tr>
<tr>
<td>الأرز</td>
<td></td>
</tr>
<tr>
<td>الزبدة</td>
<td></td>
</tr>
<tr>
<td>السمن النباتي (المكسرات)</td>
<td></td>
</tr>
<tr>
<td>الكسكس (مثل الجوز واللوز والخوز السوداني)</td>
<td></td>
</tr>
<tr>
<td>البطاطس</td>
<td></td>
</tr>
<tr>
<td>الحليب</td>
<td></td>
</tr>
<tr>
<td>البيض</td>
<td></td>
</tr>
<tr>
<td>وجهات سريعة (مثل البرجر)</td>
<td></td>
</tr>
</tbody>
</table>

2) سكن مرة في الأسبوع يقوم طفلك بممارسة رياضة شديدة لفترة طويلة تجعله يت نفسها بمصر؟

<table>
<thead>
<tr>
<th>مرارة أو مرة أو احيانا</th>
</tr>
</thead>
<tbody>
<tr>
<td>ثلاث مرات أو أكثر في الأسبوع</td>
</tr>
</tbody>
</table>

3) خلال أيام الأسبوع، سكن ساعة في اليوم (فترة 24 ساعة) يقوم طفلك بمشاهدة التلفاز (الساعتين)؟

<table>
<thead>
<tr>
<th>أقل من ساعة واحدة</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 ساعات فأكثر</td>
</tr>
</tbody>
</table>

mahodnas@yahoo.com

263
٤) ما هو الوقود المستخدم في الطبخ عادة في التكييف؟

５) ما هي وسيلة التكييف في البيت؟

６) ما نوع الططلب عند الطبيب؟

٧) ما حيوانات المزينة (مثل الأغنام والماض والخرافان)؟

٨) هل ولد طفلك في المدينة المغيرة؟

٩) وزن الطفل عند مولوده؟

١٠) هل رفع الطفل رضاعة طبيعية؟

١١) خلال السنة الأولى من عمر الطفل، هل أخذ الطفل أي مضادات حيوية؟

١٢) خلال السنة الأولى من عمر الطفل، هل سكن عند مسجد فقط (على البيت؟

١٣) خلال السنة الأولى من عمر الطفل، هل سكن عند مسجد فقط (على البيت؟

١٤) لحيوانات المزينة (مثل الأغنام والماض والخرافان)؟

١٥) خلال الأشهر من عمر الطفل، هل سكن عند مسجد فقط (على البيت؟
16 - حجم عدد أخوة وأخوات الطفل الذي أعتبر منه إخوة وأخوات
17 - حجم عدد أخوة وأخوات الطفل الذي أعتبر منه إخوة وأخوات
18 - حجم سنة عاش الطفل في المدينة المذكورة
19 - خلال أيام العمل في الأسبوع، حجم مرة بمرتين تشرن الشاحنات في الشارع المجاور للمنزل
265 - ولا مرة نادرًا بشكل متكرر أثناء النهار طوال اليوم تقريبًا.
20 - هل أم الطفل تدخن السجائر؟ 

21 - إذا مكثت إجابتك (نعم)، حجم سجارة بعد اليوم تقريبًا

22 - خلال السنة الأولى من عمر الطفل، هل طالبت أم الطفل تدخن السجائر؟ 

23 - حجم عدد الأشخاص الذين يعيشون في البيت يدخن السجائر (بما فيهم الأبوين)...

شيا، لست على نسخ المقابل.
# PARENTAL CONSENT FORM

**Notice:** This form is written in Arabic and English, with the Arabic text appearing first. **Translation:** Parental Consent Form

**Notice:** This form is written in Arabic and English, with the Arabic text appearing first. **Translation:** Parental Consent Form

<table>
<thead>
<tr>
<th>رقم الم роли</th>
<th>رقم الد رسة</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-0683358</td>
<td></td>
</tr>
</tbody>
</table>

**Name of Investigator:** د. محمود بن عبد الفتاح فحاس

**University:** جامعة أدنبرة - بريطانيا

**Consent Requirements:**

- [ ] أُعلِنَت في قراءة مطلوبة بالدراسة المتوقعة أعلاه، وقد انتهى على فكرة الاتصال بالباحث ومسائلة عن الاستفسارات التي تمثل في نمطية حول مراحل الدراسة المختلفة.

- [ ] أعظم تفاهمًا أن مشغولة ما، هي إما مشغولة في هذا البحث فإن المشاركة ستكون معافاة ومن حقك التمتع في أي مرحلة من مراحل الدراسة.

- [ ] اتفقت في عملية طاقم الفحوصات لابنتي وهي تتضمن:
  - اختبار التحليل البشري (الطول، الوزن، قياس ضغط الدم، الشحم).
  - قياس ضغط الدم في الحمل.

- [ ] اختبار التحصين.

**Parental Consent:**

<table>
<thead>
<tr>
<th>التوقيع</th>
<th>الامام الطالبة</th>
</tr>
</thead>
</table>
|         | ١٤٣٠ هـ / / |}

<table>
<thead>
<tr>
<th>التوقيع</th>
<th>الامام الباحث</th>
</tr>
</thead>
</table>
|         | ١٤٣٠ هـ / / |}

**Thanks:**

Thank you for your cooperation. This form is available in Arabic and English, with the Arabic text appearing first. **Translation:** Thanks for your cooperation. This form is available in Arabic and English, with the Arabic text appearing first.
مع تحيات
فريق البحث للدراسة

للتواصل مع الباحث
د / محمود بن عبد الفتاح نحاس

جوال: 09966005000، فاكس: 76763230
البريد الإلكتروني: mahodnas@yahoo.com
Appendix 18: Cross-sectional survey (Boys questionnaire and consent forms)
المحتويات

خطاب الدعوة للمشاركة

التعريف بالدراسة

الاستبانة

موافقة ولي الأمر

للاتصال والاستفسارات - الغلاف الخارجي

شكركم تعاونكم وتبظяем المشاركة ابتكار في الدراسة

محمود بن عبد الله نحاس
جاكوة
للمشاركة في الدراسة
المكرم ولي أمر الطالب / ... وفقه الله
السلام عليكم ورحمة الله وبركاته...

يسريني دعوكم للتفضيل بالموافقة على مشاركتكم في الدراسة التي اعتبرنا القيام بها بالتعاون مع الإدارة العامة للتربية والتعليم بمدينة المنوفية (صحة الرياضة) بعنوان "بحث العلاقة السببية بين مشاركات مختارة لجسم 어بطة بسيط بين الأطفال في منطقة الدراسة من منطقتي مدينة المنوفية وذللك بهدف التحقق من صحة هذه العلاقة وأسباب حدوثها بين الأطفال في منطقة الدراسة من خلال مدارس البنين والبنات مختارة لأحد مناطق مملكتنا الحبيبة ومن ثم المساهمة في التخطيط لوضع الحلول المناسبة للفوقية من هذه المشكلة.

عليه فإنه يعدضني تعاونكم لتعزيز الإستبانة المرفقة وإعطاء المعلومات اللازمة التي تتصل بالموضوع الذي تم اختياره للمشاركة فيه هذه الدراسة. علماً بأنه سيتم تزويدكم بتقرير مفصلي عن الحالة الصحية للأطفال وقت إجراء الدراسة والتصائيح التي قد تحتاج لها من واقع نتائج الدراسة مع الالتزام الكامل بالمحافظة على سرية هذه المعلومات والتصائيح عند عدم استخدامها تغري الدراسة الحالية. كما أمل تفاؤلكم بالتوافق على النموذج المرفق إما بالموافقة أو عدم الموافقة بشكل واضح على اشتراك ابنكم في الدراسة ومن ثم التفضل بإعادتها إلى المدرسة وذلك خلال يومين من تسلمكم لخطابي هذا.

شاكراً ومقرباً لكم حسن تعاونكم لما فيه صالح أطفالنا.

الحمد لله...
المخرجات التدريسية الخاصة بالدراسة

فقام الله

السلام عليكم ورحمة الله وبركاته...

يرجى دعوكم للمشاركة في الأبحاث التي أجريت في الدراسة التي اقتصرت القيام بها بالتشاور مع الإدارة العامة للتدريب والتعليم بإدارات المدينة المنورة ومحافظة مكة حسب الدراسة المكونة من مؤشرات مختلطة الجسم والغذاء الشعبي بين أطفال المدارس في منطقة المدينة المنورة. ويعتبر الاستنتاج نشرة الدراسات المرتبطة وفجوات جاذبة أن أحبب على الاستنتاجات التي تم توفيره وقد تحتاجن لتوفرها.

ويجس على الأخص الشعبي بناء التوام بفرض الاستنتاج عن أي من تطبيقات قطاع المحافظات لها أمل لا تتردد في ذلك فإنه يعتمد في الإجابة على طفلكة تشجيعكم على وسائل التواصل وبدائمل التواصل مع الباحث المرافق.

هل تعلم؟

أن زيادة الوزن والرحو الشعبي من الأمراض المتزمنة التي تثير القلق، وإن هذه الأمراض بدأت في التنامي بشكل متزايد، بشكل متزايد، بشكل متزايد، بشكل متزايد.

تتعلق سنوات الأخيرة غالباً وتحديدياً مما جعلها تثير قلق العلماء والمختصين، ويوجد في المملكة العربية السعودية ما يزيد على مليوني مصاب بدمار التنبؤ اغلبيتهم من الأطفال.

أهداف الدراسة:

1- تحديد معدل انتشار الرحو الشعبي بين طلاب المدارس في منطقة المدينة المنورة.
2- دراسة العلاقة بين زيادة الوزن والرحو الشعبي بين طلاب المدارس في منطقة المدينة المنورة.

لماذا تم اختياري لمشاركتي في الدراسة؟

تم اختياري لأن الدراسة تشمل أبناء المدينة المنورة الذين تتراوح أعمارهم ما بين 6-8 سنوات.

هل لا تعلم أن الأبحاث التي أجريت في الدراسة كا في الدراسة في الدراسة تشمل أبناء المدينة المنورة الذين تتراوح أعمارهم ما بين 6-8 سنوات.

ليس هناك أي إطار في الدراسة، ويمكنك اتباعنا إذا كان من الدراسة ودعم رغبتك فيما بعد الاستثمار بها يمكن أن تكون الانسحاب من الدراسة في أي وقت بدون إيداع الأسيا، وسيتلقى الدعم على مستوى رعاية الطلاب المساهمين في.

ما الذي سيحصل لا يتجاوز علي المشاركة في البحث؟

سيتم إدراجه في الدراسة التي ستفتح في المدارس بطريقة منطقي معدل مرن على مستوى عالية من الخبرة والمؤسسات وسيكون ذلك على مرتين.

الوضوع الأول: لا تتخطى الاستثناء المرتفع بكفر المواقع على الاشتراك في الدراسة ومن ثم إرساله إلى المدرسة خلال اليومين.

mahodnas@yahoo.com
المرحلة الثانية: سيعقد فريق البحث العلمي بزيارة مدرسة إبنك خلال الفترة القريبة القادمة لإجراء الفحوصات الطبية المتجهة للبحث.

هل سيتم تجربة أدوية أو سيتم إعطاء إياه أي أدوية؟
لا... أبدا، فقط تهدف الدراسة إلى تحديد العلاقة بين زيادة الوزن والربو الشعبي فقط.
ما هي المضاعفات أو الخطر الناتجة من مشاركتك في الدراسة؟
لا يوجد أي مضاعفات مطلقة.
ما هي النافذة التي سيحصل عليها إبنك من المشاركة في الدراسة؟
تعد مشاركتك في الدراسة بمثابة المساهمة في إيثرات حقيقية علمية يسعى العديد من الخصائص في إيثراتها ويساعد ذلك أيضًا على دراسة مشكلة الربو الشعبي ومشكلة زيادة الوزن لدى الأطفال بمدينة العاصمة صلى الله عليه وسلم.
هل سيتم استخدام المعلومات التي سيتم الحصول عليها لأي غرض آخر؟
ستراعي الخصوصية الكاملة ولن نستخدم البيانات لأي غرض آخر غير الدراسة الحالية.
ماذا لو رفضت مشاركتك في الدراسة؟
في حالة رفضك، سيتم إلغاء هذا الخطاب غير وصوله إلينا، وفي حالة الموافقة يمكنك الانسحاب في أي وقت دون إبداء الأسباب، ولن يؤثر ذلك على إبنك مطلقا.
ماذا لو مكنا لدي بعض الملاحظات التي أو اضافتها مستكشف من مترشحات؟
يمكن طرح أي شكوك أو مشاكل والحث بالإتصال بالباحث الرئيسي (د/ محمود بن عبد الفتاح فهاس) - مرفق ببيانات التواصل.
ما هو المطلوب من فعالة الآن؟
في حال موافقتك على المشاركة، فعلى التكنولوجيا بتحديد الاستبان المرضى والتفويض على إقرار الموافقة على الاشتراك في الدراسة وإرسالها إلى المدرسة في موعد أقصاه يومين من استلامك لخطابنا هذا.
ارغب في الحصول على بعض المعلومات الإضافية عن الدراسة؟
يمكنك التواصل مع الباحث الرئيسي (د/ محمود بن عبد الفتاح فهاس) - مرفق ببيانات التواصل.

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الاستيقاء
نأمل التكرم بتعيينه وإعادته إلى المدرسة

معلومات عن الطالب:

اسم الطالب:

المدرسة:

الصف:

تاريخ الميلاد بالهجري:

يوم شهر سنة

تاريخ الميلاد بالميلادي:

يوم شهر سنة

العمر عند تعيينه الاستيقب:

العمر عند تعيينه:

معلومات عن والدي الطالب:

الرجل الإجابة عن الأسئلة التالية بوضع علامة (✓) أمام الاختيار المناسب أو الكتابة في الأماكن المحددة لذلك:

1) عمر الأب:

(أ) مصطلح:

العمر:

(ب) مكان الميلاد:

المملكة العربية السعودية

(ج) أعلى شهادة حصل عليها:

لا يوجد

(د) المرحلة:

الكليات الابتدائية

2) عمر الأم:

(أ) مصطلح:

العمر:

(ب) مكان الميلاد:

المملكة العربية السعودية

(ج) أعلى شهادة حصل عليها:

لا يوجد

(د) المرحلة:

الكليات الابتدائية

3) من أجاب على هذا الاستيقب؟

الأم

الأب

شخص آخر:

تاريخ الإجابة على الاستيقب:

/ 1430 هـ

mahodnas@yahoo.com
استبيان عن حساسية الصدر
Core Questionnaire For Chest

الرجاء الإجابة عن الأسئلة التالية بوضوح علامة (√) أمام الاختيار المناسب:

لا نعم

1) هل أصيب طفلك微量元素 في ليلة حساسية الصدر، هل أي وقت مضى؟

إذا أجاب الإجابة ب (√) الرجاء الاتصال مباشرة بالإجازة على الأسئلة 87، 87.

لا نعم

2) خلال الأشهر العشرة الماضية هل أصيب طفلك微量元素 في ليلة حساسية الصدر؟

إذا أجاب الإجابة ب (√) الرجاء الاتصال مباشرة بالإجازة على الأسئلة 87، 87.

لا نعم

3) خلال الأشهر العشرة الماضية، هل مرت مرة أصيب طفلك微量元素 في الصدر؟

لا نعم

1 - 3 مرات

4 - 12 مرة

أكثر من 12 مرة

4) خلال الأشهر العشرة الماضية، هل مرت مرة استيقاظ أو قام فيها طفلك微量元素 من النوم نتيجة لإصابته بصغر الصدر؟

لا نعم

أكثر من ليلة في الأسبوع

ليلة واحدة في الأسبوع

5) خلال الأشهر العشرة الماضية، هل وجدت أن احتكاك الصدر شديد لدرجة أنه لا يستطيع أن يكلم إلا أحكام أو

لا نعم

نعملتين بين نطقنها أخر؟

6) هل أصيب طفلك微量元素 أو عاني من الررب (مضيق التنفس أو الكرب) في أي وقت مضى؟

لا نعم

7) خلال الأشهر العشرة الماضية، هل أصيب طفلك微量元素 في الصدر أثناء أو بعد اللعب أو عمل أي مجهود؟

لا نعم

8) خلال الأشهر العشرة الماضية، هل أصيب طفلك微量元素 بكحة جافة (بدون بلغم) في الليل، ولم تحدث من غير الأيام التي

لا نعم

mahdrnas@yahoo.com

د/ محمود بن عبد النافذ، نحاس
جوال: 0599, 30000, مكتب: 7711344, البريد الإلكتروني: mahdnas@yahoo.com

المؤسسات: Allergy & Respiratory Research Group
Mahmoud Nahhas
PhD Student
Center for Population Health Sciences, General Practice
The University of Edinburgh
29 West Richmond Street
Edinburgh, EH8 9AG
استبيان عن حساسية الأنف

Core Questionnaire For Nose

الأسئلة التالية هي عن مشاكل الأنف عندما لا يكون طفح الجلد بعناب من البرد أو الزكام:

1) هل أصيب طفح الجلد من قبل مشاكل مثل العطس أو نزول مخاط من الأنف أو إسداد الأنف، من غير المرات التي يكون فيها مصاباً بالزكام أو البرد؟

نعم لا

إذا سقطت الإجابة بـ (لا) (1) الرجاء الإجابة مباشرة للإجابة على السؤال رقم 2.

2) خلال الأشهر عشرة الماضية، هل أصيب طفح الجلد مشاكل مثل العطس أو نزول مخاط من الأنف أو إسداد الأنف، من غير المرات التي يكون فيها مصاباً بالزكام أو البرد؟

نعم لا

إذا سقطت الإجابة بـ (لا) (2) الرجاء الإجابة مباشرة للإجابة على السؤال رقم 3.

3) خلال الأشهر عشرة الماضية، هل سقطت هذه المشاكل الأنفية مصحوبة بدء أو حكة في العينين؟

نعم لا

4) خلال الأشهر عشرة الماضية، في أي شهر من أشهر السنة أصيب طفح الجلد بهذه المشاكل الأنفية؟

ضع علامة (✓) أمام الأشهر التي أصيب فيها:

- يناير
- فبراير
- مارس
- أبريل
- مايو
- سبتمبر
- يونيو
- يوليو
- أغسطس
- ديسمبر

5) خلال الأشهر عشرة الماضية، كيف أثرت هذه المشاكل الأنفية على نشاطات طفح الجلد اليومية؟

أثرت بصورة بسيطة
أثرت بصورة متوسطة
أثرت بصورة شديدة

6) هل أصيب طفح الجلد بما يسمى حمى القش، وهي حساسية حادة في الأنف والعينين؟

نعم لا

mahodnas@yahoo.com
استبيان عن حساسية الجلد
Core Questionnaire For Skin

1. هل أصيب أو عانى طفلاً من قبل بطفح جلدي (حبوب على الجلد) معه حكة بصورة مستمرة أو متقطعة استمرت لمدة سنة أقصر على الأقل؟
نعم لا

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة للإجابة على السؤال رقم 7

2. خلال الإلتهاب عشرة أعراض هن أصيب أو عانى طفلاً بهذا الطفح الجلدي (حبوب على الجلد) مع الحكة؟
نعم لا

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة للإجابة على السؤال رقم 7

3. هل مثان هذا الطفاح الجلدي (حبوب على الجلد) مع الحكة يصيب أي من المواقع التالية: السحاب، لسان، فم، البنكرياس، العين، الرأس، القالب، اللسان، الثدي؟
نعم لا

4. في أي سن أصيب طفلاً لأول مرة بهذا الطفاح الجلدي (حبوب على الجلد) مع الحكة 5 سنوات فأكثر
سنتين إلى 4 سنوات تحت سن السنتين

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة للإجابة على السؤال رقم 7

5. خلال الإلتهاب عشرة أعراض هن مثان هذا الطفاح الجلدي (حبوب على الجلد) مع الحكة تشفي (تعافي) بصورة مماثلة (لا) أي وقت؟
نعم لا

6. خلال الإلتهاب عشرة أعراض هن مثان هذا الطفاح الجلدي (حبوب على الجلد) مع الحكة؟
نعم لا

إذا كانت الإجابة ب (لا) الرجاء الانتقال مباشرة للإجابة على السؤال رقم 7

7. هل أصيب أو عانى طفلاً من مرض الأكزيميا (حساسية الجلد)؟
نعم لا

mahodnasy@yahoo.com

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استبيان عن البيئة الغشبية

Environmental Questionnaire

(1) خلال الاثنين عشر شهراً الماضية،كم مرة تم المتوسط لناول طلخات الأطعمة أو المشروبات النباتية؟

<table>
<thead>
<tr>
<th>النوع</th>
<th>ثلاثة مرات أو أكثر في الأسبوع</th>
<th>مرة أو مرتين في الأسبوع</th>
<th>لا مرة أو أحياناً</th>
</tr>
</thead>
<tbody>
<tr>
<td>اللحوم (مثل الدجاج)</td>
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<td></td>
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<tr>
<td>المنتجات البحرية (مثل الأسماك)</td>
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<tr>
<td>الفواكه</td>
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<tr>
<td>الخضروات</td>
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<tr>
<td>البقالات (مثل الخضروات والفواكه والبيض)</td>
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<tr>
<td>الحبوب (مثل القهوة والذرة)</td>
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<tr>
<td>المعكرونة</td>
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<td>الأرز</td>
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<tr>
<td>الزبدة</td>
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<tr>
<td>السمن الشبائي (المرغوبين)</td>
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<tr>
<td>المكسرات (مثل الجوز واللوز والقنب السوداني)</td>
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<tr>
<td>البطاطا</td>
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<tr>
<td>الحليب</td>
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<tr>
<td>البيض</td>
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<tr>
<td>وجبات سريعة (مثل البرجر)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(2) حكم مرة في الأسبوع يقوم طلخات بممارسة رياضة لمدة طويلة تجعله يتنفس بصعوبة؟

(3) خلال أيام الأسبوع،كم ساعة في اليوم ( فترة 24 ساعة) يقوم طلخات بممارسة التمياز (التليفزيون)؟

<table>
<thead>
<tr>
<th>ساعات</th>
<th>من 3 ساعات إلى أقل من 5 ساعات</th>
<th>أقل من 3 ساعات واحداً</th>
<th>5 ساعات فأكثر</th>
</tr>
</thead>
</table>
4) في البيت، ما هو الوقود المستخدم في الطبخ عادة؟
تار بالخشب أو الفحم
الغاز
الكهرباء
5) ما هي وسيلة التكييف في البيت؟
مكيف فريون
مرحة ميكانيكية
مكيف صحراوي
6) خلال السنة الأولى من عمر طفلك، هل صفت عادة تعطيه دواء الباراسيتامول (مثل أدول، فيفايول) عندما يصاب بالحمي؟
لا
نعم
7) خلال الأشهر الثلاثة الماضية، صممت مرة في المتوسط فم بإعطاء طفلك دواء الباراسيتامول (مثل أدول، فيفايول)؟
مرة واحدة في الأسبوع على الأقل
مرة واحدة في الشهر على الأقل
مرة واحدة في السنة على الأقل
8) عندما طفلك الأول حاملًا هذا الطفل، هل طفلك تعرضا بصورة منتظمة (مرة واحدة في الأسبوع على الأقل) للحيوانات المزعجة (مثل الأغنام والmAhوم والخرافان)؟
لا
نعم
9) هل ولد طفلك في المدينة المثورة؟
لا
نعم
10) حجم مساحته وزن طفلك عند الولادة؟
مليمترات
11) هل رفع طفلك رضاعة طبيعية؟
لا
نعم
12) خلال السنة الأولى من عمر طفلك، هل أخذ طفلك أي مضادات حيوية؟
لا
نعم
13) خلال السنة الأولى من عمر طفلك، هل صفتك عند ممت قط (مر) في البيت؟
لا
نعم
14) خلال السنة الأولى من عمر طفلك، هل صفتكم تعرضا بصورة منتظمة (مرة واحدة في الأسبوع) على الأقل لحيوانات المزعجة (مثل الأغنام والماز والخرافان)؟
لا
نعم
15) خلال الأشهر الثلاثة الماضية، هل صفتكم عند ممت قط (مر) في البيت؟
لا
نعم
16) حكم عدد أخوة وأخوات طلائلكم الذين هم أصغر منه ؟ إخوة وأخوات

17) حكم عدد أخوة وأخوات طلائلكم الذين هم أصغر منه ؟ إخوة وأخوات

18) حكم سنة عاش طلائلكم في المدينة المنورة ؟

19) خلال أيام العمل في الأسبوع، حكم مرة في المتوسط تمر الشاحنات في الشارع المجاور لنزلكم ؟

20) هل أم الطفل تدخن السجائر ؟

21) هل أب الطفل يدخن السجائر ؟

22) خلال السنة الأولى من عمر طلائلكم هل سكنت أم الطفل تدخن السجائر ؟

23) حكم عدد الأشخاص الذين يعيشون في البيت يدخنون السجائر (أيما فيهم الأب/الأمه) ؟

شراً لحمكم على هذه الأسئلة

mahodnas@yahoo.com مم/ محمود بن عبد الفتاح يحاس

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**PARENTAL CONSENT FORM**

**Research Project**

The research project involves a study of pediatric patients suffering from asthmatic attacks in the study area.

**Parental Consent**

To proceed with the study, consent must be provided by the parent or legal guardian. Please indicate your agreement with the following statements:

1. Authorize the research team to collect personal and medical information about the participant and their family.
2. Authorize the research team to contact me for any urgent matters.
3. Authorize the research team to perform diagnostic tests (blood tests, genetic tests, and others) as required.
4. Authorize the research team to store and use the collected data for research purposes.

**Parent Information**

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Thank you for your cooperation.

For more information, please contact:

mahodny@yahoo.com

Date: 1430 / /

D. Mohamad bin Abd al-Aziz Al-Nahas
مع تحيات
فريق البحث للدراسة

لل التواصل مع الباحث
د / محمود بن عبد الفتاح نحاس

جوال: 399 000 007 007
فاكس: 216 484 83
البريد الإلكتروني: mahodnas@yahoo.com
Appendix 19: Images of the training programme for research team

Images of the training programme for the research team and the revision day with Professor Aziz

Revision Day in the presence of Professor Aziz

Talk to the research team

A further talk to the research team

Professor Aziz checking the procedure

Measuring height

Skin prick test in the presence of Professor Aziz
With the volunteer children and their fathers

Professor Aziz checking the accuracy of Skin prick test

Measuring the height of a volunteer child

Professor Aziz presenting the certificate for the research

Professor Aziz presenting the certificate for training
Appendix 20: Image from pilot study

Images from pilot study

Professor Aziz with Dr. Bahjat
The General Directorate of Education (Boys)

Professor Aziz with Dr. Yousif
The General Directorate of Education (Girls)

Professor Aziz checking the skinfold thickness procedure

Professor Aziz checking the height procedure

Pulmonary function test

Professor Aziz checking the blood samples
Processor Aziz checking the accuracy of skin prick test
Processor Aziz checking the accuracy of blood-taking
Processor Aziz checking the accuracy of PFT
Processor Aziz checking the accuracy of child’s details
Processor Aziz visiting children in their classroom
Appendix 21: Images from final study

Images from final study

Cheeking the data information on the children

Measuring skin fold thickness in the large study

Measuring highs in the large study

Measuring skin fold thickness in the large study

Measuring highs in the large study

Measuring waist circumference in the large study
Skin prick test in the large study

Pulmonary function test in the large study

Skin prick test in the large study

Pulmonary function test in the large study

Skin prick test in the large study

Pulmonary function test in the large study
Appendix 22: Contributions to science

Poster presentations


Oral presentations


Publications in peer-refereed journals


Thanks to my teachers