DIETARY AND ENVIRONMENTAL FACTORS ASSOCIATED WITH SYMPTOMS OR DIAGNOSIS OF ASTHMA IN CAPE TOWN SCHOOL CHILDREN: FINDINGS FROM THE INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC) PHASE THREE STUDY

Unati Mahlati

MBChB (Natal)

Thesis presented for the degree of

Masters in Medicine (MMed) (Public Health)

School of Public Health and Family Medicine

University of Cape Town

August 2007

CONTENTS

I dedicate this thesis to my family. Their constant support and encouragement made it possible to complete this work. My beloved children, Liza Mulalo and Takalani, deserve special mention, they are my inspiration.

DECLARATION

The work presented in this report represents analyses of data collected as part of a larger international multicentre collaborative study, the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. The role of the author in the study was data analyses and writing up of all chapters of this thesis, under the supervision of Professors Rodney Ehrlich and Heather Zar. In this regard the analyses presented in this thesis are the original work of the author and have not been submitted for other degree purposes, or publication before. To date results of disease prevalence trends from the project have been recently published by Zar, Ehrlich and Weinberg [5]. From a subset of the same dataset Graham (2005) presented the relationship between socio-economic deprivation and asthma prevalence and severity as part of a BSc Honours research project [26]. All sources used for this report have been appropriately cited.

ACKNOWLEDGEMENTS

I would like to express my most sincere gratitude to my co-supervisors for this project, Professor Heather Zar and Professor Rodney Ehrlich. I would like to thank them for allowing me to use the ISAAC 3 dataset for this project. Their guidance, expert input and patience have been invaluable. On behalf of my co-supervisors and myself, I thank the field researchers, Ms E Ngxabi and Mr S Abrahamse. We are grateful to the Dept. of Education in the Western Cape, the school principals, teachers, children and parents for participating. The study was supported by a grant from the Medical Research Council, South Africa, an AstraZeneca Respiratory fellowship awarded by the South African Thoracic Society (Heather Zar), and sponsorship from the following pharmaceutical companies: AstraZeneca, Boehringer-Ingelheim, 3M and Schering-Plough. We thank the International ISAAC centre, New Zealand for a start up grant and for advice and support.

***ABSTRACT*:**

Background:

The prevalence of current wheeze and asthma in school children in Cape Town has been reported to be increasing. The multicentre International Study of Asthma and Allergies in Childhood Phase 3 (ISAAC 3) offered an opportunity to investigate the relationship between environmental or dietary risk factors and asthma symptoms or diagnosis.

Methods:

A cross sectional survey of self- reported symptoms and diagnoses in 13 to 14 year old school children using standardized ISAAC written and video questionnaires was performed in 2002. The associations between environmental and dietary predictors and the 12-month prevalence of wheeze on written and video questionnaires or asthma diagnosis were estimated using logistic regression.

Results:

A school based sample of 5 037 pupils participated. The 12-month ("recent") prevalence of wheeze on written and video questionnaire was 20.3% and 11.2% respectively. On written questionnaire 14.4% of participants reported an asthma diagnosis. The following environmental and dietary variables were associated on multivariate analysis with a diagnosis of asthma or with the prevalence of recent wheeze:

Environmental variable	Current wheeze on written questionnaire OR (95% CI)	Asthma diagnosis OR (95% CI)	Current wheeze on video questionnaire OR (95% CI)
Xhosa speaking (reference: Afrikaans)	0.92 (0.71- 1.19)	0.73 (0.54- 1.00)	0.85 (0.64- 1.12)
English speaking (reference: Afrikaans)	1.82 (1.50- 2.19)	1.22 (0.99- 1.49)	1.28 (1.02- 1.62)
Mother with tertiary education	1.32 (1.11- 1.56)	1.32 (1.09- 1.60)	1.11 (0.89- 1.38)
Eating maize at least once or twice a week	0.71 (0.60- 0.84)	0.91 (0.75- 1.10)	0.83 (0.68- 1.02)
Eating maize 3 or more times a week	0.80 (0.64- 1.00)	0.77 (0.59- 1.00)	Not included in final model
Exercise once or twice a week	1.47 (1.24- 1.74)	1.57 (1.30- 1.91)	1.40 (1.13- 1.74)
Exercise = 3 times a week	1.39 (1.14- 1.70)	1.40 (1.11- 1.75)	1.39 (1.08- 1.79)
Taking paracetamol at least once a month	1.45 (1.26- 1.68)	1.22 (1.04- 1.44)	1.62 (1.35- 1.94)
Maternal smoking	1.20 (1.02- 1.42)	1.07 (0.89- 1.28)	1.32 (1.08- 1.62)
Respondent smoking	1.45 (1.15- 1.82)	Not included in final model	1.35 (1.01- 1.79)
Using paraffin as cooking/heating* fuel	1.05 (0.83- 1.33)	0.75 (0.53- 1.04)	Not included in final model
Using wood as cooking/heating* fuel	Not included in final model	1.94 (1.13- 3.32)	2.35 (1.36- 4.05)
Body Mass Index (BMI) > 95th centile for age	1.71 (1.30- 2.24)	1.27 (0.92- 1.74)	1.89 (1.38- 2.60)

Conclusion:

The study confirms the association of asthma with improved socio-economic status as reflected in language, maternal higher education and diet. Maternal and respondent smoking, obesity and exposure to wood fumes may have more direct causal significance. The association with exercise is probably a result of cross sectional bias. Paracetamol intake may indicate either a direct association or be confounded by symptom severity. Although inferences are limited by the cross-sectional study design, the results add to the growing body of evidence on factors associated with asthma. It is likely that the associations are multi-factorial and also dependent on gene-environment interactions.

Funding: MRC, South Africa, an AstraZeneca Respiratory fellowship from South African Thoracic Society (HZ), and sponsorship from the following pharmaceutical companies: AstraZeneca, Boehringer-Ingelheim, 3M and Schering-Plough. We thank the International ISAAC centre, New Zealand for a start up grant.

CHAPTERS AND SUBHEADINGS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: INTRODUCTION

1.1 **Background:**

The International Study of Asthma and Allergies in Childhood (ISAAC) is a multicentre collaborative study of the prevalence of asthma, allergic rhinoconjuctivitis and eczema. ISAAC was initiated to apply standardised methodology and to compare prevalence of these diseases between study centres and/ or countries. Phase One (ISAAC 1) commenced in 1991 and documented the baseline prevalence of the three allergic conditions across all the centres participating in the study. This was followed by Phase Two (in which fewer centres took part) to investigate objective markers of disease. Phase Three (ISAAC 3) was conducted an average of seven years later, with the objectives of investigating trends in the prevalence of disease and associations between possible dietary and environmental risk factors and these conditions.

ISAAC I included eight study centres from six African countries, and results showed that asthma symptom prevalence in these countries was similar to that in many European countries [4]. In particular, in Cape Town, South Africa, prevalence of wheeze in the past 12 months was considered to be high, with a prevalence of 16.1% (compared to a regional prevalence of 11.7% and a global prevalence of 13.8%) [1].

Results from the ISAAC 3 study showed that although trends in the prevalence of symptoms and diagnoses of asthma, allergic rhinoconjuctivitis and eczema varied worldwide, increases were twice as common as decreases. The only exception was asthma symptoms in the 13 to 14 year age group, where particularly in high prevalence centres decreases were more common than increases. However in the South African study population (13 and 14 year old schoolchildren from Cape Town), significant increases were documented in all three allergic disorders [3].

ISAAC 3 included 22 centres from 16 African countries [4], of which the Cape Town study centre had the second highest prevalence of current wheeze on written questionnaire (20.3%, following Reunion Island with 21.5%). Similarly the second South African study centre, Polokwane (which did not participate in Phase 1) recorded a high prevalence of 18.0% [4].

The high prevalence of asthma, which has been documented to be increasing in Cape Town, is of public health concern and increased efforts should be made to investigate possible causal factors.

Internationally the associations between asthma and several risk factors, including dietary and environmental factors, have been investigated and there is reasonable consensus on the role of some, most notably the positive association with maternal smoking, environmental tobacco smoke, and socioeconomic status [20,21,22,23,24]. However the evidence is inconclusive on other risk factors.

Some of these studies (especially those derived from the ISAAC study) have been of ecological study design, and findings may not be applicable to associations at the individual level.

Despite the increasing prevalence of asthma occurring in developing countries (both urban and rural settings), there is little information on the contribution of dietary, environmental and socioeconomic variables in these settings. Africa may have unique characteristics that may be associated with the increasing prevalence of asthma in childhood, but research in this field is sparse. It may well be that the influence of genetics, burden of infectious diseases, diet etc. is different from developed country settings.

1.2 Purpose:

The purpose of this study was to investigate associations between the prevalence of asthma and dietary and other environmental factors, with the aim of adding to existing evidence and identifying modifiable risk factors for which local public health interventions could be developed.

1.3 Objectives:

1.3.1 To measure the prevalence of current wheeze and lifetime diagnosis of asthma in a population of adolescents in Cape Town, South Africa.

1.3.2 To measure the association of dietary factors with prevalence of current wheeze and lifetime diagnosis of asthma in this population.

1.3.3 To measure the association of environmental risk factors with prevalence of current wheeze and asthma ever. Environmental factors of particular interest included those related to the hygiene hypothesis [tuberculosis (TB), overcrowding, number of siblings], socioeconomic status (as indicated by maternal education, type of housing and overcrowding), maternal smoking and environmental tobacco smoke, exercise, body mass index (BMI), paracetamol intake, type of fuel used for cooking and heating (wood or paraffin compared with electricity).

1.4 Structure of the thesis:

The thesis begins in Chapter 2 with a comprehensive literature review. In this chapter relevant research findings on prevalence of asthma in childhood, and dietary and environmental factors which have been shown to have an association with asthma symptoms and diagnosis in childhood are presented and discussed. Thus the chapter presents the research evidence pertinent to this study's research questions.

Chapter 3 describes the methods used to conduct the study. The section describes the study design, sampling method, data collection, data analysis and ethical considerations.

In Chapter 4 the results of the study are presented. Selected outputs from the bivariate analysis and the multivariate logistic regression are presented in tables preceded by summaries of important results. Odds ratios with the 95% confidence intervals represent the associations between risk factors and the outcomes of interest in the study (asthma symptoms and diagnosis).

This is followed by a detailed interpretation and discussion of the study findings and limitations.

The thesis ends in Chapter 6 with a conclusion of the study findings and considers the public health implications thereof. Recommendations based on the study findings are proposed.

References and appendices are presented at the end of the thesis. Appendices include extended bivariate results for all variables considered too detailed to include in the main body of the thesis.

CHAPTER 2: LITERATURE REVIEW

2.1 Asthma in childhood: prevalence estimates worldwide and in South Africa

2.1.1 Global asthma prevalence estimates and trends

The results of ISAAC 1 indicated that world wide estimates of the prevalence of asthma varied widely between centres and countries, ranging from a low of 2.1% in the Bandung study centre in Indonesia to a high of 32.2% in the United Kingdom (including 15 study centres) [1]. Differences in prevalence were reported to be generally bigger between countries than within countries, with a tendency towards higher prevalence in English speaking developed countries [1]. The results suggest that genetic factors play a lesser role than environmental factors in the causation of asthma and allergic conditions [1].

ISAAC 3 was conducted an average of seven years after ISAAC 1. Reporting on the prevalence trends from ISAAC 1 to ISAAC 3, recently published results indicate that world-wide there has been change of one or more standard errors in the prevalence of allergic diseases (asthma, eczema and rhino-conjunctivitis) in most study centres, with variations in the size and direction of the change [3].

With particular reference to asthma in the 13 to 14 year age group [most centres (including South Africa) included this age group only, with fewer centres studying the 6 to 7 year age group], almost the same number (42) of study centres had increased asthma symptom prevalence as those with decreased prevalence (40 centres). Increases were noted to be more common in centres with lower mean prevalence. In contrast, decreases in asthma symptom prevalence were more common in centres with higher mean prevalence [3].

These variations provide additional evidence that environmental factors play a significant role in asthma causation even over a relatively short period of time.

2.1.2 Africa: asthma prevalence estimates and trends

Table 2.1 below presents ISAAC 1 data. It can be seen that the African regional prevalence at the time was quite similar to the global prevalence for all three outcome measures. Of the six countries in the African region that participated in ISAAC 1 Nairobi (Kenya) had the highest prevalence of current wheeze on both written and video questionnaire, whilst Ibadan (Nigeria) had the highest lifetime asthma diagnosis prevalence. South Africa (Cape Town study centre) had a higher prevalence of current wheeze on the written questionnaire than both the regional and global prevalence, with the prevalence of current wheeze on video questionnaire being similar to the global figure [1].

Table 2.1: Prevalence of current wheeze (written and video questionnaire) and lifetime diagnosis of asthma in 13 to 14 year age group, ISAAC 1 study results in Africa [1].

Study centre	Current wheeze (written questionnaire)	Lifetime diagnosis of asthma	Current wheeze (video questionnaire)
Regional prevalence	11.7%	10.2%	9.2%
Global prevalence	13.8%	11.3%	7.3%
Addis Ababa (Ethiopia)	10.7%	2.8%	Not done
Jima (Ethiopia)	1.9%	2.2%	Not done
Eldoret (Kenya)	10.4%	6.8%	3.5%
Nairobi (Kenya)	17.1%	15.4%	18.7%
Ibadan (Nigeria)	10.7%	18.4%	Not done
Cape Town (South Africa)	16.1%	13.1%	6.5%
Algiers (Algeria)	7.8%	6.4%	Not done

From table 2.1 it is noted the both regionally and globally the prevalence reported from the video questionnaire is consistently lower than that reported from the written questionnaire. Several authors have suggested several possible explanations for this [47,54]. In their paper on the agreement between the written and video questions (current wheeze) for comparing asthma symptoms in ISAAC 1, Crane et al. reported that whilst the overall correlation between the two questions was high, negative agreement was high (i.e. most respondents who responded negatively to the written question had the same negative response for the video question, but in contrast positive agreement was low/poor (indicating that a large proportion of respondents who responded in the affirmative for the written question, responded negatively for the video question) [54]. This resulted in low level of agreement as measured by Kappa statistic. The authors suggested three possible reasons for this:

i) The inherent "omnibus" nature of the kappa statistic, which make it vulnerable to difference in prevalence across populations (as noted between the written and video questionnaires).

ii) Differential understanding of the term "wheeze" by 13-14 year old children, compared to medical practitioner's understanding of the term, and the context for the terminology.

iii) Interpretation of the video sequence to be depicting a more severe wheeze state than that experienced by the respondents, resulting in a high proportion of respondents with mild wheezing to under-report wheeze at rest.

The authors further report that the differences in agreement (kappa statistic) varied between centres, regions and language (with English speaking centres having the poorest positive agreement [54].

Twenty two (22) centres from 16 African countries participated in ISAAC 3. Similar to the international prevalence, wide variation within and between the African countries was observed, ranging from a low prevalence of current wheeze on the written questionnaire of 4.4% in Marrakech, Morocco (North Africa) to a high prevalence of 21.5% in Reunion Island. Overall, the prevalence in most countries was intermediate to high (=10% and

=20% respectively), with several Sub-Saharan centres (including the two South African centres) having prevalence similar to that seen in study centres in Europe [4].

This was an unexpected finding given the high burden of infectious diseases in these African countries, as it goes against the hygiene hypothesis [4]. Generally, the urban centres had higher prevalence than the rural centres and therefore this suggests that environmental factors related to "urbanization" and changing socioeconomic status are associated with asthma symptom prevalence in developing countries like Africa [4].

Prevalence of current wheeze on the video questionnaire varied less between the seven centres that conducted the video questionnaire than on the written questionnaire, ranging from 7.1% in Boulmene to 12.9% in Casablanca (both Moroccan centres).

2.1.3 South Africa: asthma prevalence estimates and trends

Several studies using different methodologies have measured prevalence of self- or parent - reported asthma symptoms and asthma as diagnosed by bronchial hyperresponsiveness (BHR) to either exercise challenge or histamine challenge tests in South Africa. The results of these studies are presented below in chronological order, from earliest to latest reported. Tables are presented for ease of transposition.

a) Prevalence of exercise induced bronchospasm (EIB)

In 1979 Van Niekerk et al. were the first to report a relatively low EIB prevalence in Xhosa speaking African children in Cape Town and Transkei [6]. The study included 694 Black children aged 6 to 9 years old residing in the peri-urban black township of Gugulethu, Cape Town and a corresponding sample of 671 children from a rural village in Transkei. Asthma was diagnosed by exercised induced reduction in the forced expiratory volume in 1 second (FEV_1) and peak expiratory flow rate (PEFR).

Van Niekerk's study showed a significant urban- rural difference in asthma (EIB) prevalence. Whilst the urban prevalence of EIB was 3.17%, the rural prevalence was reported to be 0.14% [6].

Following Van Niekerk's study Vermeulen went back to rural Transkei to investigate whether Van Niekerk's finding that "there was no asthma in Transkei" was true, and published his results in 1990. Vermeulen had previously concluded from a pilot study designed to compare the exercise challenge test to the histamine challenge test that the latter was more reliable in diagnosing asthma, and thus used the histamine provocation test in his study. In addition Vermeulen included clinical history and full allergy work-up, whilst Van Niekerk used exercise challenge testing only [7]. From Vermeulen's study, 14.2% of children were diagnosed with bronchial hyperresponsiveness, and of this group 6.1% were diagnosed with asthma. Thus Vermeulen confirmed that "there definitely is asthma in (rural) Transkei" [7].

In 1990 Terblanche and Stewart compared prevalence of exercise induced bronchospasm in White and Coloured schoolchildren aged 6 to19 years old from the northern suburbs of Cape Town. They reported a statistically significantly higher prevalence in White schoolchildren (5.87%) compared to their Coloured counterparts who had a prevalence of 4.05% [8]. This was an unexpected finding since higher prevalence in Coloured children was previously reported from study populations drawn from hospital based studies [8].

The authors suggest that this may represent one of two reasons. The first may be that the lower rates observed in older Coloured children may have reflected higher drop-out rates in older Coloured children from poor backgrounds. This is supported by the finding that although the White children had *on average* a higher prevalence than the Coloured children, in the youngest age band (6 to 9 years) the Coloured children had a much higher prevalence than the White children (6.3% compared to 1.08% respectively) [8].

The second reason cited by the authors was that White asthmatic children were more likely to seek medical care from the private sector, whilst Coloured children were more likely to attend public provincial hospitals, where all the earlier prevalence surveys had been conducted [8].

Although the study was not designed to be analytic and therefore no analysis of association between risk factors and EIB could be done, it is interesting to note that the White children were recruited from schools attending predominantly social class 1 and 2, whilst the Coloured children came from schools serving predominantly social classes 3 and 4 [8]. This indicates that the White children were from better socio-economic status background than the Coloured children.

Following this, in 1992 Nagel reported prevalence of EIB to be 4.15% in White children aged 12 years attending schools in the southern suburbs of Cape Town [9]. Nagel proposed that the reason for the lower prevalence in his study compared to that found in White children by Terblanche and Stewart was due to the fact that Terblanche and Stewart's diagnostic criteria included milder cases of post exercise bronchospasm (outcome

measure >10% reduction in FEV_1 compared to Nagel's of >15% reduction in FEV_1), which "was not severe enough to be generally not be accepted as EIB" [9].

It is worth noting that both Terblanche and Nagel concluded that the exercise challenge test is not sensitive enough for epidemiological studies [8,9]. Terblanche had shown that whilst the exercise challenge test was highly specific, it had a sensitivity of 0.37 and a positive predictive value of 46% [8]. Nagel further reported that for various reasons the reported prevalence of 4.15% was most likely to be an underestimate of the true prevalence [9].

Twenty years after van Niekerk's study, Steinman et al. also went back to rural Transkei to study prevalence of asthma. They also employed the histamine challenge test and found the prevalence of histamine induced bronchospasm in rural children aged 10 to 14 years to be 17% (compared to 0.14% reported by van Niekerk in 1979 and 14.2% reported by Vermeulen in 1990) [10]. They compared the prevalence of bronchial hyperresponsiveness in children in rural Transkei to that of African children from the Marconi Beam peri-urban settlement in Cape Town (recently urbanised families) and that of white children in the Kirstenhof suburb of Cape Town. The prevalence of bronchial hyperresponsiveness was reported to be 34.4% in African children from recently urbanized families, and 33% in white fully urbanized children [10].

In 2005 Calvert and Burney also reported significant urban-rural difference in prevalence of EIB. The survey was conducted in 18 schools in rural Transkei and six urban schools in the Khayelitsha township of Cape Town, and included African children between the ages of 8 and 12 years. They reported the prevalence of EIB to be 8.9% in the rural population and 14.9% in the urban population, unadjusted OR 1.76 (95% CI 1.47- 2.10) and adjusted OR 1.31 (0.99- 1.74) [11].

The consistent urban-rural difference in prevalence of asthma symptoms and diagnosis is in keeping with the general observation in other African countries; that urban centres tend to have higher prevalence than the rural centres [4].

Outside of Cape Town, in 2006 Mashalane et al. reported EIB prevalence of 7.2% (95% CI 4.5- 10.3%) in 9 to 10 year old children from Thokoza township in the Gauteng province. The authors suggested environmental pollution to be a risk factor contributing to the high prevalence in this study population [12].

Table 2.2 below illustrates the trend of trends in prevalence of bronchial hyperresponsiveness in South African children over the last three decades.

Table 2.2: Comparison of asthma prevalence in South African children as measured by exercise induced bronchospasm (EIB) or histamine induced bronchospasm (HIB)[#].

Study name/authors	Year study published, study population	Age range and race of respondents (years)	EIB prevalence	HIB prevalence
Van Niekerk et al.	1979, rural Transkei and Gugulethu township, Cape Town	6 to 9 years, Black	0.14% rural, 3.17% urban	--
[#] Vermeulen	1990, rural Transkei	8- 16 years	--	14.2% rural
Terblanche and Stewart	1990, Northern suburbs Cape Town	6 to 19 years	5.1%	--
Nagel	1992, Southern suburbs, Cape Town	12 years	4.1%	--
[#] Steinman et al.	2003, rural Transkei and Cape Town suburbs	10- 14 years	--	17% rural, 34.4% *, 33% **
Calvert	2005, rural Transkei and Khayelitsha township, Cape Town	8 to 12 years 8 to 12 years	8.9% rural 14.9% urban	--
Mashalane et al.	2006, Thokoza, Gauteng province	9 to 10 years	7.26%	--

*: recently urbanized

**: fully urbanized

b) Prevalence of parent- or self- reported asthma symptoms and diagnosis

In 1994, Burr et al. reported on results of a survey conducted in 4 countries to compare asthma prevalence in 12 year old children from four countries (New Zealand, Wales, South Africa and Sweden).The South African study included white children living in the Southern suburbs of Cape Town. They found the prevalence of current wheeze (in the past 12 months) in the South African study population to be 17.8%, comparable to New Zealand (with prevalence of 17.9%), and higher than the other two study centres (15.2% in Wales and 9.2% in Sweden) [13]. Prevalence of lifetime asthma diagnosis in Cape Town was found to be 11.5%, similar to the prevalence of 12% in Wales [13]. New Zealand had the highest prevalence of lifetime diagnosis of (16.8%), whilst the lowest prevalence was found in Sweden (4.0%) [13].

A year later, in 1995 Ehrlich et al. reported a prevalence of 26.8% for current wheeze and that of 10.8% for reported asthma diagnosis in school children aged 6 to 13 years old in Mitchells Plain. Mitchells Plain is a predominantly coloured township in Cape Town [14].

In 1998, the ISAAC Phase One Steering Committee reported the prevalence of current wheeze to be 16.1%, and that of asthma diagnosis to be 13.1% in Cape Town school children of *all* races aged 13 to 14 [1]. More than 30 schools were included in ISAAC 1.

Whilst Ehrlich's study referred to above used similar methodology (outcome measures and questionnaire), the study population was different to that of the ISAAC study. Ehrlich's study included younger children (ranging from 6 to 13 years old, 80% between 7 and 8 years of age) from 15 schools in the coloured township of Mitchells Plain. This may account for the marked difference in prevalence of recent wheeze between the two studies.

This explanation is supported by the fact that in 2002 Pather reported similar prevalence to that reported by Ehrlich in 1995. Similar to Ehrlich, Pather also conducted his study on a similar study population from Mitchells Plain township. He reported the prevalence of

current wheeze to be 27.5% and that of reported asthma diagnosis to be 11.2% [15]. Comparing Ehrlich and Pather's findings in the predominantly coloured township of Mitchells Plain to the reported prevalences reported in other predominantly White suburbs and Black townships in Cape Town suggests that there must be some exposure/risk factors in these different settings that accounts for the reported differences in reported prevalence of asthma symptoms and diagnosis.

In 2003 White et al. reported very high prevalence of current wheeze and reported asthma diagnosis (33% and 23.7% respectively) in 9 to 15 year olds from the North-western suburbs of Cape Town [15]. Of note is that these are residential suburbs which are in close proximity to a petrochemical refinery and other industries, which may account for the very high reported prevalence [15].

In 2005, Obihara et al. reported the prevalence of lifetime diagnosis of asthma in children aged six to fourteen years from two poor suburbs of Cape Town to be 12.3% [16]. The racial composition of the sample was not reported.

Recent reports showed that the prevalence of current wheeze in 13 and 14 year old school children residing in Cape Town had increased from 16.1% in Phase One (data collected in 1995) to 20.3% in Phase Three (data collected in 2002), a rate of 0.60% per year [3,4,5]. The two study centres from South Africa (both urban cities) had similar prevalence (Cape Town 20.3% and Polokwane 18.0%) [4]. The variation in reported prevalence between the different residential areas and racial groups in the city of Cape Town suggests differential exposure to risk factors which to date have not been adequately investigated in a representative study in this setting.

Fewer asthma symptom prevalence studies have been reported outside of Cape Town. In 1999 Nriagu et al. reported the prevalence of wheeze associated with shortness of breath and that of doctor diagnosed asthma in children younger than 17years residing in predominantly coloured and Indian suburbs of Durban to be 16% and 10% respectively [17].

Table 2.3: Comparison of parent- or self- reported asthma symptom and diagnosis prevalence studies conducted in children in Cape Town, South Africa.

Study name/authors	Year study published	Study population (age group, area)	Asthma symptom prevalence	Reported asthma diagnosis prevalence
Burr et al.	1994	12 year olds, Southern suburbs, Cape Town	17.8%	11.5% (lifetime diagnosis), 8.7% (current asthma)
Ehrlich et al.	1995	6 to 13, Mitchells Plain township, Cape Town.	26.8%	10.8%
ISAAC 1	1998	13 to 14, across city of Cape Town (all races)	16.1%	13.1%
Pather	2002	7 to 12, Mitchells Plain township, Cape Town	27.5%	11.2%
White et al.	2003	9 to 15, Northwest suburbs, Cape Town	33.0%	23.7%
Obihara et al.	2005	6 to 14, two low income suburbs, Cape Town	--	12.3%
ISAAC 3	2007	13 to 14 across city of Cape Town (all races)	20.3%	14.4%

remaining strongly significant in males. However the authors note that the formal test of interaction was not significant [26].

In an attempt to clear the uncertainties regarding causality, especially the temporal relationship between asthma and obesity, Flaherman and Ruderford recently conducted a systematic review and meta analysis, including 12 cohort studies fulfilling the studies' inclusion criteria, which confirmed that high weight (as indicated by a body mass index/BMI of $\geq 85^{th}$ centile) increases the risk of developing asthma (at any time compared to baseline) by 50% (OR 1.5, 95% CI 1.2- 1.8) [25].
The same review showed that the risk of incident asthma is increased by high birth weight (as indicated by a birth weight >3.5 kg or high Ponderal index) (OR 1.2, 95% CI 1.1- 1.3) [25].

The problem with interpreting cross sectional studies, as in Luder et al's study noted above, is temporality. Severe asthma may lead to inactivity and weight gain as exercise induced bronchospasm is one of the hallmarks of asthma diagnosis. However the fact that a significant number of cohort studies (included in Flaherman and Rutherford's meta analysis discussed above) also found a strong positive association strengthens the evidence for the association between high body mass index and asthma. One of the significant limitations of the meta- analysis is that with this methodology it was not possible to adjust for possible confounding factors, although some of the individual studies did control for confounding [25].

An additional criterion that is fulfilled for a causal relationship between high BMI and asthma is consistency of results in studies of different design as shown above, conducted in different study populations (adults and children). There is also evidence that moderate weight loss is associated with an improvement in signs of asthma (airway obstruction and peak exploratory variability) in obese asthmatics [26].

Authors attribute the association between underweight and asthma to be possibly due to poor nutrition in the perinatal period and/or low birth weight, resulting in both poor lung and airway development and underweight later in life [27].

The postulated mechanisms for the association between obesity and asthma are not clear but include hormonal changes (mainly oestrogen related), systematic inflammation and mechanical factors related to high body mass [26,27]. Obesity is associated with increased caloric intake. It is plausible that the predominant foodstuff in the diet of subjects with normal BMI are different from those of subjects with high BMI, and since diet has also been independently associated with asthma prevalence it may be an important cofactor in the association between obesity and asthma.

Obesity is also associated with increased levels of inactivity in children. Inactivity is in turn associated with reduction in deep breathing, which is hypothesised to lead to "latching" of the airway smooth muscles, leading to increased airway reactivity and obstruction as seen in asthma [26].

Authors attribute the association between underweight and asthma to be possibly due to poor nutrition in the perinatal period and/or low birth weight, resulting in both poor lung and airway development and underweight later in life [27].

The postulated mechanisms for the association between obesity and asthma are not clear but include hormonal changes (mainly oestrogen related), systematic inflammation and mechanical factors related to high body mass [26,27]. Obesity is associated with increased caloric intake. It is plausible that the predominant foodstuff in the diet of subjects with normal BMI are different from those of subjects with high BMI, and since diet has also been independently associated with asthma prevalence it may be an important cofactor in the association between obesity and asthma.

Obesity is also associated with increased levels of inactivity in children. Inactivity is in turn associated with reduction in deep breathing, which is hypothesised to lead to "latching" of the airway smooth muscles, leading to increased airway reactivity and obstruction as seen in asthma [26].

2.4 Maternal smoking and environmental tobacco smoke (ETS) and asthma

Parental smoking, in particular maternal smoking has been shown in many studies to be associated with wheeze after the first year of life in children [29,30]. There is some debate as to whether this association is true for allergic asthma as some studies have suggested that the association is mainly found in children suffering from non-specific "wheezy illness", rather than atopic/allergic asthma. With allergic asthma, the association with smoking seems to be present in severe cases of asthma, suggesting that rather than cause asthma, smoking triggers or provokes wheezing attacks. This theory is proposed by Cook and Strachan, who performed a meta analysis of studies investigating the association between parental smoking and bronchial hyper-responsiveness. Although the meta-analysis confirmed significantly increased odds of BHR in children whose mothers smoked, the authors suggested that the observed association was due to publication bias [31].

2.4.1 Epidemiology of smoking in South Africa

In 1995 South Africa had a recorded smoking prevalence of 17% for females and 52% for males with consumption per capita of 1 720g (consumption data from 1990-1992) [28]. In contrast, the range for consumption per capita internationally varied between 90g in Ethiopia to 3 620g in Poland [28]. These figures illustrate that prevalence of smoking in South Africa is high enough to be of concern. Further a high prevalence of maternal smoking during pregnancy has been documented in South Africa [30].

From the first Demographic and Health Survey (DHS) in South Africa Steyn et al. reported lower figures of smoking prevalence. In the 1998 DHS, in adults older than 15 years male smoking prevalence was documented at 44.2%, and female smoking prevalence at 11.0% [50], which were much lower than those reported previously (in 1995) [28].

Some racial differences were noted, specifically that Coloured female smoking rates were recorded to be 39% (previously reported to be as high as 41% [5]), compared to only 5.4%

in African females. Also noted was the fact that African females tended to use smokeless tobacco [50].

Environmental tobacco smoke exposure was reported by 28% and 19% of all non-smokers reporting exposure at home and at work [50]. Further, light smoking was more prevalent in the most socio-economically deprived, with heavy smoking being more prevalent in the highest educated group.

The authors attribute the observed reductions in smoking prevalence to the enactment and implementation of the Tobacco Products Control Act of 1993 [50]. In light of the varied and changing patterns in smoking prevalence in South Africa, and the more recent amendments (1999 and 2006) of the Tobacco Products Control Act of 1993, it is important to monitor the impact of such on the prevalence trends of asthma.

2.4.2 Passive smoke exposure (ETS) and asthma in children

Mitchell et al. performed an ecological analysis to study the association between prevalence of asthma symptoms and prevalence of smoking by gender for all the countries participating in the ISAAC 1 study where smoking prevalence by gender and cigarette consumption per capita data were available. They confirmed a positive association between prevalence of smoking in females older than 15 years of age and asthma symptoms in the 13-14 year age group, although there was no significant association in the younger (6-7 years) age group [28]. This result is consistent with previous findings of a positive association between maternal smoking and environmental tobacco exposure at the individual level. Interestingly the study revealed a negative association between smoking prevalence in males and prevalence of asthma symptoms in children [28]. The authors attributed this negative association to the hygiene hypothesis in that high adult smoking prevalence has been shown to be associated with higher infection rates in infancy, which in turn is suggested to be protective for asthma or atopy [28].Further they emphasized that this negative association at the ecological level does not dispute the

positive association at the individual level that has been shown in several other studies, but rather indicates that differences in smoking prevalence between countries are unlikely to account for the differences in prevalence in asthma and other atopic diseases [28].

Looking at evidence from studies employing more rigorous methodology to study causal associations, numerous case control and cohort studies have been undertaken worldwide to study the association between parental smoking and asthma in childhood. Most of these studies will not be discussed individually in this review, as they have been included in the systematic review and meta analysis conducted by Strachan and Cook in 1998, which is discussed below.

In their review Strachan and Cook confirmed a positive association between maternal smoking and incidence of wheezing illness after the first two years of life.
19 case control studies were included in the systematic review. The meta analysis from 14 case control studies confirmed the association between either of the parents smoking and wheezing illness (pooled OR 1.37, 95% CI 1.15- 1.64) [29]. When the results were stratified by maternal or paternal smoking, in contrast to maternal smoking (pooled OR 1.59, 95% CI 1.27- 1.99) paternal smoking failed to show an association (pooled OR 0.94, 95% CI 0.78- 1.12) [29].

I will single out and report one of the cross sectional studies included in the meta-analysis, as it was conducted in Cape Town, which is the study setting for the study reported in this thesis. In 1993, Ehrlich et al studied the association between parental smoking/ environmental tobacco exposure in schoolchildren from Mitchells Plain, Cape Town. Antenatal maternal smoking (OR 1.87, 95% CI 1.25- 2.81), current maternal smoking (OR 1.70, 95% CI 1.23- 2.34), current paternal smoking (OR 1.38, 95% CI 0.93- 2.05), more than 3 persons smoking in the household (OR 1.21, 95% CI 1.10- 1.34) and urinary Cotinine Creatinine Ratio (CCR) (an objective marker of environmental tobacco smoke) were all found to be positively associated with current asthma/wheeze in school children aged 7 to 9 years old [30]. In the multivariate models only maternal

smoking during pregnancy and increasing number of smokers in the household remained significant [30].

Moving on to prospective studies, Strachan and Cook's review included six longitudinal studies. Three studies were conducted in American states, two were from the 1958 and the 1970 British births cohorts and the sixth study was conducted in Christchurch, New Zealand. The results of the meta analysis were similar to those of the case-control studies, with a pooled odds ratio (OR) of 1.31 (95% CI 1.22- 1.44) for incident wheezing illness in the first 5 to 7 years and of 1.13 (95% CI 1.15- 1.64) throughout childhood and the school years [29].

The authors attributed the greater association in the younger age groups to the stronger association of tobacco smoke exposure with non-atopic wheezing illness and wheezing associated with viral respiratory illness inducing/ exacerbating wheeze which is commoner in early childhood. In contrast they suggest a weaker association with incidence of atopic asthma which tends to start later in childhood [29].

Evidence to support this suggestion is found in a subsequent systematic quantitative review by the same authors [31]. In the second review the authors tested the hypothesis that environmental tobacco smoke (ETS) triggered asthma rather than caused it. To do this they looked at the association between ETS/ parental smoking and presence of bronchial hyperresponsiveness (BHR), which is assumed to be a marker of underlying susceptibility to asthma in children. Of the 19 studies included in the review, ten could be included in meta analysis, five did not report findings in odds ratios, and four were not published at the time. Although the pooled OR from the ten studies included in the meta analysis showed a significant positive association between ETS and BHR, the associations reported from the other five published studies was not significant [31]. The authors therefore concluded that although the pooled OR showed a significant positive association, it may have been biased upwards due to publication bias [31].

2.5 Indoor (cooking/ heating fuel) and out door pollution and asthma

The type of fuel used for cooking and heating and exposure to diesel smoke have been implicated as associated with asthma and other respiratory conditions including acute respiratory infections and bronchitis.

In their study, Wong et al reported a strong positive association between exposure in infancy to use of gas as cooking fuel and presence of current wheeze (OR 1.68, 95% CI 1.03- 2.75) [41]. Whilst the authors reported that other studies in Canada and England reported similar results and one study in Britain did not show any association, they emphasized that where families live in smaller dwellings (as in Hong Kong), the effects of gas would be more evident than in those living in bigger dwellings [41].

Schei et al., using the ISAAC questionnaire, studied the association between asthma symptom prevalence in children aged 4 to 6 years in rural Guatemala, Latin America, and exposure to indoor open wood-fire cooking. Amongst the three exposure groups (wood stove with flue/chimney, mixed use of gas stove and open fire, and indoor open fire cooking) exposure to open fire cooking indoors increased the risk of asthma symptoms significantly. Indoor open fire cooking increased the odds of wheeze in the last twelve months by between 2.1 and 3.4 times compared to households cooking on stoves with chimneys [unadjusted OR 2.1 (95 CI 1.06- 4.19) ; adjusted OR 3.4 (95% CI 1.3- 8.5)], and similarly that of diagnosed asthma [adjusted OR 1.8 (95% CI 0.76- 4.19)] [44].

In a case-control study of asthma and indoor environment in rural Kathmandu Valley in Nepal, subjects between 11 and 17 years of age were identified as either cases or controls for asthma using ISAAC methodology. Results showed that exposure to "smoky biomass cooking fuel" as defined by living in a house with an open fire or cooking stove without a flue (compared to use of a gas or kerosene stove) increased the risk of asthma [adjusted OR 2.2 (95% CI 1.0- 4.5)] [46].

However, closer to home, in Kenya, Ng'ang'a et al studied the relationship between asthma as indicated by exercise induced bronchospasm (EIB) and several environmental exposures in grade 4 children aged between 8 and 12 years. The results showed that contrary to the studies in Guatemala and Nepal discussed above, in Kenya use of biomass fuel was negatively associated with exercise induced bronchospasm (OR 0.58, 95% CI 0.37- 0.90), with the measure of association becoming statistically insignificant after adjusting for area of residence (rural or urban) [OR 0.73 (95% CI 0.46- 1.15)] and all other risk factors (including sex, age, family history of asthma, animals in the homestead, ventilation, parental education, exposure to motor vehicle fumes and area of residence) [OR 0.64 (95% CI 0.37- 1.11)]. On the other hand, cooking with kerosene increased the risk of EIB [unadjusted OR 1.50 (95 CI 1.07- 2.10); area of residence- adjusted OR 1.80 (95% CI 1.27- 2.55) and all other risk factors- adjusted OR 1.17 (95% CI 0.74- 1.84)] [45].

The differences between the results of the first two studies and the Kenyan study are difficult to explain. It would seem that the findings of the studies from Guatemala and Nepal are biologically plausible given that there is a growing body of evidence from toxicological studies showing a positive association between smoky fuels which upon combustion emit a complex mix of carbon monoxide, nitrogen dioxide, polycyclic organic matter and suspended particulate matter (respirable particles <10 μm being important) and asthma [44,46]. The question remains whether these air pollutants cause or merely trigger/ exacerbate asthma. Evidence for a causal association is supported by findings that diesel particles (similar in many ways to biomass fuel emissions) stimulate production of inflammatory mediators like IgE, eosinphic degranulation and cytokine/chemokine production [44].

The different results seen in the Kenyan study probably represent the association between socio-economic status and other environmental factors associated with urban setting and asthma. Use of wood as cooking fuel was associated with rural and/or poor households (thus the protective unadjusted effect), whereas paraffin was associated with urban and perhaps better socio-economic status (although after adjusting for area of residence the

odds ratio increased, one would expect it to decrease if area of urban residence was a significant confounder of the kerosene use- asthma association).

2.6 Socioeconomic status and asthma

Socioeconomic status has come under the spotlight as a risk factor for asthma prevalence and severity. The exact mechanism for this association is not easy to understand as other factors which may be independently associated with asthma may also be mediators of the association. These include parental education (which is usually a component of socioeconomic status), diet, type of housing and household exposures, area of residence and environmental pollution and access to health care.

2.6.1 South Africa: Political demography in relation to health status in South Africa

The history of apartheid has had a persisting impact on the health status of the population of South Africa [21].

During the apartheid era (pre 1994), the government implemented policies to segregate people according to their race (mainly defined by skin colour), and thus imposed limitations on the area of residence, education and employment opportunities for its different people. Persons of European descent (classified as White) were advantaged in every regard, compared to their non-European counterparts (now also classified as Africans or Black, Coloured/Mixed descent and Asian). In turn Coloured and Asian persons enjoyed better status than African people. This meant that Africans were confined to reside in urban "townships" or rural areas with often un-serviced inferior quality housing, had inferior quality education (the "Bantu education system" for "natives"), and had poor access to medical care and services [19]. This resulted in significant disparities between Whites and Africans in socioeconomic and health status.

Post democracy (1994) there has been significant shifts with government policies attempting to redress the historic disparities (for example a Reconstruction and Development Policy for housing, an integrated education system, and several health policies which culminated in the new National Health Act of 2003). As a result the

African population has since enjoyed better opportunities overall than before, and indeed a Black middle class is emerging.

However, despite recent government economic policies, the level of unemployment continues to be very high and the gap between the poor and rich has not been reduced; indeed South Africa has the second highest Gini coefficient in the world [21]. The situation is compounded by high levels of migration of people from the rural areas into the urban cities looking for employment. This has contributed to the rising population of peri-urban informal settlements characterised by overcrowded "shanty towns" with limited or no municipal services (electricity, clean piped water and sewerage facilities) and consequently an undesirable impact on the health of persons residing in these informal settlements [19].

Thus the South African population is a population in transition, with persisting impact of apartheid policies, an emerging Black middle and upper class, and a large unemployed sector. Factors associated with the socio-political, demographic and epidemiologic transitions currently being experienced are thus of particular interest. Although the focus seems to be on the HIV/AIDS and other acute childhood conditions, impact on chronic diseases of childhood, of which asthma is the commonest, needs study.

The country's last census (2001) statistics reflect the following disparities related to race and socio-economic status: annual median income was R12,213 (US$ 1,836) for Black Africans, R16,354 (US$ 2,458) for Coloured people, R42,803 (US$ 6,434) for Indian/ Asian people and R64,968 (US$ 9,765) for White people [49].
The inverse association between socioeconomic status and general health status (morbidity and mortality) is internationally accepted.

These disparities resulting from apartheid are borne out in the country's health statistics. In particular the Western Cape (with a total population of 4,524,335 in 2001, composed of 53.9% Coloureds, 26.7% Blacks, 18.4% White and 1% Indian/Asian racial groups) [49] is a good province to illustrate this. The infant mortality rate (IMR) (per 1000 live births)

is a sensitive health indicator that reflects socioeconomic status and health care access of a population [19]. In 1998 South Africa had a recorded IMR of 45.0 per 1000 live births [18]. Significant differences in IMR were observed between provinces [30.0 in the Western Cape (mixed urban and rural farm areas), 36.3 in Gauteng Province (predominantly urban), and 61.2 in Eastern Cape Province (predominantly rural)] [18]. Whilst the IMR was 45.0 for South Africa as a whole, it was 52.2 in the rural areas compared to 32.2 in the urban areas [18]. This difference highlights to some extent access to health care and socioeconomic disparities in urban and rural areas. Similar findings were documented by Bachman et al in 1996 [19]. They investigated IMR inequalities in the Western Cape Provinces and showed that besides place of residence (urban, rural, farms, and informal settlements) racial categorisation revealed more information in socio-economically heterogenous residential areas. In this regard they found that IMR was highest in Coloureds living in informal settlements (60 per 1000), whilst similar in Blacks living in informal settlements (35 per 1000) and Coloureds living on rural farms (34 per 1000). Using racial classification only, IMR was lowest for Whites (11 per 1000), followed by Coloureds (19 per 1000) and highest for Blacks (33 per 1000) [19].

Asthma does not contribute (as a cause of death) to the IMR statistic, and is relatively low in the list of causes of under 5 mortality (accounting for 0.9% of all deaths under the age of 5 years and ranked number 12 in the top 20 causes of under 5 mortality in Cape Town in 2001) [20]. However, it is the most common chronic disease in childhood [22], causing significant morbidity and significant school absenteeism in the school going ages [17]. In a study in south-central Durban, South Africa, asthma diagnosis was strongly correlated with the missing of school by children (OR 44; 95% CI 13-141) [17].

It is worth noting that mortality from asthma is an indicator of overall asthma care. Despite being ranked number 25 in global prevalence, South Africa has the fourth highest asthma mortality rate [52]. Deaths from asthma are largely avoidable and a high mortality rate from asthma indicates failure of the health system and other broader contributing factors.

2.6.2 Socioeconomic status and asthma: international evidence

An ecological analysis of the relationship between prevalence of asthma and other allergy symptoms and the economic standing of countries participating in ISAAC 1 found the lowest median centre symptom prevalence of asthma at the lowest quartile of GNP per capita in the 13-14 year age group, and a similar association for asthma and eczema symptom prevalence for the 6-7 year age group [32]. This means that countries with higher socio-economic status had a higher prevalence of asthma and atopic eczema. However, infant mortality rate and the Human Development Index (HDI), which are also considered to be good measures of a country's level of development, did not show any consistent associations with asthma symptom prevalence [32].

2.6.3 Socioeconomic status and asthma: South African evidence

In Cape Town, an analysis by Poyser et al. of the ISAAC Phase 1 data found that after geocoding (using Geographic Information Systems/ GIS) the study participant's residential addresses and assigning a socioeconomic deprivation (SED) score to each enumerator area, there was negative association between level of socioeconomic deprivation and the lifetime and 12 month prevalence of asthma symptoms, but positive association between SED and the frequency of asthma symptoms. In other words whilst improved socioeconomic status was associated with an increased prevalence of asthma, the more socioeconomically deprived experienced greater severity of asthma [33]. The authors postulated that these associations may be due to non-reporting of mild symptoms in more deprived groups. Less adequate disease management and/or poorer access to medical care in the more socioeconomically deprived would explain the greater severity in the more deprived groups [33].

A similar analysis to that of Poyser et al. (using the same database) focusing on the other allergies (allergic rhinoconjuctivitis and atopic eczema) revealed similar associations for eczema, but no significant associations for allergic rhinoconjuctivitis [34].

Interestingly, a more recent unpublished paper (BSc Honours thesis) by Graham comparing the findings of the Poyser study with data from the ISAAC Phase 3 Cape Town study centre, reported somewhat different findings, with socioeconomic deprivation being positively associated with asthma symptom prevalence and, similarly to the Poyser findings, severity of symptoms [35]. The different direction and strength of association between asthma symptom prevalence and socioeconomic deprivation in the two studies are intepreted by Graham as possibly related to the social change which Cape Town has undergone in the seven years between phase One and phase Three [35]. However Graham's interpretation was mainly based on the video questionnaire prevalence of asthma symptoms, with emphasis on the point estimates, although most of the confidence intervals tended to include one, whereas the written questionnaire results tended to be similar to those of Poyser.

2.7 Early infections, tuberculosis (TB), Antibiotics and asthma

2.7.1 The hygiene hypothesis

The hygiene hypothesis has enjoyed some popularity as a theory accounting for the observed increase in prevalence of allergic asthma especially in developed countries, where the burden of disease from infectious diseases, including TB, has dropped significantly in past decades. The hygiene hypothesis proposes that improved hygiene, tendency towards smaller family sizes and successful vaccination programmes for infectious diseases in childhood in recent times, have led to a reduction in infectious diseases. The effect is that the immune system develops a predominantly Th2 response, which is characteristic seen with atopic disorders (as opposed to Th1 response which suppresses atopic disorders). This traditional simplistic exposition of the hygiene hypothesis has recently been challenged by more complex models. These include the suggestion that other than an imbalanced Th1/Th2 immune response, the key feature of the hygiene hypothesis is the reduction in activity of regulatory T cells (Treg), commonly $CD4^+$ and $CD25^+$ which normally inhibit Th2 cytokine activity in response to allergen exposure in non-atopic persons. Exposure to bacterial endotoxin or lipopolysaccharide (LPS) enhances the suppressive function of Treg. Thus reduced exposure to endotoxin would result in increased Th2 cytokine expression, which encourages atopic disease expression [38]. This hypothesis is supported by evidence from a European study that showed that higher endotoxin, lipopolysaccharide (LPS) and TLR2 levels in European children living on farms was associated with lower prevalence of atopic diseases in children (compared to children not living on farms) [38].

2.7.2 Early infections and asthma

Cohet et al. reported a weak protective effect (OR 0.86, 95% CI 0.74- 1.00) of childhood notifiable infectious diseases (at ages 0 to 4) on current wheeze (at age 6-7 years) [42]. The study, conducted in New Zealand, compared asthma symptom prevalence (using the ISAAC questionnaire) between a group of children who had been diagnosed with confirmed childhood notifiable diseases and included the national EpiSurv database, and the control group, which were children included in the general population dataset and who were included in the ISAAC Phase III study conducted in Wellington during the same period. Restricting the analysis to only children who were reported not to have used antibiotics in the first year of life somewhat increased the strength of the association, although the confidence interval widened (OR 0.78, 95% CI 0.55- 1.10) [42]. The study also reports a negative association between number of younger siblings =2, compared to one sibling, and current wheezing (OR 0.66, 95% CI 0.51- 0.84) [42].

The same study also reports strong positive associations between antibiotic use in the first year of life and asthma (OR 1.78, 95% CI 1.49- 2.14 for current wheezing and OR 2.10, 95% CI 1.79-2.48 for asthma diagnosis) [42].

2.7.3 Antibiotics and asthma

The hygiene hypothesis is also supported by some evidence that use of antibiotics, by reducing the "anti-allergy" effect of infections and/or disruption of normal gut flora in early life, increases the risk of developing asthma later [37].

An ecological analysis of the ISAAC 1 data (age group 13-14 years) from 28 countries with data for per capita antibiotic sales was used to study the association between antibiotic sales and symptoms of asthma. Although the study showed weak positive associations between symptoms of asthma and per capita antibiotic sales, the associations became insignificant and/or negative once adjusted for GNP [40].

Thus the study could not confirm the postulated association derived from the hygiene hypothesis. From the discussion in that paper it is clear that there is conflicting evidence on the matter and that confounding cannot be ruled out (frequent childhood upper respiratory symptoms associated with development of asthma are often treated with antibiotics) [40]. Furthermore the authors emphasize that whilst the results of this ecological analysis do not rule out significant positive association between antibiotic use and later development of asthma, they do refute such an association accounting for the large differences in prevalence of asthma between countries [40].

2.7.4 Tuberculosis and asthma

In an ecological analysis, von Mutius et al. measured the association in 13 and 14 year old school children between tuberculosis *notification* rates and the prevalence of symptoms of asthma (wheeze ever and wheeze in the past 12 month on written and video questionnaire) and asthma-ever diagnosis, in 23 countries participating in the ISAAC Phase 1 study where the notification rates were regarded as valid. This excluded developing countries including Africa where notification rates were considered not to be valid. The results confirmed a strong significant negative association between TB notification rates and prevalence of asthma symptoms (including after adjustment for GNP) [36].

A similar analysis using the same database and World Health Organisation (WHO) estimated tuberculosis incidence rates (considered to be of greater validity than notification rates) was later conducted by Shirtcliffe et al., expanding the number of countries included in the analysis to 55 countries, including those from developing countries including Africa. Both the 6-7 and the 13-14 year age groups were included in this analysis. The results confirmed a consistent significant inverse relationship between estimated TB incidence rates and all asthma symptoms and diagnosis in the 6-7 year old group. However this relationship was only maintained with the outcome of "asthma ever" in the 13-14 year age group, with the other associations (wheeze ever, wheeze in the past 12 month on written and video questionnaire) becoming statistically insignificant after adjusting for GNP, alluding to significant confounding by socioeconomic status/level of affluence [37].

The authors interpret the stronger association in the younger age group as indicating that the anti-atopic effect of tuberculosis has greater impact in earlier life, and recommend that this ecological association requires investigation at the individual level [37].

Obihara et al, in their recent review of experimental and epidemiological literature investigating the association between *mycobacterium* exposure and atopic disease,

conclude that it is not just the development of a predominantly Th2 immune response in infancy/ childhood that predisposes to atopy but that more likely the dose and persistence of antigen exposure have a bigger role to play [38].

This view is supported by evidence that, contrary to the traditional view that the window period (neonatal period up to about 5 years of age) is critical to the development of the Th1/Th2 immune balance, even in later life persons who have grown up in developing (and thus "infection- rich") countries, and subsequently migrated to developed/ industrialised countries may still develop atopy/ allergic conditions. Thus it seems that genetically exposed individuals may still be at risk of developing atopy in the absence of sustained/ persistent exposure to certain infectious agents. Similarly previously "atopic" persons may experience remission of symptoms after acquiring infections in adult life [38].

This view concurs with results from other studies which failed to show an association between prevalence of atopic disease and once off BCG vaccination (administered in the neonatal period) compared with multiple BCG vaccination. Children in the latter category (a Japanese study) received BCG vaccination at birth, 6 and 12 years and were shown to have lower prevalence of atopic disease compared to children who received the once-off BCG immunization [38]. The Japanese study, the only one showing a protective effect of BCG vaccination against asthma, has been criticized for weak methodology. There is little evidence to support a protective effect of BCG against asthma.

Lastly, Obihara et al. propose that together with *mycobacterium tuberculosis* exposure concurrent allergen exposure is required for the development of an allergen specific protection against atopic disease. They derived this from their study in South Africa study which showed a significant inverse association between positive tuberculin skin test (indicating *mycobacterium tuberculosis* infection) and both atopic and allergic rhinitis [39]. In this study (conducted in Cape Town) both *mycobacterium tuberculosis* infection and allergen exposure were highly prevalent in the community. Atopy was diagnosed by positive skin prick test (SPT) and total serum IgE. *Ascaris lumbricoides* IgE, and stool parasite eggs were measured so as to enable correction of the serum IgE [39]. Thus it would

seem that in addition to endotoxin exposure, several factors including dose of and timing of exposure to the infectious agent; genetic factors and other environmental factors are involved in developing protection against atopic disease [38].

Since it seems that evidence may suggest that the dose of *mycobacterium tuberculosis* found in regular vaccines is neither enough nor sustained long enough to confer protection against atopy (compared to frequent exposure to mycobacteria) [38], Obihara et al. argue that future research should investigate a recombinant mycobacterial vaccine that is primed simultaneously with allergens, resulting in long term protection against allergen specific atopy [38].

It is also worthy to note that recently, the authors of the African ISAAC phase 3 prevalence paper indicated that in study centres in Sub- Saharan Africa, where there is high prevalence of infections like tuberculosis and human immunodeficiency virus (HIV) and parasitic infestations in childhood, there is a somewhat unexpected contradiction of the hygiene hypothesis, in that intermediate to high and rising asthma prevalences have been recorded [4].

2.8 Paracetamol (acetaminophen) and asthma

Paracetamol intake has been reported to increase the risk of asthma in several studies [40,41,42].

The possible mechanism for the positive association between paracetamol use and asthma was first reported and discussed in detail by Shaheen et al., who reported results from a case control study of young adults aged 16- 49 years living in Greenwich, London [43]. In this case control study, the results indicated that overall, frequent (weekly or daily) paracetamol use (compared to none and less frequent use) was a strong risk factor for asthma (OR 1.73, 95% CI 1.29- 2.31). A dose- response relationship was demonstrated by the fact that for weekly use the OR was 1.79 (95% CI 1.21- 2.65) and for daily use 2.38 (95% CI 1.22- 4.64) [43].

The strength of the association between frequent use of paracetamol and asthma has also been shown to increase with increasing severity of asthma [43].

Confounding by associated conditions (co-morbidities) or other conditions which require use of analgesia was controlled for. For example B_2 agonists which are used in the management of asthma may cause headaches, which in turn may be treated with paracetamol. The positive association between frequent paracetamol use and asthma was not restricted to respondents taking paracetamol only, but was also found in those taking both paracetamol and aspirin. The study did not find an independent association between aspirin use and asthma [43].

Following Shaheen et al.'s study, Cohet et al. found a strong positive association between paracetamol use in the first year of life and risk of current wheezing and asthma at age 6-7 years (OR 1.38, 95% CI 1.04- 1.83) and (OR 1.72, 95% CI 1.32- 2.23) respectively [42].

In the same study, a stronger positive association was also reported with recent paracetamol use at least once a month (OR 2.10, 95% CI 1.78- 2.49 for current wheezing, and OR 1.57, 95% CI 1.34-1.84 for asthma diagnosis) [42].

Similarly, in their recently published paper, Wong et al, report that in 2-6 year old preschool children living in China, paracetamol use in the first year of life increased the risk of symptoms of current wheeze compared to no paracetamol exposure in infancy. A dose- response was demonstrated with paracetamol use at least once a year increasing the risk of current wheeze by 53% (OR 1.53, 95% CI 1.04- 2.00) and paracetamol use at least monthly increasing the risk by more than double (OR 2.41, 95% CI 1.50- 3.87) [41].

Thus findings from the different studies show a consistent positive association between paracetamol use and asthma. The association is biologically plausible, as reports from animal studies have shown that paracetamol reduced levels of the pulmonary antioxidant glutathione in the lungs [43]. Glutathione has been shown to be increased in the airways of persons exposed to inhaled oxidants, like cigarette smoke, as a response to oxidative damage. It is therefore postulated that paracetamol, by reducing the protective effect from glutathione in the lungs, increases asthma morbidity [43].

2.9 Literature review: Conclusion

A significant volume of published research on risk factors for asthma in childhood exists. Evidence from ISAAC phase 1 supports an ecological association between diet and asthma prevalence. Foodstuff with antioxidant and anti-inflammatory properties were shown to have a protective effect against asthma, whilst mono- and polyunsaturated fatty acids the former were associated with increased asthma prevalence in childhood.

The association between high body mass index and asthma has been shown to be consistent. A causal association is supported by evidence from prospective cohort studies. Effect modification by gender of the association between BMI and asthma has been reported in some studies.

Similarly, environmental tobacco smoking, particularly from maternal smoking has been positively associated with asthma prevalence. Some researchers have proposed that rather than causing asthma, smoke exposure triggers asthma attacks and is associated with severity of asthma.

Other airway irritants including biomass fuel exposure from cooking fuel like wood have also been found to be positively associated with asthma symptom prevalence.

Results from analyses of South African ISAAC 1 and ISAAC 3 data support evidence from other studies that suggests an inverse association particularly in the developing worlds, between socioeconomic deprivation and asthma prevalence.

The hygiene hypothesis is supported by several studies showing an inverse association between early childhood infectious diseases including TB and increased asthma symptom prevalence. Similarly, early antibiotic exposure is associated with increased risk of asthma.

The evidence seems to be consistent and biologically plausible for most of the associations summarized above. However most of the research was conducted in the developed world. With the increasing asthma prevalence in developing countries, which most probably have a different environmental constitution from that of the developed world, it is important to study dietary and environmental factors associated with asthma prevalence in this setting. Thus this analysis of ISAAC 3 data should provide insight into possible risk factors that may be responsible for the observed increasing trend in asthma prevalence in South Africa.

The results from this analysis will hopefully assist in developing appropriate interventions to stem the trend.

CHAPTER 3: METHODS

The ISAAC study methodology is standardised across all participating centres and is described in detail in the ISAAC Phase Three manual [51] and elsewhere [2]. This methodology is summarized in what follows.

3.1 Study design

The ISAAC 3 study employs cross sectional surveys, using two written questionnaires (a core questionnaire on symptoms and diagnosis of asthma, allergic rhinitis and eczema, and an environmental questionnaire) and a video questionnaire, which are completed by school learners, aged 6 to 7 years and/or 13 to 14 years.

3.2 Study population and sampling

The study population in this study included school children aged 13 and 14 years of both genders attending schools in the city of Cape Town.

The sampling unit was the school. ISAAC requires a minimum of 10 schools to be included in each participating centre. For the sample to be representative, stratified random sampling was employed. A list of all schools in the City of Cape Town was obtained from the Department of Education, and stratified into 3 strata by predominant racial group of student body i.e. predominantly White/ integrated, predominantly Coloured and predominantly Black, which given the socio-political history of South Africa reflects stratification on socio-economic and other environmental conditions. Schools were then randomly selected from each stratum, and all children aged 13 and 14 years from the selected schools were eligible to be included in the study. All pupils in the two grades with the highest proportion of 13 and 14 year olds in the selected schools were surveyed. Each school was visited twice so that eligible children who were absent at the first visit could be enrolled.

3.3 Sample size calculation

Sample size was predetermined by the ISAAC methodology. The required sample size was calculated to be a minimum of 3000 children. Such sample size would give the study 99% power to detect a significant difference in prevalence in two centres with a true prevalence of 25% and 30%, respectively at the 1% significance level, and 90% study power to detect a significant difference in prevalence of severe asthma between centres with a true difference of 3% and 5% respectively, at the 1% confidence level [2].

3.4 Measurement tools

ISAAC 3 employs three standardized and validated questionnaires:

1. The core written questionnaire;
2. The video questionnaire
3. The environmental written questionnaire

The development and validation of the instruments is described in the ISAAC Phase 1 manual, and the methods and rationale papers for phase 3 [2].

The core written questionnaire (Appendix A) is comprised of demographic questions and questions which are used to estimate prevalence of asthma, allergic rhinoconjuctivitis and eczema.
The two questions that are relevant to this analysis are: "have you had wheezing or whistling of the chest in the past 12 months" to indicate "current wheeze", and "have you ever had asthma" to indicate "asthma ever".

The environmental questionnaire was developed by the ISAAC Steering Committee. It consists of standardized questions which were developed based on specific hypotheses and sources as described by the ISAAC Steering committee [55]. To quote from the reference "Validated questions were sought in an extensive literature review and used where available. Because the ISAAC context is unique in studying children in a wide

range of world environments, validated questions were not available for all factors or for all possible environments. The SC adapted questions or used questions from the ISAAC Phase Two risk factor questionnaire where necessary. The EQ (environmental questionnaire) was piloted in New Zealand, Latin America, French speaking Africa and the Asia-Pacific regions, and appropriate modifications were made. The hypotheses and question source and the EQ for both age groups are available on the ISAAC website."

The environmental questionnaire provides a measure of the individual's dietary and environmental exposures and frequency of dietary exposure (never, 1 or 2 times a week, and more than 3 times a week) (Appendix B). ISAAC international centre allowed for modification of the questionnaire either by excluding certain questions from the original questionnaire, or addition of questions on additional risk factors that are locally relevant. Thus one additional dietary risk factor was added to the Cape Town questionnaires, maize. This was based on the fact that maize is part of staple diet for a significant proportion of the South African population, especially Black Africans. An additional 11 questions on other environmental exposures which were deemed to be locally relevant were added to the standard ISAAC environmental questionnaire. These were:

1. **Do you smoke cigarettes?**
2. **Is your house damp or wet inside?**
3. **Has anyone in your household ever had TB?**
4. **Have you ever been treated for TB?**
5. **Do you have taps for running water in your house?**
6. **Do you have electricity in your house?**
7. **Do you have a TV in your house?**
8. **Type of home**

- House
- Flat
- Shack
- Other

9. **Number of people working in the household**
10. **Number of people not working in the household**
11. **Number of people sharing a room with the respondent at night**

All three questionnaires were self-administered, as recommended by the ISAAC Steering Committee. The standardized sequence was to complete the core written, the environmental, and lastly the video questionnaire, all on the same day. In cases where learners were absent from school on the first visit, the investigators visited the school again within a week of the first visit. Although the learners were not specifically trained, a facilitator was present and explained the process in a standardized way at each school in the language in which the questionnaire was administered and showed video [51]. The video questionnaire contained five sequences portraying the symptoms of asthma as follows: wheezing at rest, exercise induced wheeze, nocturnal wheezing, nocturnal cough, and severe wheezing with shortness of breath. The questions refer to "ever", "in the past 12 months" and "monthly or more often". In this analysis response to the presence of wheeze at rest in the past 12 months was analyzed.

The questionnaire was compiled in English and translated and back translated into Xhosa and Afrikaans (see Appendices C and D).

The learners completed the questionnaires in the language that was used as medium of instruction at the particular school i.e. Xhosa, English or Afrikaans. It is important to note that whilst the language used as medium of instruction at a school probably represents the predominant home language of the learners, in the post democracy (post 1994) period in the case of the mixed schools in the city/suburbs (previously predominantly White schools) a considerable number of learners may be travelling to these schools from Black or Coloured townships. These learners' home language may be Afrikaans or Xhosa while attending schools where in most cases the medium of instruction is English.

The standardized video questionnaire is used as a means of overcoming language interpretation/ terminology problems which may be encountered with the written questionnaire [2]. This is especially relevant in Cape Town since the Western Cape Province has three official languages. English is spoken predominantly by the White population, some of whom speak Afrikaans. Afrikaans is also the home language of a

significant proportion of the Coloured population, whilst Xhosa is spoken by the majority of the Black population.
The height and weight of each respondent was measured prior to completing the questionnaire. BMI was calculated using the formula BMI= weight/height^2.

All data analysed for the purposes of this paper were obtained from the original dataset.

3.5 Data analysis

Data were analysed using the software package Stata version 8 (Stata Corporation).

Data Management/ Data recoding:

Dependent variable e.g. wheeze in the past 12 months:

The core questionnaire was designed to have "stem and branch" questions. For example "have you ever had wheezing or whistling in the chest at any time in the past?" is a stem question, followed by "if yes, have you had wheezing or whistling in the chest in the past 12 months (branch question). As a result of this design, the dependent variable of interest (wheeze in the past 12 months) could be coded yes (1)or no (2) for respondents who had responded in the affirmative for the stem question, or be coded 9 (skipped) if the responded had responded negatively for the stem question.
Technically this meant that code 9 really represented code 2's (that is respondents with both these codes never had wheeze in the past 12 months). Thus for the analysis code 2 and 9 responses were recoded as code 0, and the variable then treated as a binary variable. Contradictory branch responses were not included in analyses.

Independent variables:

In the questionnaire, the dietary exposures were graded from "never or occasionally eat (particular diet item)", "eat (particular diet item) once or twice a week" to "eat particular diet item three or more times a week". Thus the categories represented increasing

frequency of exposure to the foodstuff. For the analysis the independent variables were therefore treated and analyzed as ordinal categorical variables. Thus dummy variables were created and compared to the reference category of "never or occasionally eat (particular diet item), which was interpreted to represent "no or minimal exposure to particular diet item" and Stata 8 commands for multivariate logistic regression analysis employed. For example "never or occasionally eat maize" was recoded as "Maize0", eat maize once or twice a week as "maize2", and eat maize more than three times a week as "maize3". During model building "maize2" and "maize3" would then be independently and sequentially added to the model, thus allowing them to be independently compared to the reference category "maize0"

Some of the other environmental exposures were measured as discrete numerical variables e.g. number of siblings; some as binary categorical variables e.g. cooking/heating fuel: exposed vs. not exposed and others as ordinal categorical variables e.g. paracetamol use: "no exposure" vs. "at least once in the past 12 months" vs. "at least once a month in the past 12 months".

The following data analyses were undertaken:

a. Demographic data (age, gender, language, etc.) were tabulated in one way frequency tables and/ or graphically.
b. Two way frequency distribution tables were used to cross tabulate categorical variables of interest.
c. Measures of central tendency (mean or median) and dispersion were calculated for numeric variables e.g. mean/ median, and ranges..
d. Bivariate analysis was performed, computing the odds ratio (OR), with the 95% confidence interval and p value, to measure associations between an exposure and the outcome variable of interest.
e. Multivariate logistic regression was performed fitting the statistically significant and biologically plausible risk factors against the outcome variables of interest. In this way potential known confounders were controlled.

f. Effect modification by certain risk factors of *a priori* interest was tested for using the appropriate statistical tests.

g. Chi^2 test for trend was performed where appropriate to test whether there was a linear trend between exposure/ risk factor categories and the outcome variable/s of interest. The Chi^2 test for trend provided a more powerful test than the unordered Chi^2 independence test, e.g. for the association of exposure categories of BMI (underweight, normal weight, overweight and obese) with asthma.

3.6 Ethical considerations

The 2002 study was approved by the Research Ethics Committee of the University of Cape Town (*Ethics approval no. 203/2001*).

Permission for the study was obtained from the Western Cape Department of Education and the school principals, with parents/guardians of included learners being informed through a letter with an opt out option in the event that they did not want their child to participate in the study. In addition respondents also provided signed assent.

4 RESULTS

4.1 Background characteristics of the study population

A total of 54 schools and 5 037 learners were included in the study. The response rate was 83.4% [3]. Non-responder rates were similar across schools. ISAAC requires only the number of non- responders, and thus no further data on this group was collected or available for further analysis.

For all tables represented in this section, "n" represents the number of affirmative responses to a particular question/risk factor and "N" represents the relevant denominator. For example in table 4.1 (prevalence) 1 289 (n) learners out of total study population of 5 037 (N) spoke Afrikaans, whereas in table 5.4 (bivariate analysis) 204(n) of the 1 289 (N) Afrikaans speaking learners had experienced wheeze in the past 12 months.

Table 4.1 shows the background characteristics of the respondents. Females were over represented in this study. All three official languages spoken in the province were well represented. Most participants were born in Cape Town. Although the majority of respondents lived in a house, 11% lived in a shack (informal housing structure). Whilst the majority of respondents were of normal weight for age, 6.5% were underweight for age, 12% at risk for overweight and 5.6% overweight for age.

Table 4.1: Background characteristics of the respondents (N = 5 037):

Variable	n= positive responses	percentage
Language (of instruction at school)		
Afrikaans	1 289	25.5
English	2 059	40.8
Xhosa	1 689	33.5

Age		
13 years	2 605	51.7
14 years	2 432	48.2
Sex		
Male	2 025	40.2
Female	2 994	59.4
Place of birth		
Cape Town	4 074	80.8
Outside of Cape Town	934	18.5
Type of residential dwelling		
House	3 936	78.1
Flat	263	5.2
Shack	573	11.3
Other house type (unspecified)	60	1.1
Invalid response	205	4.0
BMI		
Underweight for age (BMI <5TH centile)	323	6.4
Normal weight for age (5^{th} = BMI <85^{th} centile)	3 772	75.8
At risk for overweight (85^{TH} = BMI <95^{th} centile)	601	12.0
Overweight for age (BMI =95TH centile)	278	5.5
Maternal education		
Tertiary education	1 086	21.5
No tertiary education	3 951	78.4

4.2 Prevalence of outcome measures and risk factors in the study population

For ease of exposition only those variables that were significant on bivariate analysis are presented in the following sections (Tables 4.2- 4.4). Appendix E details all the tested variables, including those that were not significant on bivariate analysis and therefore not included in the multivariate models.

Table 4.2 presents the prevalence of the three outcomes of interest in this study. The 12-month ("recent") prevalence of wheeze on written and video questionnaire was 20.3% and 11.2% respectively. On written questionnaire 14.4% of participants reported an asthma diagnosis "ever".

Table 4.2: Prevalence outcomes of interest in the entire study population (N=5 037)

Outcome variable	n	percentage
Wheeze in past 12 months (Written questionnaire)	1 025	20.3
Lifetime diagnosis of asthma	725	14.3
Wheeze in past 12 months (Video questionnaire)	559	11.1

Table 4.3 presents the prevalence of dietary risk factors that were found to be significantly associated with asthma symptom prevalence or diagnosis, by frequency of consumption. Notably a greater proportion of the respondents (48.2%) ate pasta than maize (32.7%) at least once or twice a week, whilst the proportions of respondents eating both foods three or more times a week were similar.

Table 4.3: Prevalence of dietary risk factors significantly associated with symptoms and diagnosis of asthma (N=5 037).

Dietary variable	n	percentage
Maize		
Never or rarely	2 224	44.1
Once or twice a week	1 651	32.7
Three or more times a week	879	17.4
Invalid response	283	5.6
Pasta		
Never or rarely	1 332	26.4
Once or twice a week	2 434	48.3
Three or more times a week	827	16.4
Invalid response	444	8.8

Table 4.4 below presents the prevalence of environmental risk factors that were found to be significantly associated with asthma symptom prevalence or diagnosis, by frequency of consumption. Of interest is that a significant proportion of respondents used paraffin for cooking and heating. In contrast, less than 2% of respondents used wood use for cooking, although a little more (6%) used it for heating purposes.

About 70% of the study population used paracetamol at least once a year, with half the number using it more frequently (at least once a month).

More than a quarter (27.8%) of mothers or female caregivers and 42.2% of fathers or male caregivers smoked cigarettes. 3.7% of the respondents reported themselves to be smokers.

Table 4.4: Prevalence of environmental and behavioural risk factors significantly associated with symptoms and diagnosis of asthma (N=5 076).

Environmental risk factor	n	percentage
Exercise (enough to make one breathe hard)		
Never or occasionally	1 572	31.2
Once or twice a week	2 103	41.7
Three or more times a week	1 181	23.4
Invalid response	181	3.5
Paraffin for cooking		
Yes	892	17.7
No	4 145	82.2
Wood (including open fires) for cooking		
Yes	83	1.6
No	4 954	98.3
Paraffin for heating		
Yes	1 177	23.3
No	3 860	76.6
Wood for heating		
Yes	303	6.0
No	4 733	93.9

Paracetamol use		
Never or occasionally	1 333	26.4
At least once a year	1 764	35.0
At least once a month	1 741	34.5
Invalid response	199	3.9
Mother or female caregiver smokes cigarettes		
Yes	1 405	27.8
No	3 419	67.8
Invalid response	213	4.2
Father or male caregiver smokes cigarettes		
Yes	2 130	42.2
No	2 626	52.1
Invalid response	281	5.5
Respondent smoking		
Yes	187	3.7
No	4 417	87.6

4.3 Wheeze in the past 12 months (written questionnaire)

Table 4.5 presents the results of the bivariate analysis of demographic, dietary and environmental factors associated with current wheeze prevalence from the written questionnaire. Variables which were not statistically significant and were therefore not included or serially excluded in the sequential model building during the multivariate analysis have been excluded in the subsequent sections, but for reference all the outputs can be found in Appendix F.

Language was the only demographic factor found to be significantly associated with current wheeze. Afrikaans was arbitrarily taken as the reference group. 15.8% of Afrikaans speaking respondents reported current wheeze. English speaking respondents had a higher odds of current wheeze (prevalence of 28.9%, OR 2.1, 95% CI 1.8- 2.6) compared to Afrikaans speakers, whilst the Xhosa speaking learners had a reduced odds of current wheeze (prevalence of 13.2%, OR 0.8, 95% CI 0.6- 1.0) compared to Afrikaans speakers.

Of note was that gender was not associated with current wheeze.

Of the dietary variables, maize consumption was consistently negatively associated with current wheeze; whilst eating pasta once or twice a week (compared to never eating pasta) increased the odds of current wheeze.

Maternal higher education, living in a shack and overcrowding (as indicated by more than 4 people sharing a room with the respondent at night) were considered before the analysis to be proxy measures for socioeconomic status. Whilst maternal higher education increased the odds of current wheeze, living in a shack and overcrowding reduced the odds of current wheeze. Use of paraffin as cooking and heating fuel also reduced odds, whilst use of wood, including cooking on open fires, increased the odds of current wheeze. Exercise, paracetamol use, overweight (BMI $\geq 95^{th}$ centile) also increased risk of current wheeze.

Table 4.5: Bivariate analysis: Association of selected dietary and environmental factors with current wheeze

Risk factor	n	N	OR	95% CI
Demographic factors				
Language of instruction at school				
Xhosa	224	1,689	0.8	0.6- 1.0
Afrikaans	204	1,289	1.0	-
English	597	2,059	2.1	1.8- 2.6
Mother has tertiary education				
No	728	3951	1.0	-
Yes	297	1 086	1.6	1.4- 1.9
Dietary variables				
Maize				
Never or rarely	573	2 224	1.0	-
Once or twice a week	265	1 651	0.5	0.4- 0.6
Three or more times a week	138	8 79	0.5	0.4- 0.6
Pasta				
Never or rarely	247	1 332	1.0	-
Once or twice a week	557	2 434	1.3	1.0- 1.5
Three or more times a week	167	8 27	1.1	0.8- 1.3
Environmental risk factors				
Indicators of socio-economic status				
Type of residential dwelling				
House	836	3 936	1.0	-
Flat	53	263	0.9	0.6- 1.2
Shack	86	573	0.6	0.5- 0.8
Other (unspecified)	12	60	0.9	0.4- 1.7

Number of people sharing room with respondent at night				
< Four	865	4108	1.0	-
≥ Four	61	417	0.5	0.3- 0.7
Other environmental risk factors				
Fuel used for cooking				
Paraffin use vs. no paraffin use	136	892	0.6	0.5- 0.8
Wood (including open fires) use vs. no wood use	23	83	1.5	0.8- 2.4
Fuel used for heating				
Paraffin use vs. no paraffin use	176	1 177	0.6	0.5- 0.7
Wood (including open fires) use vs. no wood use	81	303	1.4	1.1- 1.9
Exercise (enough to make one breathe hard)				
Never or occasionally	255	1 572	1.0	-
Once or twice a week	490	2 103	1.5	1.3- 1.8
=3 times a week	257	1 181	1.4	1.1- 1.7
Paracetamol use				
Never or occasionally	214	1 333	1.0	-
At least once a year	351	1 764	1.2	1.0- 1.5
At least once a month	434	1 741	1.7	1.4- 2.0
Mother or female caregiver smokes cigarettes				
No	652	3 419	1.0	-
Yes	339	1 405	1.3	1.1- 1.5
Father or male caregiver smokes cigarettes				
No	524	2 626	1.0	-
Yes	455	2 130	1.0	0.9- 1.2

Respondent smoking				
No	868	4 417	1.0	-
Yes	126	433	1.6	1.3- 2.1
BMI				
Underweight for age (BMI <5th centile)	52	323	0.7	0.5- 1.0
Normal weight for age (5th = BMI <85th centile)	741	3 772	1.0	-
At risk for overweight (85th = BMI <95th centile)	131	601	1.1	0.9- 1.4
Overweight (BMI =95th centile)	89	278	1.9	1.4- 2.5

Tables 4.6 below illustrates the multivariate model for associations of selected dietary and environmental factors which were shown on bivariate analysis to be statistically significantly associated with current wheeze, before and after addition of language into the model.

Comparing the two models, it is evident that with the addition of language to the model, some risk factors become statistically non-significant (eating maize three or more times a week. eating pasta at least once or twice a week, more than 4 people sharing the room with the respondent at night, paraffin use as heating fuel). For some, whilst the associations remain significant, the strength of association is somewhat weakened (the protective effect of eating maize once or twice a week and maternal higher education).

In summary, the multivariate models show consistent positive association with English language, maternal education, exercise, frequent paracetamol intake (at least once a month), maternal smoking, active smoking by the respondent and high BMI for age. Other factors (dietary, fuel use and overcrowding) are attenuated by the addition of language into the model.

Table 4.6: Multivariate analysis: association of dietary and environmental factors with current wheeze before adding language to the model

RISK FACTOR	OR	95% CI
Dietary factors (reference unless otherwise stated is no or occasional exposure)		
Eating maize at least once or twice a week	0.6	0.5- 0.7
Eating maize three or more times a week	0.6	0.5- 0.8
Eating pasta at least once or twice a week	1.1	1.0- 1.3
Environmental factors (reference unless otherwise stated is no or occasional exposure)		
Mother has tertiary education	1.5	1.2- 1.7
≥ Four people sharing room with respondent at night vs. < four	0.7	0.5- 0.9
Paraffin use as cooking fuel	0.8	0.6- 1.0
Exercise (enough to make one breathe hard) once or twice a week	1.5	1.2- 1.8
Exercise (enough to make one breathe hard) ≥3 times a week	1.4	1.1- 1.7
Paracetamol use at least once a month	1.4	1.2- 1.7
Mother or female caregiver smokes cigarettes	1.2	1.0- 1.4
Respondent smoking	1.5	1.2- 1.9
Overweight (BMI =95th centile)	1.7	1.3- 2.3
vs normal weight for age (5th = BMI <85th centile)		

Table 4.7: Multivariate analysis: association of dietary and environmental factors with current wheeze after adding language to the model

RISK FACTOR	OR	95% CI
Language of instruction at school		
Xhosa	0.9	0.7- 1.1
Afrikaans	1.0	-
English	1.8	1.5- 2.1
Dietary and environmental factors (reference unless otherwise stated is no or occasional exposure)		
Eating maize at least once or twice a week	0.7	0.6- 0.8
Eating maize three or more times a week	0.8	0.6- 1.0
Eating pasta at least once or twice a week	1.0	0.9- 1.2
Mother has tertiary education	1.3	1.1- 1.5
≥ Four people sharing room with respondent at night vs. < four	0.7	0.5- 1.0
Paraffin use as cooking fuel	1.0	0.8- 1.3
Exercise* once or twice a week	1.4	1.2- 1.7
Exercise* ≥3 three or more times a week	1.3	1.1- 1.7
Paracetamol use at least once a month	1.4	1.2- 1.6
Mother or female caregiver smokes cigarettes	1.2	1.0- 1.4
Respondent smoking	1.4	1.1- 1.8
Overweight (Respondent's BMI =95th centile) vs normal weight for age (5th = BMI <85th centile)	1.7	1.3- 2.2

** exercise enough to make one breathe hard*

4.4 Lifetime diagnosis of asthma (written questionnaire)

Results for the outcome of asthma diagnosis as determined from the written questionnaire are fairly similar to those for the outcome of current wheeze. Although the strength of association of associations for many of the variables was not as strong and in some instances bordered on not being significant (upper/lower limit of the 95% confidence interval = 1.0), the direction of associations were all similar to that observed with the outcome of current wheeze on the written questionnaire.

Table 4.8 presents the results of the bivariate analysis of dietary and environmental factors and asthma diagnosis. Similar to the findings for current wheeze on written questionnaire, maize was significantly protective for asthma diagnosis, as was living in a shack and use of paraffin as cooking and heating fuel.

Factors that increased the odds of asthma diagnosis included maternal education, exercise, paracetamol intake, and maternal smoking. Interestingly, contrary to the findings with current wheeze on written questionnaire, active smoking by the respondent was not significant at the 95% confidence level, and the same was observed for high BMI for age.

One factor that had not been observed to be significantly associated with current wheeze , but was significantly (and strongly) positively associated with asthma diagnosis, despite the wider confidence interval caused by the small number of respondents exposed, was exposure to wood smoke as cooking fuel.

Table 4.8: Bivariate analysis: association of dietary and environmental factors with lifetime diagnosis of asthma.

Risk factor	n	N	OR	95% CI
Demographic factors				
Language of instruction at school				
Xhosa	150	1 689	0.5	0.4- 0.7
Afrikaans	183	1 289	1.0	-
English	392	2 059	1.4	1.1- 1.7
Mother has tertiary education vs. no tertiary education	210	1 086	1.5	1.3- 1.9
Dietary variables				
Maize				
Never or rarely	378	2 224	1.0	-
At least once or twice a week	219	1 651	0.7	0.6- 0.8
Three or more times a week	88	879	0.5	0.4- 0.6
Pasta				
Never or rarely	174	1 332	1.0	-
At least once or twice a week	401	2 434	1.3	1.0- 1.5
Three or more times a week	112	827	1.0	0.7- 1.3
Environmental risk factors				
Indicators of socio-economic status				
Type of residential dwelling				
House	591	3 936	1.0	-
Flat	49	263	1.2	0.9- 1.7
Shack	49	573	0.5	0.3- 0.7
Other type (unspecified)	8	60	0.8	0.3- 1.8
=4 people sharing room with respondent at night vs. <4 people	48	417	0.7	0.5- 1.0

Other environmental risk factors				
Cooking and heating fuel used				
Fuel used as cooking fuel				
Paraffin use vs. no paraffin use	72	892	0.4	0.3- 0.6
Wood (including open fires) use vs. no wood use	19	83	1.7	1.0- 3.0
Fuel used for heating				
Paraffin use vs. no paraffin use	112	1 177	0.5	0.4- 0.6
Wood (including open fires) use vs. no wood use	52	303	1.2	0.8- 1.7
Exercise (enough to make one breathe hard)				
Never or occasionally	168	1 572	1.0	-
Once or twice a week	358	2 103	1.7	1.4- 2.0
≥3 times a week	179	1 181	1.4	1.1- 1.8
Paracetamol use				
Never or occasionally	171	1 333	1.0	-
At least once a year	249	1 764	1.1	0.9- 1.3
At least once a month	285	1 741	1.3	1.0- 1.6
Female caregiver smokes cigarettes vs. does not smoke	232	1 405	1.2	1.0- 1.4
Male caregiver smokes cigarettes vs. does not smoke	321	2 130	1.0	0.9- 1.2
Respondent smokes vs. does not smoke	72	433	1.2	0.9- 1.5
BMI and current wheeze				
Underweight for age (BMI <5th centile)	39	323	0.8	0.5- 1.7
Normal weight for age (5th = BMI <85th centile)	539	3 772	1.0	-
At risk for overweight (85th = BMI <95th centile)	84	601	0.9	0.7- 1.2
Overweight (BMI =95th centile)	52	278	1.3	0.9- 1.9

Tables 4.9 and 4.10 present the results of the multivariate analysis before and after addition of language. A similar effect to that noted with the outcome of current wheeze is observed. After addition of language to the model, the association between eating maize three or more times a week and asthma diagnosis becomes statistically on- significant (95 % confidence interval includes 1). The same is observed for maternal education and use of paraffin as cooking and heating fuel.

Associations that remain unaffected by the addition of language to the model are exercise, paracetamol use, exposure to fire/wood exposure, and obesity.

Table 4.9: Multivariate analysis: association of dietary and environmental factors with lifetime diagnosis of asthma before adding language to the model

RISK FACTOR	OR	95% CI
Dietary factors (reference is no or occasional exposure)		
Maize at least once or twice a week	0.8	0.7- 1.0
Maize three or more times a week	0.6	0.5- 0.8
Pasta at least once or twice a week	1.1	1.0- 1.3
Environmental factors (reference is no or occasional exposure)		
Mother has tertiary education	1.4	1.1- 1.7
Usually use paraffin as cooking fuel	0.6	0.4- 0.8
Usually use wood (or open fires) as cooking fuel	1.9	1.1- 3.3
Paraffin use as heating fuel	0.8	0.6- 1.0
Exercise (enough to make one breathe hard) once or twice a week	1.6	1.3- 1.9
Exercise (enough to make one breathe hard) ≥ 3 times a week	1.4	1.1- 1.7
Paracetamol use at least once a month	1.2	1.0- 1.4
Mother or female caregiver smokes cigarettes	1.1	0.9- 1.3
Overweight (BMI =95th centile) vs. normal weight for age (5th = BMI <85th centile)	1.2	0.9- 1.7

** Some of the variables which were analyzed in the bivariate analysis were not included in the final multivariate model for this outcome either because they were not significantly associated with the outcome (at the 5% significance level) on bivariate analysis or testing of a multivariate model that included them was shown not to be the best model (lrtest).*

Table 4.10: Multivariate analysis: association of dietary and environmental factors with lifetime diagnosis of asthma after adding language to the model

RISK FACTOR	OR	95% CI
Language of instruction at school		
Xhosa	0.7	0.5- 1.0
Afrikaans	1.0	-
English	1.2	0.9- 1.4
Dietary factors (reference is no or occasional exposure)		
Maize at least once or twice a week	0.9	0.7- 1.1
Maize three or more times a week	0.7	0.5- 1.0
Pasta at least once or twice a week	1.1	0.9- 1.3
Environmental factors (reference is no or occasional exposure)		
Mother has tertiary education	1.3	1.0- 1.6
Paraffin use as cooking fuel	0.7	0.5- 1.0
Wood use as cooking fuel (incl. open fires)	1.9	1.1- 3.3
Paraffin use as heating fuel	0.9	0.7- 1.2
Exercise* once or twice a week	1.5	1.3- 1.9
Exercise* ≥3 times a week	1.4	1.1- 1.7
Paracetamol use at least once a month	1.2	1.0- 1.4
Mother or female caregiver smokes cigarettes	1.0	0.8- 1.2
Overweight (BMI =95th centile) vs. normal weight for age (5^{th} = BMI <85th centile)	1.2	0.9- 1.7

** exercise enough to make one breathe hard*

4.5 Wheeze in the past 12 months (video questionnaire)

Table 4.11 presents results of the bivariate analysis of those dietary and environmental factors which were found to be significantly associated with current wheeze on video questionnaire.

As with the outcomes of current wheeze on written questionnaire and asthma diagnosis, language was significantly associated with current wheeze, with the associations in the same direction (Xhosa speakers having lower odds and English speakers having higher odds of current wheeze compared to Afrikaans speakers (the reference group). The same direction in associations was noted for dietary factors.

Although living in a shack was negatively associated with current wheeze, the association was not significant as the confidence interval included 1. The same was noted for overcrowding.

Although the confidence interval was somewhat wide, the use of wood as cooking fuel significantly increased the odds of current wheeze by over double compared to no wood exposure. In contrast, wood use as heating fuel was not significantly associated with current wheeze; in fact the point estimate was in the opposite direction (weakly negative).

Exercise once or more times a week and frequent paracetamol use (at least once a month) were strongly positively associated with current wheeze, as was maternal smoking and active smoking by the respondent. The latter increased the odds of current wheeze by 70% compared to non-smoking respondents.

Respondents who were overweight for age (BMI =95th centile) had more than double the odds of current wheeze compared to respondents with a normal BMI for age.

Table 4.11: Bivariate analysis: association of selected dietary and environmental factors with current wheeze on video.

RISK FACTOR	n	N	OR	95% CI
Demographic factors				
Language of instruction at school				
Xhosa	132	1 689	0.7	0.5- 0.9
Afrikaans	135	1 289	1.0	-
English	292	2 059	1.4	1.1- 1.7
Mother has tertiary education	142	1 086	1.2	1.0- 1.5
Dietary variables (reference is no or occasional exposure)				
Maize consumption				
Never or rarely	278	2 224	1.0	-
At least once or twice a week	156	1 651	0.7	0.5- 0.9
Three or more times a week	92	879	0.8	0.6- 1.0
Pasta consumption				
Never or rarely	126	1 332	1.0	-
At least once or twice a week	308	2 434	1.3	1.1- 1.7
Three or more times a week	83	827	1.0	0.7- 1.4
Environmental risk factors (reference is no or occasional exposure)				
Indicators of socio-economic status				
Type of residential dwelling				
House	443	3 936	1.0	-
Flat	31	263	1.0	0.6- 1.5
Shack	51	573	0.7	0.5- 1.0
Other (unspecified)	9	60	1.3	0.5- 2.8

≥ four people sharing room with respondent at night				
vs. < four people	43	417	0.9	0.6- 1.2
Fuel used for cooking				
Paraffin use vs. no paraffin use	74	892	0.6	0.5- 0.8
Wood use (including open fires) vs. no wood use	18	83	2.2	1.2- 3.8
Fuel used for heating				
Paraffin use vs. no paraffin use	103	1 177	0.7	0.5- 0.8
Wood use (including open fires) vs. no wood use	33	303	0.9	0.6- 1.4
Other environmental risk factors				
Exercise (enough to make one breathe hard)				
Never or occasionally	136	1 572	1.0	-
Once or twice a week	266	2 103	1.5	1.2- 1.9
Three or more times a week	140	1 181	1.4	1.0- 1.8
Paracetamol use				
Never or occasionally	118	1 333	1.0	-
At least once a year	171	1 764	1.1	0.8- 1.4
At least once a month	256	1 741	1.7	1.4- 2.2
Smoking exposure (reference no exposure)				
Female caregiver smokes cigarettes vs. doe not smoke	199	1 405	1.4	1.2- 1.8
Male caregiver smokes cigarettes vs. does not smoke	266	2 130	1.2	1.0- 1.5
Respondent smokes vs. does not smoke	70	433	1.6	1.2- 2.1
BMI				
Underweight for age (BMI <5th centile)	30	323	0.8	0.5- 1.2
Normal weight for age (5th = BMI <85th centile)	400	3 772	1.0	-
At risk for overweight (85th = BMI <95th centile)	67	601	1.0	0.7- 1.3
Overweight (BMI =95th centile)	54	278	2.0	1.4- 2.8

Table 4.12: Multivariate analysis: association of dietary and environmental factors with current wheeze on video questionnaire before adding language to the model

RISK FACTOR	OR	95% CI
Dietary factors (reference is never or rare consumption)		
Maize at least once or twice a week	0.7	0.6- 0.9
Pasta at least once or twice a week	1.2	1.0- 1.5
Environmental factors (reference is no or occasional exposure)		
Mother has tertiary education	1.2	0.9- 1.5
Wood used as cooking fuel	2.2	1.3- 3.8
Exercise* once or twice a week	1.4	1.1- 1.7
Exercise* three or more times a week	1.3	1.0- 1.7
Paracetamol use at least once a month	1.6	1.3- 1.9
Mother or female caregiver smokes cigarettes	1.4	1.1- 1.7
Respondent smoking vs. respondent not smoking	1.4	1.0- 1.8
Overweight (BMI =95th centile) vs. normal weight for age (5^{th} = BMI <85^{th} centile)	1.9	1.4- 2.7

* *exercise enough to make one breathe hard*

Table 4.12 depicts the results of the multivariate logistic regression for analysis of associations between selected risk factors (those that were statistically significant on the bivariate analysis) and the presence of current wheeze on video questionnaire. Of note is that unlike with the two outcomes of current wheeze on written questionnaire and lifetime diagnosis of asthma, with current wheeze on video questionnaire paraffin either as cooking or heating fuel was not included in the multivariate model (becomes insignificant and inclusion weakens the model).

Table 4.13: Multivariate analysis: association of dietary and environmental factors with current wheeze on video questionnaire after adding language to the model

RISK FACTOR	OR	95% CI
Language of instruction at school		
Language: Xhosa	0.8	0.6- 1.1
Afrikaans	1.0	-
Language: English	1.2	1.0- 1.6
Dietary and environmental factors (reference is never/rare consumption/exposure)		
Maize at least once or twice a week	0.8	0.6- 1.0
Pasta at least once or twice a week	1.1	0.9- 1.4
Mother has tertiary education	1.1	0.8- 1.3
Wood use (incl. open fires) as cooking fuel	2.3	1.3- 4.0
Exercise* once or twice a week	1.4	1.1- 1.7
Exercise* ≥ 3 three or more times a week	1.3	1.0- 1.7
Paracetamol use at least once a month	1.6	1.3- 1.9
Mother or female caregiver smokes cigarettes	1.3	1.0- 1.6
Respondent smoking	1.3	1.0- 1.7
Overweight (BMI =95th centile) vs. normal weight for age (5^{th} = BMI <85^{th} centile)	1.8	1.3- 2.6

* *exercise enough to make one breathe hard*

Tables 4.12 and 4.13 present the results of the multivariate associations between selected dietary and environmental factors and current wheeze on video questionnaire. The observations made are similar to those on current wheeze on written questionnaire and lifetime diagnosis of asthma. Although not much change is noted in the *strength* of association, when language is included in the model the point estimates of the associations with maize and pasta, maternal education, maternal smoking and to a lesser

extent active smoking by the respondent do get attenuated, moving closer to the null with or without the associations becoming non-significant.

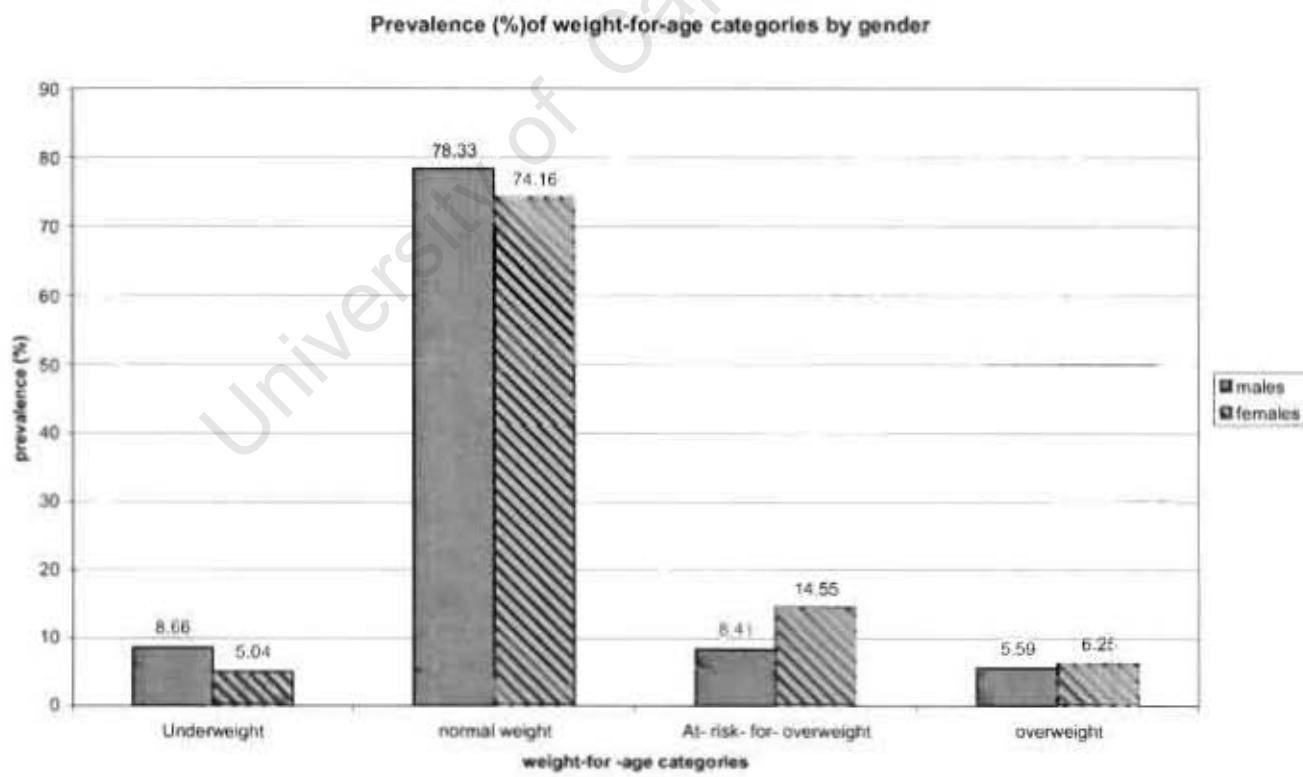
Factors whose odds ratios remain unchanged are use of wood as cooking fuel, exercise at least once a week, paracetamol use at least once a month and being overweight for age.

4.6 Gender, BMI and asthma

From the results in the preceding section, high BMI has been shown to be consistently significantly associated with asthma symptoms and diagnosis. Since there is conflicting evidence regarding the role of gender in this association, further analysis was undertaken.

Figure 4.1 below illustrates the prevalence of weight for age categories by gender. A bigger proportion of females than males had a BMI that was higher than normal for age (20.8%), and 5.04% were underweight. In contrast, a higher proportion of males were underweight (8.66%) and 17.67% had a BMI higher than normal for age.

Figure 4.1: Prevalence (%) of weight-for-age categories by gender



On bivariate analysis, gender was thus a risk factor for being overweight (Table 4.14). Females were between 30% to 60% less likely to be underweight than males, and had a

higher risk (between 50% to over double) of being at- risk- for- overweight (85^{th} = BMI $<95^{th}$ centile) and between 10 and 80% higher risk of being overweight (BMI $=95^{th}$ centile) than males.

Table 4.14: Bivariate associations, female gender vs. male gender and weight for age categories

Wt category*	Male OR	Female OR (95% CI)
Underweight	1.0	0.6 (0.4- 0.7)
At risk for overweight	1.0	1.8 (1.5- 2.2)
Overweight	1.0	1.4 (1.1- 1.8)

* Reference standard is normal weight for age males.

Tables 4.15 to 4.17 and figure 4.2 below illustrate the associations between asthma symptoms, diagnosis and BMI. Whilst the only statistically significant association was with the overweight category, it is worthwhile to note that for the outcomes of current wheeze on both written and video questionnaire there is a statistically significant linear trend from the underweight to the overweight category as evidenced by the statistically significant Chi2 test for trend (z= 4.0 and 3.3 respectively and p=0.00 for both outcomes), whilst the trend was not statistically significant for the outcome of asthma diagnosis "ever" (z= 1.01 and p= 0.31).

Effect modification by gender was shown for the association between current wheeze at rest on the video questionnaire and the- at- risk- for- overweight category (OR 0.6 and 1.1 for males and females respectively, p= 0.029). Effect modification was not evident with any of the other associations. Thus except for current wheeze on the video questionnaire associations between body mass index and asthma were shown to be linear (in odds ratios) generally for both males and females in this study.

Table 4.15: Gender stratified associations between current wheeze on written questionnaire and weight for age categories

Weight category*	Male OR (95% CI)	Female OR (95% CI)	All OR (95% CI)
Underweight	0.8 (0.5- 1.2)	0.7 (0.4- 1.1)	0.7 (0.5- 1.0)
At risk for overweight	1.0 (0.6- 1.5)	1.1 (0.9- 1.5)	1.1 (0.9- 1.4)
Overweight	1.6 (0.9- 2.6)	2.0 (1.4- 2.8)	1.9 (1.4- 2.5)*

Table 4.16: Gender stratified associations between lifetime asthma diagnosis and weight for age categories

Weight category*	Male OR (95% CI)	Female OR (95% CI)	All OR (95% CI)
Underweight	0.9 (0.5- 1.5)	0.6 (0.3- 1.1)	0.8 (0.5- 1.1)
At risk for overweight	0.7 (0.4- 1.2)	1.0 (0.7- 1.4)	0.9 (0.7- 1.2)
Overweight	1.1 (0.6- 2.1)	1.5 (0.9- 2.2)	1.3 (0.9- 1.9)

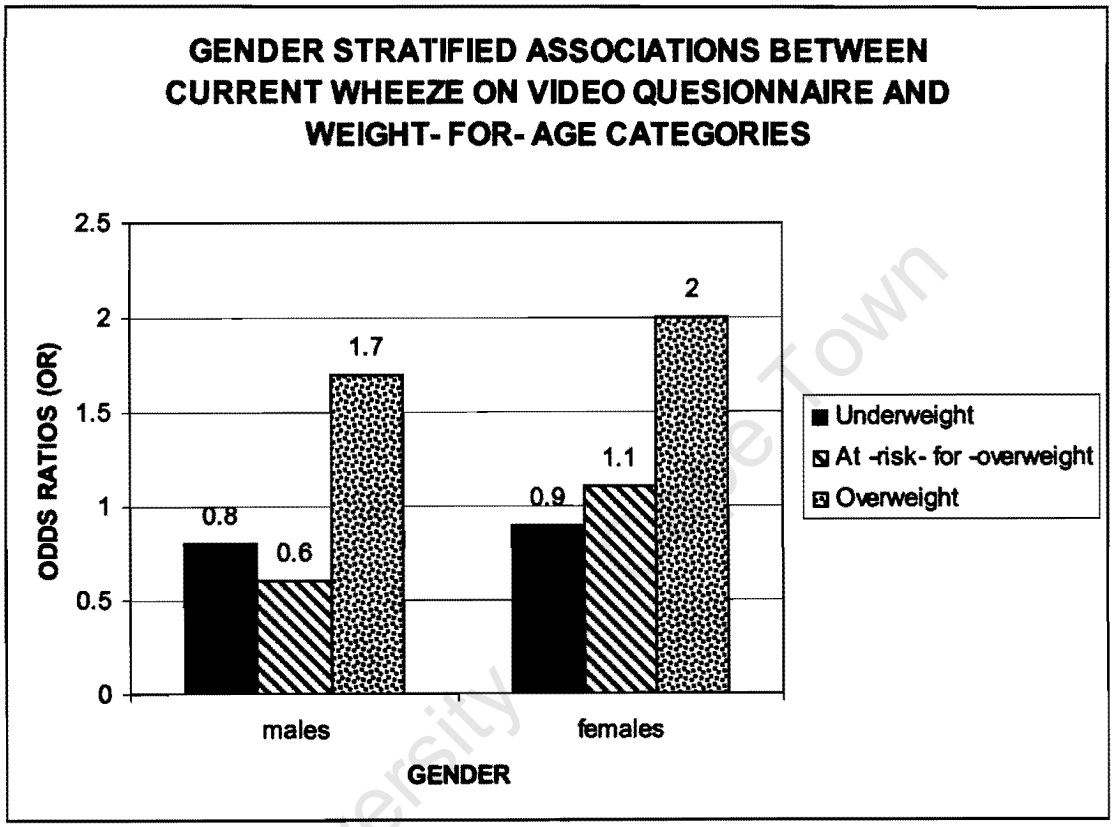
Table 4.17: Gender stratified associations between current wheeze on video questionnaire and weight for age categories

Weight category*	Male OR (95% CI)	Female OR (95% CI)	All OR (95% CI)
Underweight	0.8 (0.4- 1.5)	0.9 (0.4- 1.5)	0.8 (0.5- 1.2)
At risk for overweight	0.6 (0.3- 1.3)**	1.1 (0.8- 1.5)**	1.0 (0.7- 1.3)**
Overweight	1.7 (0.8- 3.2)	2.0 (1.4- 3.0)	2.0 (1.4- 2.8)

* Reference standard is normal weight for age

** Effect modification by gender evident (p= 0.029)

Figure 4.2 Gender stratified associations between current wheeze on video questionnaire and weight-for-age categories



4.7 Results: all outcomes combined

Table 4.19 below depicts the multivariate associations between the dietary and environmental risk factors and all three outcome measures for asthma in one table.

There is consistency in the direction of all associations across the three outcome measures. However, it is noted that students at English medium schools have a significantly higher odds of wheezing in the past 12 months on written questionnaire than on video questionnaire. This is in contrast to the general observation that the strengths of association (point estimates) for most risk factors are similar for current wheeze on both written and video questionnaire.

This is different for lifetime diagnosis of asthma, as the point estimates tend to be slightly weaker for asthma diagnosis (as in the case of paracetamol use, maternal smoking and active smoking by the respondent, and being overweight) than those for current wheeze on both written and video questionnaires. Exceptions to this are the associations with exercise and wood exposure, which are stronger for asthma diagnosis.

Table 4.18: Summary of multivariate associations for all outcome measures

	Current wheeze (Written questionnaire)		Asthma ever diagnosis (Written questionnaire)		Current wheeze (Video questionnaire)	
	OR	95% CI	OR	95% CI	OR	95% CI
Language of instruction at school						
Xhosa	0.9	0.7- 1.1	0.7	0.5- 1.0	0.8	0.6- 1.1
Afrikaans (reference level)	1.0	-	1.0	-	1.0	-
English	1.8	1.5- 2.1	1.2	0.9- 1.4	1.2	1.0- 1.6
Dietary risk factors (reference is no or occasional exposure)						
Maize at least once or twice a week	0.7	0.6- 0.8	0.9	0.7- 1.1	0.8	0.6- 1.0
Maize ≥ 3 three or more times a week	0.8	0.6- 1.0	0.7	0.5- 1.0	not included in model	
Pasta at least once or twice a week	1.0	0.9- 1.2	1.1	0.9- 1.3	1.1	0.9- 1.4
Environmental risk factors (reference is no or occasional exposure)						
Mother has tertiary education	1.3	1.1- 1.5	1.3	1.0- 1.6	1.1	0.8- 1.3
≥four people sharing room with respondent	0.7	0.5- 1.0	not included in model		not included in model	

Paraffin as cooking/ heating	1.0	0.8- 1.3	0.7	0.5- 1.0	not included in model	
Wood use as cooking/ heating fuel	not included		1.9	1.1- 3.3	2.3	1.3- 4.0
Exercise* once or twice a week	1.4	1.2- 1.7	1.5	1.3- 1.9	1.4	1.1- 1.7
Exercise* ≥ 3 times a	1.3	1.1- 1.7	1.4	1.1- 1.7	1.3	1.0- 1.7
Paracetamol use at least once a month	1.4	1.2- 1.6	1.2	1.0- 1.4	1.6	1.3- 1.9
Mother smokes cigarettes	1.2	1.0- 1.4	1.0	0.8- 1.2	1.3	1.0- 1.6
Respondent smoking	1.4	1.1- 1.8	not included in model		1.3	1.0- 1.7
Overweight (BMI ≥95th centile)	1.7	1.3- 2.2	1.2	0.9- 1.7	1.8	1.3- 2.6

* Enough exercise to make one breathe hard

CHAPTER 5: DISCUSSION AND STUDY LIMITATIONS

The study has demonstrated several consistent associations between the three outcome measures for asthma and certain dietary and environmental risk factors, which will be discussed in some depth below. A discussion on the consistency between results from the written and video questionnaire is also included at the end of the chapter.

a) Dietary associations:

Admittedly it is difficult to study diet robustly, especially to quantify exposure and make comparisons for different populations with different dietary practices, the dietary questionnaire as indicated in the methods section was developed, standardized and validated by the ISAAC Steering Committee, but at the same time allowing for locally relevant adaptation. A dietician working at the Red Cross Children's Hospital was consulted for expert advice on the inferences that could be drawn the observed associations.

Of the sixteen dietary variables included in the questionnaire, maize and pasta were the only dietary risk factors that were consistently associated with asthma symptom prevalence. Whilst maize consumption reduced the odds, eating pasta once or twice a week increased the odds of having wheeze on both written and video questionnaires. The maize association is consistent with findings from the ISAAC 1 ecological analysis that showed consistent negative association between asthma and starch from cereal (and rice) intake [23]. In South Africa maize is the traditional staple food for the majority of Africans. Post democracy (1994), in an effort to reduce high rates of protein energy malnutrition, the South African government enforced fortification of maize-meal with vitamins and trace elements. Vitamins like A and E are known for their antioxidant properties, and micronutrients (specifically those derived from vegetables) were demonstrated in the ISAAC 1 ecological analysis to be associated with reduced asthma prevalence [23]. This may be the mechanism for the association of (fortified) maize with reduced asthma prevalence.

Unlike maize, it is difficult to find an explanation for a direct effect of pasta on asthma prevalence.

An alternative explanation for the observed dietary associations, favoured by the authors and supported by the fact that the dietary associations were significantly confounded by language is that the two dietary factors represent proxy indicators of socioeconomic status in this study. Maize is the staple diet in the Xhosa/ African population. As discussed in the literature review in the section on political demography in relation to health status in South Africa, language to a great extent represents race and therefore the socioeconomic status of the respondents. Thus Xhosa speakers in this study would be African respondents, who due to the political history of the country are more likely to come from socioeconomically disadvantaged households compared to their English and to a lesser extent Afrikaans speaking counterparts.

On the other hand pasta (which was associated with increased asthma prevalence) is more expensive (than maize) and is more likely to be part of a "westernised" diet, and its consumption more prevalent in the socioeconomically well-off. Thus the associations with maize and pasta may be reflective of a positive association between the prevalence of asthma and socioeconomic status.

A large number of comparisons were made in the analysis of the dietary questionnaire. It is acknowledged that using a p-value pf 0.05% (threshold for type 1 error) may have resulted in 5% of observed associations being due to chance. It remains debatable whether using methods like the bonferroni correction for multiple comparisons is advisable, and in this case a decision was taken not to do so.

b) Environmental associations

Several environmental factors were found to be significantly associated with asthma symptoms and diagnosis. The variables can be grouped into those that probably represent socioeconomic status, environmental pollution, and individual constitutional or behavioural factors.

i) Indicators of socio- economic status:

Education is associated with improved socioeconomic status and access to health care. In this study maternal higher education was found to be consistently positively associated with asthma prevalence for current wheeze on written questionnaire, and asthma diagnosis but not for current wheeze on video questionnaire. Although the strength of association (the point estimate) for the association with asthma diagnosis was the same as for current wheeze on written questionnaire, the confidence interval included one.

The observed positive association with current wheeze on written questionnaire may be explained by a number of reasons, and may be as a result of either a direct association or an indirect association. In the former case, improved maternal education may have an independent effect on asthma prevalence by increasing likelihood of awareness of symptoms and signs of asthma and greater ability to access medical diagnosis and care.

The indirect association may be related to maternal education being associated with higher socioeconomic status, which in turn has been shown in several studies to be positively associated with asthma [32,33,34].

A third possibility with some evidence from the South African setting is that improvement in education and socioeconomic status of particularly African women is associated with increased smoking prevalence in this group, which otherwise has low smoking rates compared to their Coloured and White counterparts [50]. However, in this

study smoking was controlled for in the analysis and thus is unlikely to account for the observed associations.

A study conducted in Kenya in rural and urban school children failed to show an association between parental education and exercise induced bronchospasm (EIB) [45]. This may be consistent with the finding in this study in that the multivariate analysis, with adjustment for language also failed to show an association (on) with asthma diagnosis and current wheeze on video questionnaire. These two outcomes are supposed to be more objective than the written questionnaire outcomes, and thus more likely to be comparable to the objective diagnosis by EIB. This raises the question that the observed association with maternal education (a proxy for socioeconomic status) is related to subjective self reported prevalence rather than objective diagnosis or other marker of disease.

Another factor contributing evidence of the positive association between socio- economic status and asthma was the negative association with the use of paraffin as cooking fuel (since paraffin is predominantly used by the lower socio-economic groups). Although in the multivariate analysis the association between paraffin use and presence of asthma symptoms was not statistically significant, its use as cooking fuel was consistently negatively associated with asthma symptom prevalence. Similar to maize consumption, using paraffin as cooking fuel is predominantly found in the socio-economically deprived population, whereas their counterparts are more likely to use electricity as cooking fuel.

This study's finding is somewhat different from results from other studies. In a cross sectional survey conducted in rural and urban children between the ages of 8 to 12 years in Kenya Ng' ang'a and colleagues investigated the association between exercise induced bronchospasm (EIB) and environmental factors [45]. Results indicated that that the use of kerosene as cooking fuel was strongly positively associated with EIB when unadjusted [OR 1.50 (95% CI 1.07- 2.10)], or adjusted only for area of residence [OR 1.80 (1.27- 2.55)], when adjusted for all exposures (including sex, age, breastfeeding, family history of asthma, ventilation, parental education, and exposure to motor vehicle fumes on the

way to school) the OR dropped to 1.17 (95% CI 0.74- 1.84) [45].Thus whilst they found a positive association, the relationship between paraffin use and EIB was confounded by other host and environmental factors.

Another explanation for the difference in the direction of association between the Kenyan study and this one may be that in this South African study conducted in an urban setting, paraffin use is predominantly found in the poor (and thus the negative association with asthma), whereas in the Kenyan study paraffin use was more likely to be found in the urban than in the rural population (who predominantly used biomass/wood fuel) [45]. In that study parents of children residing in the urban area also had on average more years of education than those from the rural area. Since education is associated with socio-economic status it can be postulated that the rural respondents generally came from households of a lower socioeconomic status than their urban counterparts. Thus in the Kenyan study paraffin use would be associated with higher socio-economic status and thus the positive association with asthma.

ii) Environmental pollution:

Exposure to wood smoke (including open fires) was uncommon in our study [83 (1.6%) and 303 (6%) of the total study population of 5,036 children were exposed to wood used as cooking and heating fuel in the homes respectively] Contrary to paraffin use, wood was consistently and strongly positively associated with asthma prevalence. These study findings are consistent with similar findings from rural Guatemala and Nepal where use of biomass fuel ("wood fuel with an occasional supplement of crop residues" in the former and "solid fuel such as wood and grass" in the latter) increased the risk of current wheeze [OR 3.4 (95% CI 1.3- 8.5) and 2.2 (95% CI 1.0- 4.5) respectively] [44,46]. Whilst these studies both utilised the standard ISAAC questionnaire, the study population in Guatemala was much younger (4 to 6 year olds), and as a result the written questionnaire was administered to the mothers and the video questionnaire was not used since this was a door to door survey. In the Nepal study the study population was slightly older than our study population (11 to 17 year olds) and the study methodology was a case control

study. Thus this study's results are consistent with those from studies employing different study designs/ methodology, study populations of different age groups, in different countries [44,46]. This adds to evidence suggesting a *direct* if not causal association between wood smoke and asthma symptom prevalence.

More evidence to support a direct association is that in this study adjusting for socioeconomic status did not attenuate the association between use of wood as cooking fuel and asthma symptom prevalence, which would be expected as use of wood is more prevalent in households of lower socioeconomic status.

Thirdly, biological plausibility is based on the fact that biomass fuel including wood, crop residue and dung on combustion emit carbon monoxide, nitrous dioxide, formaldehyde, polycyclic organic matter and particulate matter with respirable particles <10μm (PM10) similar to that emitted by diesel combustion [44]. Exposure to the latter (diesel) has been shown to be associated with an atopic/ asthmatic predisposition by stimulating IgE production, eosinophilic degranulation and augmentation of cytokine and chemokine production [44].

Although all the studies noted above used the validated ISAAC methodology and questionnaires, it is still possible that the outcomes measured may represent non-asthmatic wheezing or chronic bronchiolitis, rather than allergic asthma.

Due to the small proportion/ sample size of respondents exposed to wood smoke reported in this study population, the possible effect of gender on the association between wood exposure and asthma symptoms and diagnosis could not be investigated.

One study was found with contradictory results. In the Kenyan study (Ng'ang'a et al.) use of biomass fuel (wood) reduced the odds of EIB [45]. Before adjusting for area of residence indoor exposure to biomass cooking fuel reduced odds of EIB [unadjusted OR 0.58 (95% CI 0.37- 0.90)] but after adjusting for area of residence the OR was attenuated to 0.73 (95% CI 0.46- 1.15). When adjusted for all exposures (including sex, age, breastfeeding,

family history of asthma, ventilation, parental education, and exposure to motor vehicle fumes on the way to school) the OR was 0.64 (95% CI 0.37- 1.11). Thus in the Kenyan study use of wood was a proxy measure for "urbanisation" as indicated by the changes following adjustment by the factors mentioned above. This illustrates that similar to kerosene, other host and environmental factors somewhat attenuated the association between indoor fuel exposure and EIB [45]. This was not evident in our study.

iii) Behavioural factors:

A couple of behavioural factors were found to be associated with asthma prevalence. These were smoking (by the mother and active smoking by the respondent) and exercise. Paracetamol use has also been included in this category.

In this study maternal smoking was found to be positively associated with current wheeze on both written and video questionnaire. For both outcomes the lower limit of the confidence interval is 1.0. The study failed to show an association between maternal smoking and asthma diagnosis.

A considerable amount of literature including cohort and case control studies and a recent systematic review and meta-analysis, has shown a positive association between maternal smoking and environmental tobacco smoke and prevalence of asthma [28,29,30].

An alarming finding was that almost 3.7% of the study population of 13 to 14 year old school children reported themselves to be smokers. The real figure may be higher than this considering that school children may be scared of admitting that they smoke, and may therefore under report this variable. The study showed that active smoking by the respondent (which is not so widely documented) positively associated with prevalence of asthma. Similar to maternal smoking, the associations were noted to be weaker for the outcome of lifetime diagnosis of asthma than for current wheeze on both written and video questionnaires.

This observation may be due to selection effect whereby parents/ relatives of respondents who had received a diagnosis of asthma from a healthcare professional would have been advised to avoid smoking in the presence of the minor. Similarly symptom exacerbation in respondents who smoke might cause them to stop/ avoid smoking. The effect of this would tend to reduce the exposure in those who have asthma and thus attenuate the real association of smoking exposure and asthma onset.

Another behavioural factor associated with asthma symptom prevalence was exercise, which was consistently positively associated with asthma prevalence for all three outcome measures. The mechanisms for this may be two-fold. The more likely explanation is that since exercise induced bronchospasm (EIB) is accepted to be a hallmark of asthma and since this was a survey, temporality may have been confused. Although the wording of the question seems clear enough "How many times a week do you engage in vigorous physical activity long enough to make you breathe hard", positive responses to the question may represent EIB, a symptom of asthma (i.e. "unmasking" of asthma), rather than representing a causal association. The alternative explanation, that there is a direct positive association, is refuted by evidence from other studies that show that lack of physical activity is associated with being overweight which is in turn positively associated with asthma [26]. The hypothesised explanation here is that lack of exercise/physical activity is associated with a reduction in deep breathing and thus airway smooth muscle latching and bronchospasm [26].

The study also showed a consistent positive association between paracetamol (acetaminophen) and asthma prevalence. This was consistent with all three outcome measures, although the confidence interval for lifetime asthma diagnosis included one.

The possibility of confounding of the association between paracetamol intake and asthma does exist i.e. use of paracetamol is associated with pulmonary viral infections which can induce or exacerbate asthma. This could explain the weaker association with asthma diagnosis, i.e. paracetamol may not be associated with true atopic asthma but rather with other "wheezing illnesses" which result in increased paracetamol intake.

Another confounding factor for the observed association may be due to the tendency for medical practitioners to discourage the use of aspirin, and instead encourage the use of paracetamol in asthmatics. This precautionary practice is because whilst the general prevalence of aspirin-induced-asthma is between 5 to 6%, up to 20% of asthmatics suffer from aspirin sensitivity. In this group use of aspirin (and other non-steroidal anti-inflammatory agents) may induce inhibit the cyclooxygenase and stimulate the lipoxygenase pathways, resulting in excess production of cysteinyl leukotrines which may induce or exacerbate bronchospasm [53].

However, a few cohort studies have shown a similar association with *incident* asthma in children and one study has shown that this association remains consistent even after controlling for aspirin use [41,42,43].

A causal relationship is further supported by evidence in animal models that paracetamol reduces the levels of pulmonary glutathione which is an antioxidant and may thus increase asthma morbidity [43].

Thus it would appear from different studies that the criteria of the strength of association, temporality, consistency and biological plausibility for the association between asthma and paracetamol use are satisfied.

iv) Individual constitutional factors:

A fair amount of literature on both children and young adults has implicated high body mass index as directly associated with asthma [25,26,27]. The results in this study population confirm the findings of these previous studies. However, whilst some studies have shown that the relationship is not always linear, for example that underweight increases the risk of asthma resulting in a U-shaped relationship [27], this study has shown a predominantly linear/monotonic association in both male and females (the exception was current wheeze on the video questionnaire, in the at- risk- for- overweight category only).

It should be noted that BMI in this paper has been reported using centile scores. The centile scores were calculated using the "antro.data" software package. The validity of this may be questionable given that the reference population/s from which these centile scores are drawn are unlikely to represent the study population.

c) Consistency of results from the written and video questionnaires:

As noted in the study methods section, the video questionnaire was added to ISAAC as a measure to overcome language related variability which may be experienced with self reported asthma symptom prevalence.

When comparing the results of the analysis between the written and video questionnaires, it is reassuring that although the written questionnaire yielded higher outcome prevalence compared to the the video questionnaire (20.3% vs. 11.1% respectively) all observed associations were in the same direction for both written and video questionnaires. Secondly most of the statistically significant associations were consistent for both questionnaires (exercise, paracetamol use, maternal and respondent smoking and BMI>95th centile). One notable exception is for language, where the OR for current wheeze is 1.8 (05% CI 1.5- 2.1) on the written questionnaire and notably lower (1.2 1.0- 1.6). Whilst this may represent language bias which is discussed in more detail in the following section on study limitations, the confidence intervals do overlap thus the difference may not be considered significant. This lends credibility to the validity of the associations.

The comparisons of the associations between the written and video questionnaire is consistent with the results of the prevalence trend study from the same study (centre), that shows that the increase in asthma symptom prevalence over seven years is consistent for all outcome measures (including written and video questionnaire) [5].

d) Study limitations:

Several factors may limit inferences from this study. The first pertains to the cross sectional study design. Due to the inability to ascertain temporality, the nature (causal or non-causal) of the associations between asthma and exercise, high body mass index (overweight) and paracetamol are difficult to interpret.

The effects of cross sectional study design on exercise have been discussed above.

With high body mass index, children with asthma may limit physical activity due to exercise induced bronchospasm and thus become overweight/obese. Thus in this scenario, the asthma precedes the weight gain rather than the reverse. However, in addition to results from cohort study designs which suggest a causal relationship between high BMI and asthma[16], other evidence for a causal relationship in this study is the presence of a dose response (from "underweight" to "at- risk- for- overweight" to "overweight" categories) as evidenced by the Chi^2 test for trend (p value of 0.029).

The possibility of confounding or reverse causation of the association between paracetamol use and asthma symptom prevalence has been discussed in the preceding section.

The second limitation of this study relates to potential selection bias, which is defined as error in the process of identifying the study population, leading to preferential selection of subjects related to either their exposure or disease status. Selection bias includes sampling, ascertainment and participation bias.

Although the study population was drawn from a clustered population, logistic regression methods for analysis of clustered data were not used in STATA. This is because the schools were randomly sampled in such a way that they represented the broader population of schools. It is acknowledged that since individuals within schools were sampled it is possible that the precision of descriptive statistics and reported associations

may be artificially small (spuriously narrow confidence intervals). However it was felt that the sample size was large enough (54 schools and 5 036 learners) to offset these concerns.

Whilst the likelihood for sampling bias has been reduced by the cluster random method employed in sampling, participation bias may have some effect on the study. This derives from the study population being school going children. Whilst the study may be valid for "school going" populations, external validity may be compromised as children of the same age group who do not attend school may have different exposure characteristics from those who attend school. This is plausible considering that children who are at school are more likely to be healthy and to come from better educated, relatively financially better-off households and besides the education of the caregiver, the respondents themselves may be more educated in avoiding unhealthy exposures e.g. diet and smoking. Unfortunately we were not able to get any data on school attendance in this population.

Similarly non-response bias may affect the results. The response rate for this study was 83.4% and reflects attendance on the day of the visit. Non-responders may have differed in some exposure/ disease characteristics in some important ways e.g. children at school on the day may be more motivated than those not at school which would include truant children who may have higher exposures like smoking. Unfortunately reasons for non response were not documented during the data collection phase.

A bias similar to that of the "healthy worker effect" or "survival bias" may be present in a school based population, whereby children with poorly controlled asthma may miss school a lot and thus not be included in the study. This was shown by Nriagu et al. in their study conducted in south- central Durban, South Africa, where asthma prevalence was strongly correlated with missing of school by children (OR 44; 95% CI 13-141) [17]. Exposures in sick children not at school may be different to those who are healthier and can attend school. The study did attempt to reduce the chances of this by visiting schools a second time at least a week apart, in order to get some of the learners who missed the

first interview. This coupled with the high response rate and the fact that the majority of children have mild asthma (only approximately 1% child asthmatics have severe asthma) would suggest that the majority of asthmatics would be present at school when surveyed a week apart.

Prevalence- incidence bias, also known as selective survivor or Neyman bias, could have occurred if the exposures were related to prognostic factors. For example, if smoking is related to prognosis of asthma, it may be that the study population included only mild cases of asthma who may be less exposed to smoking, so that smoking exposure would be under-estimated as a risk for asthma in this study population [48].

Information bias may have influenced some of the associations. Reporting bias may have occurred where respondents with asthma may have recalled exposures more than their counterparts, for example maternal smoking and active smoking by the respondent. This would result in differential misclassification, with the point estimate being biased away from the null. In this case this would mean that the real associations may be smaller than observed in the study or even spurious. However this is unlikely as most of the direct associations shown in this study have been shown to be consistent in other studies employing cohort study design such as studies of maternal smoking.

Another form of reporting bias that may have occurred is selective suppression of information on exposures such as active smoking among the respondents, as they are young learners. However, if this occurred it is more likely that all the learners would have under-reported the exposure (smoking) which would lead to non- differential misclassification and thus weakening of the observed association.

Confounding bias may have also occurred with respect to language/ medium of instruction at the school. Levin, in his study conducted at Red Cross War Memorial Children's Hospital (a tertiary paediatric hospital in the Cape Town Metropole District) found that there were significant disparities between English-speaking doctors' medical vocabularies and that of Xhosa parents of children attending the hospital's short stay

ward and the Allergy clinic [47]. He found that whilst the term "wheeze" was common in doctors' vocabularies it was almost non- existent in parents' vocabularies. An unexpected finding was that this also applied to parents of children who attended the Allergy clinic who would have been expected to be aware of this term as it was presumed that they would have been exposed to it. Similarly the Xhosa term for wheeze (*ukutswina*) was non-existent in doctors' vocabularies.

The same applied to the understanding of terminology and culture specific models of disease. For example, parents' understanding of the term "asthma" tended to be non-specific respiratory disease, as opposed to the doctors' understanding of the term. Similarly the term "tight chest" (in Xhosa *ukuminxana* or *iphika*) could also apply to healthy individuals with shortness of breath from exertion, and not necessarily due to respiratory pathology. Similarly the Xhosa term *isifuba* could apply to normal individuals as it could be understood as the anatomical chest, any chest pathology or some specific chest pathology, but not necessarily asthma. Levin concluded that assuming the same applies in the general population it would have an impact on epidemiological research findings, specifically where the research methodology is questionnaire based.

The discordance in use of medical terminology between health care workers and the general "lay" population (including English speaking laypersons) could result in underestimation of the true prevalence of asthma symptoms where the word does not exist in the vocabulary or there is limited understanding of terms like asthma or wheeze by lay persons. Alternatively overestimation of the prevalence may result where the general population have a broader understanding of the term compared to the medical profession (e.g. in the case where "asthma" can denote asthma as understood by medical professional, as a non- specific chest problem or other specific chest disease). Levin supports his argument by noting that in ISAAC invariably the response for the written questionnaire based outcome is higher than the video based equivalent outcome measure, and that the questionnaires have not been validated in most non-English speaking communities. Where this has been done, the study population has been in "homogenous populations with good socio-economic and educational background" (personal

communication and unpublished manuscript, May 2007). Levin concludes by discouraging the use of terminology like *isifuba*, asthma (*i-esma)*, and recommends exploration of revised terminology which would take into account culture specific models of disease and use of trained interpreters [47].

In the Cape Town ISAAC centre both *ukutswina* (wheeze) and *ukuminxana* (tight chest) were used in translated Xhosa questionnaire. As a result of the argument presented above, respondents may have had non-specific or broader interpretation of these terms, resulting in overestimation of the prevalence of asthma symptoms on written questionnaire compared to the video questionnaire. As discussed above the same could apply for the English speaking respondents.

However, the fact that the video questionnaire yielded similar associations to those of the written questionnaire dilutes the argument for language bias, as the video questionnaire was designed specifically to overcome any language related variability in the survey [1,2,3,4,5]. Furthermore, studies comparing ISAAC 1 and ISAAC 3 prevalence show a consistent increase in prevalence of all asthma variables e.g. recent wheeze, asthma diagnosis, severe wheeze and all five video sequences [3,4,5]. Also differences in prevalence on video and written questionnaire (approximately 1.5 to 2 times) were observed across languages i.e. including English speaking developed country settings.

In their paper describing asthma prevalence trends in the African region, Ait-Khaled et al. reported that whilst there was significant variation between and within the 16 African countries that participated in ISAAC 3 in asthma symptom prevalence recorded from the written questionnaire (4% to 21.5%), there was less variation in asthma symptom prevalence recorded for the video questionnaire (8.7% to 10%). From this it would seem that the video questionnaire may have better content validity than the written questionnaire, and language factors may contribute to this. However, only seven centres included the video questionnaire in their surveys [4].

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

The study results demonstrated a number of strong and consistent associations, some of which confirm some fairly established or plausible associations with asthma in children.

a) Summary of study findings:

Of the sixteen dietary variables included in the questionnaire, maize was consistently negatively associated while pasta consumption was consistently positively associated with asthma symptom prevalence. However after adjusting for language, the association with pasta became statistically insignificant. On the other hand, eating maize once or twice a week remained significantly "protective" for the outcome of current wheeze on written questionnaire. These findings suggest the dietary associations observed are confounded by language and socioeconomic status in this study population. However there may be another mechanism for the association with maize consumption, i.e. it may be due to the fact that all commercial maize meal in South Africa is fortified with vitamins and trace elements, some of which have been shown to have anti-oxidant properties.

Environmental factors that were found to be significantly associated with asthma symptoms and diagnosis prevalence were categorized into proxy indicators for socioeconomic status, environmental pollutants and tobacco smoke exposure, behavioural and individual constitutional factors.

Proxy indicators for socioeconomic status included maternal education, which was shown to significantly increase the odds of current wheeze on written questionnaire (association not statistically significant for asthma diagnosis and current wheeze on video questionnaire). Paraffin use as cooking fuel significantly increased the odds of asthma symptoms and diagnosis before adjusting for language and maternal education, but was significantly attenuated by adjusting for these variables, confirming that the association is not a direct effect, but is due to confounding by socioeconomic status. Living in a shack

compared to a house (indicating household of lower socioeconomic status) was also negatively associated with asthma symptom prevalence on bivariate analysis, but the association was not significant and thus this variable was not included in the multivariate analysis.

Environmental pollution from using biomass fuel (wood including open fires) for cooking and heating was strongly associated with asthma symptoms and diagnosis. Unlike with paraffin use, the association with biomass fuel was not attenuated after adjusting for socioeconomic status, indicating a direct independent mechanism for the association. Studies of different study design and population from Guatemala and Nepal have found similar associations and toxicological studies support biological plausibility for this association.

Behavioural factors found to be significantly associated with asthma symptoms and diagnosis included tobacco smoke exposure, exercise and paracetamol intake, which all increased the odds of asthma.

Numerous studies, including cohort studies have found a positive association between maternal smoking and environmental tobacco smoke, and asthma symptoms. This was confirmed in this study for the outcomes of current wheeze on written questionnaire, and (with a weaker association) for current wheeze on video questionnaire. The study failed to show an association with the outcome of asthma diagnosis. This may be a reflection of language bias or an indication that the association is more valid for "wheezy illness" rather than doctor- diagnosed asthma or asthma diagnosis by other objective means.

The study design could not help in answering the one question that remains for the association of parental smoking or environmental tobacco smoking with asthma symptom prevalence, namely, whether smoking causes asthma or triggers asthma.

This study also showed a significant association of active smoking by the respondent with current wheeze, but not asthma diagnosis. The association is entirely biologically plausible.

Exercise increased the odds of asthma symptoms and diagnosis. This association is thought to be due to cross sectional bias as it is not supported by evidence from other studies that show that exercise is associated with a reduction of asthma symptoms. It also goes against the association of exercise with BMI.

The finding that paracetamol intake at least once a month is consistently associated with increased asthma symptoms and diagnosis adds to a growing body of literature on this topic, with evidence of causation supported by results from prospective cohort studies.

BMI >95th centile was significantly associated with current wheeze on both written and video questionnaire, but the association was not statistically significant for the outcome of asthma diagnosis. The finding is consistent with other evidence from different study designs and populations (including adult populations). In this study the association between BMI and asthma symptom prevalence was linear (monotonic). Although low BMI (underweight) was more prevalent in males, this study did not show significant effect modification of the association by gender except for in the at-risk- overweight category.

b) Recommendations:

Research on environmental factors affecting asthma prevalence trends has mostly been conducted in the developed world. This study has added to this evidence from Africa. Although South Africa is generally regarded as better off than most developing countries, Cape Town represents a city with both ends of the socioeconomic spectrum, with a combination of peri-urban shack settlements with poor living standards, formal "township" households (intermediate socioeconomic status) and a suburban population. It is thus a good area in which to study environmental factors influencing disease trends.

The consistent positive association between socioeconomic status and asthma symptom prevalence in developing countries needs further unravelling, including mechanisms of "urbanisation" and factors associated with high socioeconomic status that increase asthma symptom prevalence.

Considering the strong and consistent independent association with indoor air pollution from wood/ biomass fuel, it is important to raise awareness among parents especially in rural areas and peri-urban settlements where infants and young/preschool children are exposed to wood smoke for long periods of time as they remain in the care of their mothers who spend a fair amount in the kitchen cooking every day. The infants are often on the mothers' backs for a great part of the day. It is important to monitor the trend in this association. Following democracy the government has been electrifying both peri-urban settlements and rural areas. However due to cheaper price of biomass fuel/wood compared to electric hobs, the poor may still use wood.

The Tobacco Products Control Act of 1993 was enacted to reduce the harmful effect of smoking on health. Although smoking prevalence has been reported to have reduced between 1995 and 1998, the study showed that 27.8% of mothers and 42.2% of fathers were smokers. Even more alarming was that almost 4.0% of 13 to 14 year old school children admitted to be smokers. Thus public awareness on the association between exposure to tobacco smoke exposure and health including asthma should be heightened.

The association with paracetamol is interesting and relatively new. 34.5% of respondents admitted to using paracetamol at least once a month. If the association is real/ causal as suggested in other studies, the public health implications are big, and awareness of this association needs to be raised. The government should consider regulations to implement formal controls by the pharmaceutical industry, for example the association between paracetamol and asthma should be emphasized in the product information leaflets and included in the information and counselling given to clients by healthcare providers including pharmacists on prescription and purchase of paracetamol containing products. Paracetamol use in infancy is probably high, especially since paracetamol is generally regarded as safer than other antipyretics and anti inflammatory agents. Paracetamol use is encouraged even as prophylaxis when infants have their vaccinations (at least 4 to 5 vaccination visits in the first year) and for fever even if it is associated with teething in the first year of life. Thus certain practices related to the perception that paracetamol is "harmless" need to be discouraged.

Public health efforts to address nutrition in children should be reshaped. Whilst the traditional focus of such interventions has been undernutrition, current efforts include addressing the increasing burden of overweight and obesity in children. The findings of this study add "weight" to these ongoing efforts and policies. These interventions should be multisectoral (including the departments of health and social development, education, and arts and culture in regard to sports). Health promotion is central to the approach.

In conclusion the study is the first investigation of environmental factors associated with asthma symptom prevalence in South Africa involving a cross section of the whole population of an urban area, identifying research needs and suggesting some areas for intensification of public health efforts.

REFERENCES:

1. Isaac Steering Committee. *Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC)*. Eur Respir J 1998; 12: 315- 335.

2. P. Ellwood, M.I. Asher, R. Beasley, et al. *The International Study of Asthma and Allergies in Childhood: Phase Three rationale and methods*. Int J Tuberc Lung Dis 2005; 9: 10-16.

3. M.I. Asher, S Montefort, B. Bjorksten, et al. *Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjuctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross sectional surveys*. Lancet 2006; 368: 733-43.

4. N. Ait- Khaled, J. Odhiambo, N. Pearce, et al. *Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III*. Allergy 2007; 62: 247-258.

5. H. J. Zar, R. I. Ehrlich, E.G.Weinberg. *The changing prevalence of asthma, allergic rhinitis and atopic eczema in African adolescents form 1995 to 2002*. Pediatr Allergy Immunol 2007; In Press.

6. C.H. van Niekerk, E.G. Weinberg, S.C. Shore, et al. *Prevalence of asthma: A comparative study of urban and rural Xhosa children*. Clin Allergy 1979; 9:319-324.

7. J. Vermeulen. *Airway hyperresponsiveness*. Resp Focus 1990; 2: 6- 8.

8. E. Terblanche, R. I. Stewart. *The prevalence of exercise-induced bronchoconstriction in Cape Town schoolchildren.* S Afr Med J. 1990; 78: 744-747.

9. F. Nagel. *Asthma prevalence study in primary school children.* MMed thesis, University of Cape Town, 1992.

10. H.A. Steinman, H.Donson, M. Kawalski, et al. *Bronchial hyper-responsiveness and atopy in urban, peri-urban and rural South African children.* Pediatr Allergy Immunol. 2003; 14: 383- 393.

11. J. Calvert, P. Burney. *Effect of body mass on exercise-induced bronchospasm and atopy in African children.* J Allergy Clin Immunol. 2005; 116: 773-779.

12. M.B. Mashalane, A. Stewart, C. Feldman, et al. *Prevalence of exercise-induced bronchospasm in Thokoza schoolchildren.* S Afr Med J. 2006; 96: 67- 70.

13. M. L. Burr, E. S. Limb, S. Andrea, et al. *Childhood asthma in four countries: a comparative survey.* Int J Epidemiol. 1994; 23: 341- 347.

14. R. I. Ehrlich, D. Du Toit, E. Jordaan, et al. *Prevalence and Reliability of Asthma Symptoms in Primary School Children in Cape Town.* Int J Epidemiol 1995; 24: 1138- 1145.

15. As cited in: K. Steyn, J. Fourie, N. Temple (eds). *Chapter 11: Chronic Respiratory Diseases in South Africa.* Chronic Diseases of Lifestyle in South Africa: 1995- 2005. Technical Report. Cape Town: South African Medical Research Council, 2006.

16. C.C. Obihara, B. J. Marais, R. P. Gie. *The association of prolonged breastfeeding and allergic disease in poor urban children.* Eur Respir J. 2005; 25: 970- 977.

17. J. Nriagu, T. Robins, L. Gary, et al. *Prevalence of asthma and respiratory symptoms in south-central Durban, South Africa.* Eur J Epidemiol 1999; 15: 747-755.

18. Health Systems Trust. *Health statistics: Infant mortality rate.* [On line]. Available: http://www.hst.org.za/healthsats/7/data [05 May 2007].

19. M. Bachmann, L. London, P. Barron. *Infant Mortality Rate Inequalities in the Western Cape Province of South Africa.* Int J Epidemiol.1996; 25 (5): 966- 972.

20. P. Groenewald, D. Bradshaw, B. Nojilana, et al. *Cape Town Mortality, 2001,Part 1, Cause of death and Premature Mortality.* Cape Town: City of Cape Town, South African Medical Research Council, University of Cape Town. [On line]. Available: www.mrc.ac.za/bod/bod.htm [21 March 2007].

21. L. Myer, R. I. Ehrlich, E.S. Susser. *Social Epidemiology in South Africa.* Epidemiol Rev 2004; 26: 112-123.

22. J.H. Glauber, A. L. Fuhlbrigge, J.A. Finkelstein, et al. *Relationship between asthma medication and antibiotic use.* Chest 2001; 120: 1485-1492.

23. P. Ellwood, M.I. Asher, B. Bjorksten, et al. *Diet and asthma, allergic rhinoconjucivitis and atopic eczema symptom prevalence: an ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data.* Eur Respir J. 2001; 17:436- 443.

24. S. K. Wieland, E von Matius, A Husing, et al. *Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe.* Lancet 1999; 353: 2040-2041.

25. V. Flaherman, G. W. Rutherford. *A meta-analysis of the effect of high weight on asthma.* Arch Dis Child 2006; 91: 334- 339.

26. X.M. Mai, L. Nilsson, O. Axelson, et al. *High body mass index, asthma and allergy in Swedish schoolchildren participating in the International Study of Asthma and Childhood Allergies in Childhood: Phase II.* Acta Paediatr 2003; 92: 1144- 1148.

27. E. Luder, R. I. Ehrlich, W.Y. Lou. *Body mass index and the risk of asthma in adults.* Respir Med 2004; 98: 29-37.

28. E.A. Mitchell, A. W. Stewart, on behalf of the ISAAC Phase One Study Group. *The ecological relationship of tobacco smoking to the prevalence of symptoms of asthma and other atopic diseases in children: The International Study of Asthma and Allergies in Childhood (ISAAC).* Eur J Epidemiol 2001; 17: 667- 673.

29. D. P. Strachan, D. G. Cook. *Parental smoking and childhood asthma: longitudinal and case-control studies.* Thorax 1998; 53: 204-212.

30. R. I. Ehrlich, D. Du Toit, E. Jordaan, et al. *Risk Factors for Childhood Asthma and Wheezing. Importance of Maternal and Household Smoking.* Am J Respir Crit Care Med 1996; 154: 681- 688.

31. D. G. Cook, D. P. Strachan. *Parental smoking, bronchial reactivity and peak flow variability in children.* Thorax 1998; 53: 295-301.

32. A.W. Stewart, E.A. Mitchell, N. Pierce, et al. *The relationship of per capita gross national product to the prevalence of symptom of asthma and other atopic diseases in childhood (ISAAC).* Int J Epidemiol 2001; 30: 173-179.

33. M.A. Poyser, H. Nelson, R.I. Ehrlich, et al. *Socioeconomic deprivation and asthma prevalence and severity in young adolescents.* Eur Respir J 2002; 19: 892-898.

34. M.J. Mercer, G Joubert, R.I. Ehrlich, et al. *Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents.* Pediatr Allergy Immunol 2004; 15: 234–241.

35. N. Graham. *The relationship between socio-economic deprivation and asthma prevalence and severity in Cape Town adolescents.* Unpublished (BSc Honours research project, Department of Environmental and Geographic Sciences, University of Cape Town, 2005)

36. E. von Mutius, N. Pearce, R. Beasley. *International patterns of tuberculosis and the prevalence of symptoms of asthma, rhinitis, and eczema.* Thorax 2000; 55: 449- 453.

37. P. Shirtcliffe, M. Weatherall, R. Beasley. *An inverse correlation between estimated tuberculosis notification rates and asthma symptoms.* Respirology 2002; 7: 153-155.

38. C. Obihara, J. Kimpen, N. Beyers, et al. *The Potential of Mycobacterium to Protect Against allergy and Asthma.* Curr Allergy Asthma Rep 2007; 7: 223- 230.

39. C.C. Obihara, N. Beyers, R.P. Gie, et al. *Inverse association between Mycobacterium tuberculosis infection and atopic rhinitis in children.* Allergy 2005; 60: 1121- 1125.

40. S. Foliaki, S Kildegaard Nielsen, B. Bjorksten. *Antibiotic sales and the prevalence of symptoms of asthma, rhinitis, and eczema: The international Study*

of Asthma and Allergies in Childhood (ISAAC). Int J Epidemiol 2004; 33: 558-563.

41. G. W. Wong, T. F. Leung, Y. Ma, et al. *Symptoms of asthma and atopic disorders in preschool children: prevalence and risk factors*. Clinic Experim Allergy 2007; 37:174- 179.

42. C. Cohet, S Cheng, C MacDonald. *Infections, medication use, and the prevalence of symptoms of asthma, rhinitis, and eczema in childhood.* J Epidemiol Comm Health 2004; 58: 852-857.

43. S. Shaheen, J. A Sterne, C. Songhurst, et al. *Frequent paracetamol use and asthma in adults*. Thorax 2000; 55: 266- 270.

44. M. A. Schei, J. O. Hessen, K. R. Smith. *Childhood asthma and indoor woodsmoke from cooking in Guatemala.* J Exp Analysis Environ Epidemiol. 2004; 14: S110- S117.

45. L. W. Ng'ang'a, J. A. Odhiambo, M. W. Mungai. *Prevalence of exercise induced bronchospasm in Kenyan school children: an urban-rural comparison.* Thorax 1998; 53: 919- 926.

46. T. Melsom, L. Brinch, J.O. Hessen, et al. *Asthma and indoor environment in Nepal.* Thorax 2001; 56: 477- 481.

47. M.E. Levin. *Different use of medical terminology and culture-specific models of disease affecting communication between Xhosa-speaking and English-speaking doctors at a South African paediatric teaching hospital.* S Afr Med J 2006; 96: 1080- 1084.

48. M. Delgado-Rodríguez, J. Llorca. *Bias.* J Epidemiol and Comm Health 2004; 58: 635- 641.

49. South Africa Census 2001 statistics. [On line]. Available:http://en.wikipedia.org/wiki/Demographics of_South_Africa.

50. K Steyn , D Bradshaw , R Norman, et al. *Tobacco use in South Africans during 1998: the first demographic and health survey.* J Cardiovasc Risk 2002; 9: 161-70.

51. Anonymous. *Isaac Phase 3 Manual.* [On line] Available:http://isaac.auckland.ac.nz/Phasethr/Phs3Frame.html.

52. M. Masoli, D. Fabian, S. Holt, R. Beasley. *Global Burden of Asthma Report. Global Strategy for Asthma Management and Prevention,* Global Initiative for Asthma (GINA) Report 2006. [On line]. Available: http://www.ginasthma.org.

53. K.S.Babu, S.S. Salvi. *Aspirin and Asthma.* CHEST 2000; 118(5):1470-1476. Available:http://www.medscape.com/viewarticle/405963.

54. J. Crane, J. Mallol, R. Beasley, et al. *Agreement between written and video questions for comparing asthma symptoms in ISAAC.* Eur Respir J 2003; 21: 455–461.

55. ISAAC Steering Committee. Environmental Questionnaire: Instructions and Hypotheses, 13-14 Year Age Group. [On line]. Available:http://isaac.auckland.ac.nz/phasethree/environmentalquestionnaire/instructions13_14.html.

APPENDIX A

7. Study instruments for 13/14 year olds

7.1 Instructions for completing questionnaire and demographic questions

Examples of instructions for completing questionnaires and demographic questions are given below. **The questionnaire content is fixed.** *(see pages 72–73 for 'office use only' boxes example)*

On this sheet are questions about your name, school, and birth dates. Please write your answers to these questions in the space provided.

All other questions require you to tick your answer in a box. If you make a mistake put a cross in the box and tick the correct answer. Tick only one option unless otherwise instructed.

Examples of how to mark questionnaires: Age [13] years

To answer Yes/No, put a tick in the appropriate box as per example

	YES	NO
	☐	✓

SCHOOL: _____

TODAY'S DATE: ☐ Day ☐ Month ☐ Year

YOUR NAME: _____

YOUR AGE: ☐ years

YOUR DATE OF BIRTH: ☐ Day ☐ Month ☐ Year

(Tick all your answers for the rest of the questionnaire)

Are you: MALE ☐ FEMALE ☐

Optional questions on ethnicity here

7.2 Core questionnaire for asthma

7.2.1 Questionnaire for 13/14 year olds

1 Have you 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 Have you 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 have you 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 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 speech to only one or two words at a time between breaths?
Yes ☐
No ☐

6 Have you ever had asthma?
Yes ☐
No ☐

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

8 In the past 12 months, have you had a dry cough at night, apart from a cough associated with a cold or chest infection?
Yes ☐
No ☐

7.3 Core questionnaire for rhinitis

7.3.1 Questionnaire for 13/14 year olds

All questions are about problems which occur when you DO NOT have a cold or the flu.

1 Have you ever had a problem with sneezing, or a runny, or blocked nose when you 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, have you had a problem with sneezing, or a runny, or blocked nose when you 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	☐	May	☐	September	☐
February	☐	June	☐	October	☐
March	☐	July	☐	November	☐
April	☐	August	☐	December	☐

5 In the past 12 months, how much did this nose problem interfere with your daily activities?:

Not at all ☐
A little ☐
A moderate amount ☐
A lot ☐

---

6 Have you ever had hayfever?

Yes ☐
No ☐

7.4 Core questionnaire for eczema

7.4.1 Questionnaire for 13/14 year olds

1 Have you 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 Have you 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:

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 Has this rash cleared completely at any time during the past 12 months?

Yes ☐
No ☐

5 In the past 12 months, how often, on average, have you been kept awake at night by this itchy rash?

Never in the past 12 months ☐
Less than one night per week ☐
One or more nights per week ☐

---

6 Have you ever had eczema?

Yes ☐
No ☐

7.5 ISAAC International Video Questionnaire answer sheet

If the video questionnaire is included with the core questionnaires, the demographic details will have been put onto the front of the questionnaire. If the video questionnaire is administered separately, the demographic questions will need to be added to this section.

SCENE ONE:	The first scene is of a young person at rest.		
QUESTION ONE:	Has your breathing been like this, at any time in your life?	**YES**	**NO**
if **YES:**	has this happened in the past year?	**YES**	**NO**
if **YES:**	has this happened one or more times a month?	**YES**	**NO**
SCENE TWO:	The second scene is of two young people exercising. One is in a dark shirt and the other is in a white shirt.		
QUESTION TWO:	Has your breathing been like the boy's in the dark shirt during or following exercise at any time in your life?	**YES**	**NO**
if **YES:**	has this happened in the past year?	**YES**	**NO**
if **YES:**	has this happened one or more times a month?	**YES**	**NO**
SCENE THREE:	The third scene is of a young person waking at night.		
QUESTION THREE:	Have you been woken at night like this at any time in your life?	**YES**	**NO**
if **YES:**	has this happened in the past year?	**YES**	**NO**
if **YES:**	has this happened one or more times a month?	**YES**	**NO**
SCENE FOUR:	The fourth scene is also of a young person waking at night.		
QUESTION FOUR:	Have you been woken at night like this at any time in your life?	**YES**	**NO**
if **YES:**	has this happened in the past year?	**YES**	**NO**
if **YES:**	has this happened one or more times a month?	**YES**	**NO**
SCENE FIVE:	The final scene is of another person at rest.		
QUESTION FIVE:	Has your breathing been like this at any time in your life?	**YES**	**NO**
if **YES:**	has this happened in the past year?	**YES**	**NO**
if **YES:**	has this happened one or more times a month?	**YES**	**NO**

7.6. Video questionnaire verbal instructions

(see page 83 for detailed guidelines)

Instructions to be read out once the video is running:

*THIS IS A VIDEO QUESTIONNAIRE WHICH IS BEING SEEN BY YOUNG PEOPLE ALL OVER THE WORLD.

IT IS DESIGNED TO ASK YOU QUESTIONS ABOUT YOUR BREATHING.

YOU WILL BE SHOWN SOME SCENES OF YOUNG PEOPLE IN DIFFERENT SITUATIONS, FROM DIFFERENT COUNTRIES.

AFTER EACH SCENE, SOME NUMBERED QUESTIONS WILL BE READ OUT TO YOU.

TICK YES OR NO.

PLEASE ANSWER THE QUESTIONS AS YOU GO.

*THE FIRST SCENE IS OF A YOUNG PERSON AT REST.

(First scene comes on here)

*QUESTION 1. HAS YOUR BREATHING BEEN LIKE THIS AT ANY TIME IN YOUR LIFE?

IF YES, HAS THIS HAPPENED IN THE PAST YEAR?

IF YES, HAS THIS HAPPENED ONE OR MORE TIMES A MONTH?

*THE SECOND SCENE IS OF TWO YOUNG PEOPLE AFTER EXERCISE. ONE IS IN A DARK SHIRT. AND ONE IS IN A LIGHT SHIRT.

(Second scene comes on here)

*QUESTION 2. HAS YOUR BREATHING BEEN LIKE THE BOY'S IN THE DARK SHIRT FOLLOWING EXERCISE AT ANY TIME IN YOUR LIFE?

IF YES, HAS THIS HAPPENED IN THE PAST YEAR?

IF YES, HAS THIS HAPPENED ONE OR MORE TIMES A MONTH?

*THE THIRD SCENE IS OF A YOUNG PERSON WAKING AT NIGHT.

(Third scene comes on here)

*QUESTION 3. HAVE YOU BEEN WOKEN AT NIGHT LIKE THIS AT ANY TIME IN YOUR

LIFE?

IF YES, HAS THIS HAPPENED IN THE PAST YEAR?

IF YES, HAS THIS HAPPENED ONE OR MORE TIMES A MONTH?

*THE FOURTH SCENE IS ALSO OF A YOUNG PERSON WAKING AT NIGHT.

(Fourth scene comes on here)

*QUESTION 4. HAVE YOU BEEN WOKEN AT NIGHT LIKE THIS AT ANY TIME IN YOUR LIFE?

IF YES, HAS THIS HAPPENED IN THE PAST YEAR?

IF YES, HAS THIS HAPPENED ONE OR MORE TIMES A MONTH?

*THE FINAL SCENE IS OF ANOTHER PERSON AT REST.

(Fifth scene comes on here)

*QUESTION 5. HAS YOUR BREATHING BEEN LIKE THIS AT ANY TIME IN YOUR LIFE?

IF YES, HAS THIS HAPPENED IN THE PAST YEAR?

IF YES, HAS THIS HAPPENED ONE OR MORE TIMES A MONTH?

*THANK YOU FOR TAKING PART IN THIS PROJECT.

APPENDIX B: AFRIKAANS QUESTIONNAIRE

OPNAME VAN ASEMHALINGS, NEUS EN VELPROBLEME

Alleenlik vir kantoorgebruik

Aanwysings vir die voltooing van die vraelys

Hierdie vraelys bevat vrae met betrekking tot jou naam, adres en geboortedatum.
Skryf asseblief jou antwoorde neer in die spasies voorsien.
Al die ander vrae moet beantwoord word deur 'n merkie in die blokkie te maak wat jy kiesof die antwoord in die blokkie te skryf. Indien jy jou antwoord wil verander, trek net 'n kruisie deur die blokkie en merk dan die regte een. **Merk slegs een blokkie per vraag.**

Hier is n voorbeeld: Ouderdom ☐ jaar

Ja ☐ Nee ☐

Om ja of nee te antwoord, plaas net 'n merkie In die ooreenstemmende blokkie

---

Naam:

Skool:

Huisadres:

Vandag se datum: ☐ Dag ☐ Maand ☐ Jaar

Jou ouderdom: ☐ Jaar

Jou geboortedatum: ☐ Dag ☐ Maand ☐ Jaar

Jou geslag: ☐ Seun ☐ Meisie

Is jy in Kaapstad gebore? Ja ☐ Nee ☐

Indien jy nie in Kaapstad gebore is nie, op watter ouderdom het jy hierheen verhuis? ☐

Jaar

1. Het jy al ooit 'n fluit of hygbors gehad?

Ja	Nee

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 6

2. Het jy 'n fluit of hygbors gedurende die afgelope 12 maande gehad?

Ja	Nee

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 6

3. Hoeveel aanvalle van fluit of hygbors het jy in die afgelope 12 maande gehad?

Geen	1 tot 3	4 tot 12	Meer as 12

4. In die afgelope 12 maande, hoeveel keer is jou slaap daardeur bederf?

Nooit as gevolg van fluit/hygbors wakker geword nie	Minder as 1 keer per week	1 of meer nagte per week

5. Was die fluit of hygbors ooit so erg die afgelope 12 maande, dat jy slegs 1 of 2 woorde per asemtog kon praat?

Ja	Nee

6.. Het jy al ooit asma gehad?

Ja	Nee

7. Het jou bors in die afgelope 12 maande gefluit gedurende of na oefening?

Ja	Nee

8. Het jy gedurende die afgelope 12 maande ooit 'n droë hoes gedurende die nag
ervaar buiten wanneer jy 'n verkoue of griep gehad het?

Ja	Nee

DIE VOLGENDE VRAE HANDEL OOR SIMPTOME WAT JY ERVAAR HET, MAAR NIE TEN TYE VAN 'N VERKOUE OF GRIEP NIE.

	Ja	Nee
9. Het jy al ooit 'n probleem met 'n geniesery, loop of toeneus gehad, buiten wanner jy verkoue of griep gehad het?	☐	☐

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 14

	Ja	Nee
10. Het jy in die afgelope 12 maande probleme met 'n geniesery, loop of toeneus gehad, wanneer jy nie verkoue of griep gehad het nie?	☐	☐

INDIEN JY "NEE" GEANWOORD HET, GAAN DIREK NA VRAAG 14

	Ja	Nee
11. Het jou neusprobleem in die afgelope 12 maande gepaard gegaan met jeukerige/tranerige oë	☐	☐

12. Gedurende watter van die afgelope 12 maande het jou neusprobleme geduur?
(Dui asseblief almal aan wat van toepassing is)

Januarie ☐	Februarie ☐	Maart ☐	April ☐
Mei ☐	Junie ☐	Julie ☐	Augustus ☐
September ☐	Oktober ☐	November ☐	Desember ☐

13. Hoe dikwels het jou neusprobleme in die afgelope 12 maande jou daaglikse aktiwiteite beïnvloed

Glad nie ☐	Effens ☐	Taamlik baie ☐	Baie ☐

	Ja	Nee
14. Het jy al ooit hooikoors gehad?	☐	☐

15. Het jy al ooit 'n jeukerige veluitslag gehad wat gekom gaan het oor tenminste 6 maande?

Ja	Nee

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 20

---

16. Het jy hierdie jeukerige uitslag die afgelope 12 maande gehad?

Ja	Nee

INDIEN JY "NEE" GEANTWOORD HET, GAAN DIREK NA VRAAG 20

---

17. Het hierdie jeukerige uitslag enige van die volgende areas aangetas?: Die elmboë se voue, agter die knieë, aan die voorkant van die enkels, onder die boude, om die nek, ore of oë?

Ja	Nee

18. Het hierdie uitslag ooit gedurende die afgelope 12 maande totaal opgeklaar?

Ja	Nee

19. Hoe gereeld het die jeukerige uitslag jou gedurende die afgelope 12 maande snags wakker gehou?

Nooit in die afgelope 12 maande nie	Minder as 1 keer per week	1 of meer keer per week

---

20. Het jy al ooit ekseem gehad?

Ja	Nee

STOP HIER.
LAAT NEEM JOU MASSA EN LENGTE VOORDAT JY VERDER GAAN

1. Massa: ☐ kg

2. Lengte: ☐ cm

3. Gedurende die afgelope 12 maande, hoe dikwels het jy die volgende geëet of drink?
(Laat asseblief 'n spasie indien jy nie die voedselsoort ken nie)

	Nooit of af en toe	Een of tweekeer per week	Drie of meerkeer per week
Vleis (bv. bees, lam, hoender, vark)	☐	☐	☐
Seekos (insluitend vis)	☐	☐	☐
Vrugte	☐	☐	☐
Groente (alle soorte)	☐	☐	☐
Erte, bone	☐	☐	☐
Graankos (insluitend brood)	☐	☐	☐
Mielies (mieliemeel)	☐	☐	☐
Pasta	☐	☐	☐
Rys	☐	☐	☐
Botter	☐	☐	☐
Margarien	☐	☐	☐
Neute (insluitend grondbone)	☐	☐	☐
Aartappels	☐	☐	☐
Melk	☐	☐	☐
Eiers	☐	☐	☐
Kitskos/Burgers	☐	☐	☐

4. Hoeveel keer per week doen jy oefeninge of fisiese arbeid wat jou hard laat asemhaal?

Nooit of soms ☐

Een of tweekeer per week ☐

Drie of meerkeer per week ☐

5. Gedurende 'n normale week, hoeveel uur **per dag** kyk jy televisie?:

Minder as 'n uur ☐

1 uur of meer, maar minder as 3 ure ☐

3 ure of meer, maar minder as 5 ure ☐

5 ure of meer ☐

6. Watter tipe brandstof word in jou huis gebruik vir koskook?:

Elektrisiteit ☐

Gas ☐

Paraffien ☐

Hout (insluitend oop vure) ☐

Ander – spesifiseer asseblief ☐

7. Watter tipe brandstof word in jou huis gebruik vir verhitting?:

Elektrisiteit ☐

Gas ☐

Paraffien ☐

Hout (insluitend oop vure) ☐

Ander – spesifiseer asseblief ☐

8. Hoeveel keer gedurende die afgelope 12 maande het jy Panado gedrink?:

Nooit ☐

Ten minste 1 keer per jaar ☐

Ten minste 1 keer per maand ☐

9. Hoeveel **ouer** broers en susters het jy? ☐ broers en susters

10. Hoeveel **jonger** broers en susters het jy? ☐ broers en susters

11. Is jy in Suid Afrika gebore?:

Ja ☐

Nee ☐

12. Hoeveel lank woon jy al in Suid Afrika?: ☐ jaar

13. Watter vlak van opleiding het jou moeder bereik or voltooi?:

Primêre skool ☐

Hoër skool ☐

Kollege, universiteit of ander vorm van tersiëre opleiding ☐

14. Watter vlak van opleiding het jou vader bereik of voltooi?:

Primêre skool ☐

Hoër skool ☐

Kollege, universiteit of enige ander vorm van tersiëre opleiding ☐

15. Hoe dikwels ry vragmotors in die straat af waar jy woon?:

Nooit ☐

Selde ☐

Gereeld gedurende die dag ☐

16 Het julle die afgelope 12 maande 'n kat in die huis gehad?:

Ja ☐

Nee ☐

17. Het julle die afgelope 12 maande 'n hond in die huis gehad?:

Ja ☐

Nee ☐

18. Rook jou moeder (of die vroulike persoon wat na jou kyk) sigarette?:

Ja ☐

Nee ☐

19. Rook jou vader (of die manlike persoon wat na jou kyk) sigarette?:

Ja ☐

Nee ☐

20. Hoeveel inwoners van jou huis, rook sigarette ☐ inwoners

21. Rook jy sigarette?:

Ja ☐

Nee ☐

22. Is jou huis aan die binnekant, klam of nat?:

Ja ☐

Nee ☐

23. Het enige een in jou huis al ooit TB gehad?:

Ja ☐

Nee ☐

24. Is jy al ooit vir TB behandel?:

Ja ☐

Nee ☐

25. Hoeveel mense woon in jou huis?:

Volwassenes ☐

Kinders ☐

	Ja	Nee
1. Was jou asemhaling al soos dié?:		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
2. Was jou asemhaling al ooit soos die van die seun met die **donker** hemp na oefening?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
3. Het jy ooit in jou lewe snags so wakker geskrik?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
4. Het jy al ooit soos dié gedurende die nag wakker geword?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

	Ja	Nee
5. Was jou asemhaling al ooit soos dié?		
Indien JA, het dit die afgelope jaar gebeur?		
Indien JA, het dit een of meerkeer per maand gebeur?		

APPENDIX C: XHOSA QUESTIONNAIRE

Uphando lweengxaki zokuphefumla, impumlo nolusu

Isetyenziswa yi-ofisi kuphela

Imiyalelo yokuphendula imibuzo wkiphepha lemibuzo

Kweli phepha yimibuzo malunga negama lakho, Idilesi yasekhaya, umhla wokuzalwa. Nceda bhala iimpendulo zale mibuzo kwisikhewu esinikiweyo.
Yonke eminye imibuzo ifuna **uphawule impendulo yakho okanye ubhale kwi bhokisi**. Xa wenze impazamo **Hlaba** kwibhokisi uze ufake uphawu olulungileyo kwimpendulo echanekileyo kuwe.

Imizekelo yokuphawula impendulo : Iminyaka

Iminyaka

Ukuphendula Ewe okanye hayi Faka uphawu Kwibhokisi eyiyo

Ewe Hayi

Igama lakho:

Isikolo Sakho:

Idilisi Yasekhaya:

Umhla namhlanje:

Usuku Inyanga Unyaka

Ubudala bakho:

Iminyaka

Umhla wokuzalwa:

Umhla Inyanga Unyaka

Uyi: Nkwekwe Intombazana

Wazalelwa e-Kapa? Ewe i

Ukuba akuzalwanga e-Kapa ufike uminyaka, mingaphi E-Kapa ?

☐ Yeminyaka

Ewe Hayi

1. Wakha wanaso isifuba esishinyeneyo okanye esiminxeneyo nanini na ngaphambili? ☐ ☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 6

Ewe Hayi

2. Wakha wanaso isifuba esishinyeneyo kwezi nyanga zili-12 zigqithileyo? ☐ ☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 6

3. Uhlaselwe kangaphi kwezi nyanga zili-12 zigqithileyo sisifuba esishinyeneyo?

Zange	1 kuye 3	4 kuye 12	Ngap hezu 12
☐	☐	☐	☐

4. Kwiinyanga ezili-12 ezigqithileyo uphazanyiswe kangaphi ubuncinane kubuthongo bakho kukuminxana kwesifuba?

Zange ndivuswe sisifuba esitswinayo	Ngaphantsi kobusuku obunye ngeveki	Kanye nangaphezu lu ngeveki
☐	☐	☐

Ewe Hayi

5. Kwiinyanga ezili-12 ezigqithileyo,Kwakha kwanzima ukutswina kwesifuba kangangokuba kunqumle ukuthetha kwakho de ubize igama libe linye ngexesha uzama ukuphefumla? ☐ ☐

Ewe Hayi

6. Wakha wanayo I-athsma? ☐ ☐

Ewe Hayi

7. Kwiinyanga ezili-12, ezigqithileyo sakha isifuba sakho savakala sishinyene siminxene ngethuba okanye emva komthambo? ☐ ☐

Ewe Hayi

8. Kwiinyanga ezi –12 ezigqithileyo wakha wanalo okhohlokhohlo olomileyo ebusuku,
Ingelulo olomkhuhlane okanye ulosuleleko lwesifuba? ☐ ☐

Yonke imibuzo ibhekiselele xa ungenayo ingqele okanye I-flu

9. Wakha wanayo ingxaki yokuthimla okanye impumlo evuzayo kodwa **Ungenayo** I-flu okanye ingqele?

Ewe	Hayi
☐	☐

Ukuba uphendule "hayi" Nceda tsibela kumbuzo 14

10. Kwezi nyanga zili-12 zigqithileyo, wakha wanengxaki yokuthimla okanye impumlo evuzayo enemfuxane kodwa **Ungenayo I-flu okanye ingqele?**

Ewe	Hayi
☐	☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 14

11.Kwiinyanga ezili-12, ezigqithileyo, yakha le ngxaki yempumlo yakhatshwa ngamehlo arawuzelayo alilayo/ aneenyembezi?

Ewe	Hayi
☐	☐

12. Yenzeka kuyiphi kwezi nyanga zili-12 zigqithileyo le ngxaki yeempumlo (Nceda phawula nayiphi elungileyo)

Januari	Februari	Matshi	Apreli
☐	☐	☐	☐
Meyi	**Juni**	**Julayi**	**Agasti**
☐	☐	☐	☐
Septemba	**Oktoba**	**Novemba**	**Decemba**
☐	☐	☐	☐

13. Kwiinynga ezili-12 ezigqithileyo, Ikuphazamise kangakanani le ngxaki yempumlo ukusebenza kwakho kwemihla?

Zange konkel	Kancinci	Igokuphakathi nje	Kakhulu
☐	☐	☐	☐

14. Wakha wanayo I-hayfever?

Ewe	Hayi
☐	☐

15. Wakha wanayo irashalala erawuzelayo emana ifika iphinde iphele ubuncinane iinyanga ezintandathu ?

Ewe ☐ Hayi ☐

Ukuba uphendule "hayi" nceda tsibela kumbuzo 20

---

16. Ukhe wanayo le arshalala irawuzelayo Nanini na kwezi nyanga zili –12 zigqithileyo?

Ewe ☐ Hayi ☐

Ukuba uphendule "hayi" nceda Tsibela kumbuzo 20

---

17. Yakha le rashalala irawuzelayo nanini na yakwezindawo zilandelayo?:

Ewe ☐ Hayi ☐

Kwimiphakathi yeengqiniba, emva kwamadolo, ngaphambi kwezihlahla, ezantsi kweempundu, okanye irangqe intamo, iindlebe, namehlo?

18. Yakha yaphela tu le rashalala kwesi sithuba seenyanga ezili 12 Zidlulileyo?

Ewe ☐ Hayi ☐

19. Kwezi nyanga zili-12 ezigqithileyo kukamgaphi ubuncinane,ugcinwa uhleli ebusuku Yile rashalala irhawuzelayo ?

Zange/ kwezi nyangazili-12	Ngaphantsi kobusuku obunye ngeveki	Kanye nangaphezu lu ngeveki
☐	☐	☐

---

20. Wakha wanayo I-eczema?

Ewe ☐ Hayi ☐

Yima apha.
Nceda yiya uzaliselwe ubunzima nobude bakho phambi kokuba uqhubekeke.

Ubunzima bomzimba: ☐ kg

Ubude: ☐ iiSentimitha

3. Kwezi nyanga zili -12 zigqithileyo, uzitye kangaphi, ubuncinane ezi zidlo zilandelayo?:

(Nceda ushiye kungabhalwanga ukuba akukwazi oko kutya kubuzwayo)

	Zange okanye Nqabileyo	Kanyeokan-ye kabini ngeveki	Kathathu nanga phezulu ngeveki
Inyama(umz. Yenkomo, yegusha, yenkukhu, yehagu)	☐	☐	☐
Ukutya kwasolwandle (kudibanisa nentlanzi)	☐	☐	☐
Iziqhamo	☐	☐	☐
Imifuno/ iiveji (zonke iintlobo)	☐	☐	☐
Ii-erentyisi, iimbotyi	☐	☐	☐
iiCereal (kudibanisa nesonka)	☐	☐	☐
umbona (uMielie meal, umgubo)	☐	☐	☐
iPasta	☐	☐	☐
IRice	☐	☐	☐
iBhotolo	☐	☐	☐
iMargarine	☐	☐	☐
Amandongomane	☐	☐	☐
ii-tapile	☐	☐	☐
ubisi	☐	☐	☐
amaqanda	☐	☐	☐
Ukutya okukhawulezayo umz. iiburgers	☐	☐	☐

4. Uthamba kangaphi ngeveki okanye uwenza kangaphi umsebenzi onzima ukukwenza uphefumle nzima?:

Zange okanye nqabileyo ☐

Kanye okanye kabini ngeveki ☐

Kathathu nangaphezulu ngeveki ☐

5. Kwiveki eqhelekileyo, zingaphi iiyure obukela kuzo umabona kude?:

Ngaphantsi kwe yure enye ☐

Iyure enye nangaphantsi kweeyure ezi ntathu ☐

Iiyure ezintathu nangaphantsi kweeyure ezintlanu ☐

Iiyure ezi ntlanu nangaphezulu ☐

6. Endlwini kokwenu nisebenzisa esiphi isibasi ngokuqhelekileyo xa niphekayo?:

Umbane ☐

i-Rasi ☐

i-Paraffin ☐

Iinkuni ☐

esinye- nceda cacisa ☐

7. Endlwini, kokwenu nisebenzisa esiphi isibasi ngokuqhelekileyo okwenza shushu?:

Umbane ☐

I-Rasi ☐

i-Paraffin ☐

Iinkuni ☐

Esinye-nceda cacisa ☐

8. Kwezi nyanga zili-12 zigqithileyo uzisele kangaphi ubuncinane, iiPanado?:

Zange ☐

Kanye ngonyaka ubuncinane ☐

Ubuncinane kanye ngenyanga. ☐

9. Bangaphi **abakhuluwa** noodade wenu **abakhulu**?: ☐ Oodade nabakhuluwa

10. Bangaphi **abaninawe** noodade wenu **abancinane**?: ☐ Odade nabaninawe

11. Ingaba wazalelwe e-Kapa?:

Ewe ☐

Hayi ☐

12. Mingaphi iminyaka uhlala e-Kapa?: ☐ Yeminyaka

13. U fike /ugqibe eliphi ibanga lemfundo umama wakho?:

I-Primari skolo ☐

Isikolo samabanga aphezulu (high school) ☐

I-Kholeji, idyunivesiti, okanye olunye uhlobo lwemfundo enomsila ☐

14.Ufike/ ugqibe eliphi ibanga lemfundo utata wakho?:

I- primari skolo ☐

Isikolo samabanga aphezulu (high school) ☐

I-kholeji, idyunivesiti okanye uhlobo lwemfundo enomsila ☐

15. Zigqitha kangaphi ii- truck kwisitrato ohlala kuso kwiintsuku zeveki?

Azigqithi konke konke ☐

Nqabileyo ☐

Qho imini yonke ☐

16. Kwezi nyanga zili-12 zigqithileyo ukhe wanayo ikati ekhayeni lakho?:

Ewe ☐

Hayi ☐

17. Kwezi nyanga zili-12 zigqithileyo ukhe wanayo inja ekhayeni lakho?

Ewe ☐

Hayi ☐

18. Ingaba uyazitshaya iisigarethi umama okanye umgcini wakho obhinqileyo?:

Ewe ☐

Hayi ☐

19. Ingaba uyazitshaya iisigarethi utata wakho okanye umgcini wakho oyindoda?:

Ewe ☐

Hayi ☐

20. Bangaphi abantu abatshaya iisigarethi abahlala endlwini kokwenu ?: ☐ Yabantu

21. Uyazitshaya wena ii-sigarethi?:

Ewe ☐

Hayi ☐

22. Ingaba indlu yenu imanzi okanye ifumile ngaphakathi?:

Ewe ☐

Hayi ☐

23. Ingaba ukho ubani owakha wane TB kusapho lwakowenu?:

Ewe ☐

Hayi ☐

24. Ingaba wena wakha wanyangelwa iTB?:

Ewe ☐

Hayi ☐

25. Bangaphi abantu abahlala endlini yakokwenu?:

Abantu abakhulu ☐

Abantwana ☐

26. Ingaba ninazo Ii- tepu zamanzi abalekayo endlwini yakokwenu?:

Ewe ☐

Hayi ☐

27. Ingaba ninawo umbane indlwini kokwenu?:

Ewe ☐

Hayi ☐

28. Ingaba ninaye umabona-kude (I-TV) endlwini yakokwenu?:

Ewe ☐

Hayi ☐

29. Ingaba unekhaya elinjani?:

Indlu ☐

i-flat ☐

Ityotyombe ☐

Enye Cacisa ☐

30. Ingaba bangaphi abantu abahlala kokwenu abaphangela ngokuqhelekileyo?: ☐ Yabantu

31. Ingaba bangaphi abantu abahlala kokweneu abangaphangeliyo befuna imisebenzi?: ☐ Yabantu

32. Bangaphi abantu ababelana nawe ngegumbi lokulala ebusuku?: ☐ Yabantu

Yima apha linda de kuqaliswe umfanekiso we video phambi kokuphendulaimibuzo elandelayo.

Yima ulinde umfanekiso we-video phambi kokuphendula.

	Ewe	Hayi
Ukuphefumla kwakho kukhe kwanjena?		
Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?		
Ukuba uthi EWE, ibikhe yenzeka kanye okanye kaninzi ngenyanga?		
Emva kokuthamba kukhe ukuphefumla kwakho kwafana nokwala nkwenkwe inxibe ihempe **emdaka**, nangaliphi ixesha ebomini bakho?		
Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?		
Ukuba uthiEWE, ibikhe yenzeka kanye okanye kaninzi ngenyanga?		
Wakha wavuka unjena ebusuku, nangaliphi ixesha ebomini bakho?		
Ukuba kunjalo, ibikhe yenzeka lento kulonyaka ophelileyo?		
Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?		
Wakha wavuka unjena ebusuku?		
Ukuba kunjalo, ibikhe yenzeka lento kulonyaka ophelileyo?		
Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?		
Wakhe waphefumla kanjena, nangaliphi ixesha ebomini bakho?		
Ukuba uthi EWE, ibikhe yenzeka lento kulonyaka ophelileyo?		
Ukuba kunjalo, ibikhe yenzeka kanye okanye kaninzi ngenyanga?		

APPENDIX D

1. How much do you weigh?: ☐ kg / stone / pounds
(please circle the measurement you used)

2. How tall are you?: ☐ metres / centimetres / feet and inches
(please circle the measurement you used)

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

	Never or occasionally	Once or twice per week	Three or more times a week
Meat (e.g. beef, lamb, chicken, pork)	☐	☐	☐
Seafood (including fish)	☐	☐	☐
Fruit	☐	☐	☐
Vegetables (green and root)	☐	☐	☐
Pulses (peas, beans, lentils)	☐	☐	☐
Cereal (including bread)	☐	☐	☐
Pasta	☐	☐	☐
Rice	☐	☐	☐
Butter	☐	☐	☐
Margarine	☐	☐	☐
Nuts	☐	☐	☐
Potatoes	☐	☐	☐
Milk	☐	☐	☐
Eggs	☐	☐	☐
Fast food/burgers	☐	☐	☐

4. How many times a week do you engage in vigorous physical activity long enough to make you 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 (24hours)** do you 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 past 12 months, how often, on average, have you taken paracetamol (e.g. Panadol, Pamol)?:

Never ☐

At least once a year ☐

At least once per month ☐

9. How many older brothers and sisters do you have?: ☐ brothers and sisters

10. How many younger brothers and sisters do you have?: ☐ brothers and sisters

11. Were you born in (NZ - See instructions)?:

Yes ☐

No ☐

12. How many years have you lived in (NZ - see instructions)?: ☐ years

13. What level of education has your mother received?: (local wording)

Primary school ☐

Secondary school ☐

College, university or other form of tertiary education ☐

14. How often do trucks pass through the street where you live, on weekdays?:

Never	☐
Seldom	☐
Frequently through the day	☐
Almost the whole day	☐

15. In the past 12 months, have you had a cat in your home?:

Yes	☐
No	☐

16. In the past 12 months, have you had a dog in your home?:

Yes	☐
No	☐

17. Does your mother (or female guardian) smoke cigarettes?:

Yes	☐
No	☐

18. Does your father (or male guardian) smoke cigarettes?:

Yes	☐
No	☐

19. How many people living in your house smoke cigarettes?: ☐ people

Thank you very much for your help with this questionnaire. We appreciate your assistance.

APPENDIX E: PREVALENCE- ALL TESTED VARIABLES

VARIABLE	Responses (N= 5,037)	Percentage (100%)
Socio-demographic factors		
Language/ medium of instruction at school		
Afrikaans	1,289	25.59
English	2,059	40.88
Xhosa	1,689	33.53
Age		
13 years old	2,605	51.72
14 years old	2,432	48.28
Gender		
Male	2,025	40.20
Female	2,994	59.44
Invalid response (No information)	18	0.36
City of birth		
Cape Town	4,074	80.88
Other than Cape Town	934	18.54
Invalid response	29	0.58

CORE (WRITTEN) QUESTIONNAIRE		
Have you ever had wheezing or whistling in your chest at any time in the past		
Yes	1,670	33.15
No	3,284	65.20
Invalid response	83	1.65
If yes, Have you had wheezing or whistling in your chest in the past 12 months		
Yes	1,025	20.35
No	1,896	37.64
Invalid response	2,116	42.01
How many attacks of wheezing have you had in the past 12 months?		
None	1,233	24.48
One to three	810	16.08
Four to twelve	187	3.71
More than twelve	67	1.33
Invalid response	2,740	54.40
In the past 12 months, how often on average has your sleep been disturbed due to wheezing in your chest?		
Never woken with wheezing	1,301	25.83
Less than once a week	554	11.00
One or more nights a week	252	5.00
Invalid response	2,930	58.17
In the past 12 months has your wheezing ever been severe enough to limit your speech to one or two words at a time between breaths?		
Yes	395	7.84
No	1,839	36.51
Invalid response	2,803	55.65
Have you ever had asthma?		
Yes	725	14.39
No	4,044	80.29
Invalid response	268	5.32
In the past 12 months has your chest sounded wheezy during or after exercise?		
Yes	1,641	32.58
No	3,049	60.53
Invalid response	347	6.89
In the past 12 months have you had a dry cough at night, apart form a cough associated with a cold or chest infection?		
Yes	1,846	36.65
No	2,822	56.03
Invalid response	369	7.33

DIETARY QUESTIONNAIRE		
In the past 12 months, how often on average did you eat or drink the following?		
Meat (e.g. beef, lamb, chicken, pork)		
Never or rarely	339	6.73
Once or twice a week	2095	41.59
Three or more times a week	2431	48.26
Invalid response	172	3.41
Seafood (including fish)		
Never or rarely	2174	43.16
Once or twice a week	2184	43.36
Three or more times a week	391	7.76
Invalid response	288	5.72
Fruit		
Never or rarely	335	6.65
Once or twice a week	1421	28.21
Three or more times a week	3092	61.39
Invalid response	189	3.75
Vegetables (all types)		
Never or rarely	613	12.17
Once or twice a week	1648	32.72
Three or more times a week	2549	50.62
Invalid response	226	4.49
Pulses (Peas, beans)		
Never or rarely	1561	30.99
Once or twice a week	2274	45.15
Three or more times a week	929	18.44
Invalid response	273	5.42
Cereal (including bread)		
Never or rarely	459	9.11
Once or twice a week	842	16.72
Three or more times a week	3438	68.25
Invalid response	298	5.92
Maize (Mielie meal)		
Never or rarely	2224	44.15
Once or twice a week	1651	32.78
Three or more times a week	879	17.45
Invalid response	283	5.62
Pasta		
Never or rarely	1332	26.44
Once or twice a week	2434	48.32
Three or more times a week	827	16.42
Invalid response	444	8.81
Rice		
Never or rarely	253	5.02
Once or twice a week	1155	22.93
Three or more times a week	3445	68.39
Invalid response	184	3.65
Butter		

Never or rarely	916	18.19
Once or twice a week	1125	22.33
Three or more times a week	2710	53.80
Invalid response	286	5.68
Margarine		
Never or rarely	1267	25.15
Once or twice a week	1384	27.48
Three or more times a week	1979	39.29
Invalid response	407	8.08
Nuts (including peanuts)		
Never or rarely	1951	38.73
Once or twice a week	1976	39.23
Three or more times a week	833	16.54
Invalid response	277	5.50
Potatoes		
Never or rarely	203	4.03
Once or twice a week	1292	25.65
Three or more times a week	3339	66.29
Invalid response	203	4.03
Milk		
Never or rarely	444	8.81
Once or twice a week	1317	26.15
Three or more times a week	3065	60.85
Invalid response	211	4.19
Eggs		
Never or rarely	672	13.34
Once or twice a week	2530	50.23
Three or more times a week	1588	31.53
Invalid response	247	4.90
Fast food/ burgers		
Never or rarely	980	19.46
Once or twice a week	2384	47.33
Three or more times a week	1326	26.33
Invalid response	347	6.89

ENVIRONMENTAL QUESTIONNAIRE		
How many times a week do you have enough exercise or physical effort to make you breathe hard?		
Never or occasionally	1572	31.21
Once or twice a week	2103	41.75
Three or more times a week	1181	23.45
Invalid response	181	3.59
During a normal week, how many times a day do you watch television?		
Less than 1 hour	563	11.18
1 hour but less than 3 hours	1303	25.87
3 hours but less than 5 hours	1353	26.86
5 hours or more	1620	32.16
In your house, what fuel is used for cooking?		
Electricity		
Yes	4432	88.01
No	604	11.99
Gas		
Yes	502	9.97
No	4535	90.03
Paraffin		
Yes	892	17.71
No	4145	82.29
Wood (including open fires)		
Yes	83	1.65
No	4954	98.35
Other (please specify)		
Yes	1	0.02
No	5035	99.98
In your house, what fuel is used for heating?		
Electricity		
Yes	3540	70.28
No	1497	29.72
Gas		
Yes	231	4.59
No	4806	95.41
Paraffin		
Yes	1177	23.37
No	3860	76.63
Wood (including open fires)		
Yes	303	6.02
No	4733	93.98
Other (please specify)		
Yes	8	0.16
No	5029	99.84
Use of paracetamol		
Never or occasionally	1333	26.46

At least once a year	1764	35.02
At least once a month	1741	34.56
Invalid response	199	3.95
Other environmental factors		
Number of older siblings		
Number of younger siblings		
Country of birth- South Africa	4172	82.83
Country of birth not South Africa	682	13.54
Invalid response	183	3.63
Mother has up to primary level education		
Yes	921	18.29
No	4115	81.71
Other has up to secondary level education		
Yes	2960	58.77
No	2077	41.23
Mother has up to tertiary level education		
Yes	1086	21.56
No	3951	78.44
Father has up to primary level education		
Yes	865	17.17
No	4172	82.83
Father has up to secondary level education		
Yes	2571	51.04
No	2466	48.96
Father has up to tertiary level education		
Yes	1313	26.07
No	3723	73.93
How often do trucks pass along the street where you live, on weekdays?		
Never	582	11.55
Seldom	2249	44.65
Frequently through the day	2015	40.00
Invalid response	191	3.79
In the past 12 months, have you had a cat in your home?		
Yes	1526	30.30
No	3337	66.25
Invalid response	174	3.45
In the past 12 months, have you had a dog in your home?		
Yes	2663	52.87
No	2192	43.52
Invalid response	182	3.61
Does your mother (or female care giver) smoke cigarettes?		
Yes	1405	27.89
No	3419	67.88
Invalid response	213	4.23

Does your father (or male care giver) smoke cigarettes?		
Yes	2130	42.29
No	2626	52.13
Invalid response	281	5.58
Do you smoke cigarettes?		
Yes	433	8.60
No	4417	87.69
Invalid response	187	3.71
Is your house damp or wet inside?		
Yes	507	10.07
No	4305	85.47
Invalid response	225	4.47
Has anyone in your household ever had TB?		
Yes	691	13.72
No	4133	82.05
Invalid response	213	4.23
Have you ever been treated for TB?		
Yes	325	6.45
No	4447	88.29
Invalid response	265	5.26
Do you have taps for running water in your house?		
Yes	3861	76.65
No	933	18.52
Invalid response	243	4.82
Do you have electricity in your house?		
Yes	4666	92.63
No	181	3.59
Invalid response	190	3.77
Do you have a TV in your house?		
Yes	4504	89.42
No	346	6.87
Invalid response	187	3.71
Type of home		
House	3936	78.14
Flat	263	5.22
Shack	573	11.38
Other	60	1.19
Invalid response	205	4.07
Number of people working in the household		
Number of people not working in the household		
Number of people sharing a room with the respondent at night		

VIDEO QUESTIONNAIRE		
Scene 1 (wheeze at rest). Has your breathing ever been like this?		
Yes	839	16.66
No	4102	81.44
Invalid response	96	1.91
If yes, Has this happened in the past 12 months?		
Yes	559	11.10
No	1134	22.51
Invalid response	3344	66.39
If yes, has this happened once or more times a month		
Yes	351	6.97
No	1223	24.28
Invalid response	3463	68.75
Scene 2 (Exercise induced wheeze): Has your breathing ever been like this?		
Yes	1070	21.24
No	3859	76.61
Invalid response	108	2.14
If yes, Has this happened in the past 12 months?		
Yes	692	13.74
No	1064	21.12
Invalid response	3281	65.14
If yes, has this happened once or more times a month		
Yes	466	9.25
No	1174	23.31
Invalid response	3397	67.44
Scene 3 (Nocturnal wheeze): Have you ever been woken up like this at any time in your life?		
Yes	459	9.11
No	4452	88.39
Invalid response	126	2.50
If yes, Has this happened in the past 12 months?		
Yes	265	5.26
No	1139	22.61
Invalid response	3633	72.13
If yes, has this happened once or more times a month		
Yes	194	3.85
No	1151	22.85
Invalid response	3692	73.30
Scene 4 (Nocturnal cough): Have you ever been woken up like this at any time in your life?		
Yes	1501	29.80
No	3402	67.54
Invalid response	134	2.66
If yes, Has this happened in the past 12 months?		

Yes	957	19.00
No	1009	20.03
Invalid response	3071	60.97
If yes, has this happened once or more times a month		
Yes	620	12.31
No	1173	23.29
Invalid response	3244	64.40
Scene 5 (Severe wheeze at rest): Has your breathing ever been like this?		
Yes	603	11.97
No	4295	85.27
Invalid response	139	2.76
If yes, Has this happened in the past 12 months?		
Yes	347	6.89
No	1073	21.30
Invalid response	3617	71.81
If yes, has this happened once or more times a month		
Yes	216	4.29
No	1141	22.65
Invalid response	3680	73.06

APPENDIX F: BIVARIATE ANALYSES FOR ALL EXPOSURES AND OUTCOME OF WHEEZE IN THE PAST 12 MONTHS

Table 1: BIVARIATE ANALYSIS: WHEEZE IN PAST 12 MONTHS AND DIET

EXPOSURE	Prevalence%	N= 5037	OR	95% CI	p value
Meat –1	54	339			
Meat- 2	453	2,095	1.45	1.06- 2.02	0.01
Meat- 3	492	2,431	1.33	0.97- 1.85	0.06
Meat- 9	172				
Seafood-1	439	2,174			
Seafood-2	461	2,184	1.05	0.91- 1.22	0.45
Seafood-3	80	391	1.01	0.76- 1.33	0.90
Seafood-9	288				
Fruit- 1	74	335			
Fruit- 2	281	1,421	0.86	0.64- 1.17	0.34
Fruit- 3	641	3,092	0.92	0.69- 1.22	0.56
Fruit- 9	189				
Veges- 1	107	613			
Veges- 2	325	1,648	1.16	0.90- 1.49	0.22
Veges- 3	567	2,549	1.35	1.07- 1.71	0.00
Veges- 9	226				
Pulses- 1	350	1,561			
Pulses- 2	467	2,274	0.89	0.76- 1.04	0.16
Pulses- 3	175	929	0.80	0.65- 0.98	0.03
Pulses- 9	273				
Cereal- 1	89	459			
Cereal- 2	184	842	1.16	0.86- 1.56	0.29
Cereal- 3	715	3,438	1.09	0.85- 1.41	0.48
Cereal- 9	298				
Maize- 1	573	2,224			
Maize- 2	265	1,651	0.55	0.46- 0.65	0.00
Maize- 3	138	879	0.53	0.43- 0.66	0.00
Maize- 9	283				
Pasta- 1	247	1,332			
Pasta- 2	557	2,434	1.30	1.09- 1.54	0.00
Pasta- 3	167	827	1.11	0.88- 1.39	0.34
Pasta- 9	444				
Rice- 1	65	253			
Rice- 2	259	1,155	0.83	0.60- 1.16	0.26
Rice- 3	676	3,445	0.70	0.52- 0.96	0.01
Rice- 9	184				
Butter- 1	208	916			
Butter- 2	214	1,125	0.79	0.64- 0.99	0.04
Butter- 3	558	2,710	0.88	0.73- 1.06	0.17
Butter- 9	286				

Margarine- 1	262	1,267			
Margarine- 2	266	1,384	0.91	0.75- 1.10	0.34
Margarine- 3	437	1,979	1.08	0.91- 1.29	0.34
Margarine- 9	407				
Nuts- 1	397	1,951			
Nuts- 2	453	1,976	1.16	0.99- 1.35	0.05
Nuts- 3	145	833	0.82	0.66- 1.02	0.07
Nuts- 9	277				
Potatoes- 1	33	203			
Potatoes- 2	300	1,292	1.55	1.04- 2.38	0.02
Potatoes- 3	662	3,339	1.27	0.86- 1.92	0.21
Potatoes- 9	203				
Milk- 1	93	444			
Milk- 2	227	1,317	0.78	0.59- 1.04	0.07
Milk- 3	671	3,065	1.05	0.82- 1.36	0.65
Milk- 9	211				
Eggs- 1	176	672			
Eggs- 2	507	2,530	0.70	0.57- 0.86	0.00
Eggs- 3	308	1,588	0.67	0.54- 0.84	0.00
Eggs- 9	247				
Fastfood-1	185	980			
Fastfood- 2	514	2,384	1.18	0.97- 1.43	0.08
Fastfood- 3	274	1,326	1.11	0.90- 1.38	0.28
Fastfood- 9	347				

Legend: dietary consumption:

1 = never or occasionally
2= once or twice a week
3= three or more times a week.
9= invalid response

Table 2: BIVARIATE ANALYSIS: WHEEZE IN PAST 12 MONTHS AND OTHER ENVIRONMENTAL EXPOSURES:

EXPOSURE	PREVALENCE	N=5037	OR	95% CI	P VALUE
How many times a week do you engage in vigorous physical activity long enough to make you breathe hard?					
Never or occasionally	255	1,572			
Once or twice per week	490	2,103	1.56	1. 32-1.86	0.00
Three or more times a week	257	1,181	1.43	1.17- 1.74	0.00
Invalid response	181				
During a normal week, how many hours a day (24 hours) do you watch TV?					
<1 hour	107	563			
At least 1 hour but less than 3 hours	271	1,303	1.11	0.86- 1.45	0.37
At least 3 hours but less than 5 hours	298	1,353	1.20	0.93- 1.55	0.14
5 or more hours	326	1,620	1.07	0.83- 1.38	0.56
Invalid response	198				
In your house, what fuel is usually used for cooking?					
Electricity – Yes	911	4,432	1.10	0.88- 1.37	0.38
Electricity – No	599				
Gas- Yes	96	502	0.91	0.71- 1.16	0.48
Gas- No	4,531				
Paraffin - Yes 1	136	892	0.65	0.53- 0.80	0.00
Paraffin- No	4,145				
Wood incl. open fires- Yes	23	83	1.51	0.88- 2.49	0.09
Wood incl. open fires No	4,954				
Othre cooking fuel type- Yes	0	1			
Other cooking fuel type- No	5,035				
In your house, what fuel is usually used for cooking?					
Electricity- Yes	753	3,540	1.21	1.03- 1.42	0.01
Electricity- No	1,496				
Gas- Yes	61	231	1.43	1.04- 1.94	0.01
Gas- No	4,806				
Paraffin- Yes	176	1,177	0.62	0.52- 0.74	0.00
Paraffin- No	3,856				
Wood incl. open fires- Yes	81	303	1.46	1.11- 1.91	0.00
Wood incl. open	4,733				

fires- No					
Other heating fuel type- Yes					
Other heating fuel type- No	5,028				
In the past 12 months, how often, on average, have you taken paracetamol (e.g. Panadol, Pamol)					
Never	214	1,333			
At least once a year	351	1,764	1.29	1.07- 1.57	0.00
At least once per month	434	1,741	1.73	1.44- 2.09	0.00
Invalid response	199				
How many older brothers and sisters do you have?					
0	195	900			
1	285	1,371	0.94	0.76- 1.17	0.61
2	180	933	0.86	0.68- 1.09	0.20
3	102	544	0.83	0.63- 1.09	0.18
=4	85	500	0.74	0.55- 0.98	0.03
Invalid response	789				
How many younger brothers and sisters do you have?					
0	206	986			
1	372	1,737	1.03	0.84- 1.25	0.74
2	179	977	0.84	0.67- 1.06	0.15
3	61	358	0.77	0.55- 1.07	0.11
=4	41	190	1.04	0.69- 1.53	0.83
Invalid response	789				
Were you born in S.A.?					
Yes	895	4,172	1.62	1.29- 2.06	0.00
No	98	682			
Invalid response	183				
What level of education has your mother received? (local wording)					
Primary school- Yes	192	921	1.03	0.86- 1.24	0.68
Primary school- No	4,115				
Secondary school- Yes	558	2,960	0.80	0.69- 0.92	0.00
Secondary school- No	2,077				
Tertiary education- Yes	297	1,086	1.66	1.42- 1.95	0.00
Tertiary education- No	3,951				
What level of education has your father received? (local wording)					
Primary school- Yes	166	865	0.91	0.75- 1.10	0.35
Primary school-	4,172				

No					
Secondary school- Yes	513	2,571	0.95	0.82- 1.09	0.47
Secondary school- No	2,466				
Tertiary education- Yes	344	1,313	1.585794	1.36- 1.84	0.00
Tertiary education- No	3,723				
How often do trucks pass through the street where you live, on weekdays?					
Never/ seldom	136	582			
Frequently through the day	477	2,249	0.88	0.70- 1.10	0.25
Almost the whole day	388	2,015	0.78	0.62- 0.98	0.02
Invalid response	191				
In the past 12 months, have you had a cat in your home?					
Yes	337	1,526	1.15	0.99- 1.33	0.06
No	659	3,337			
Invalid response	174				
In the past 12 months, have you had a dog in your home?					
Yes	534	2,663	0.93	0.81- 1.07	0.35
No	463	2,192			
Invalid response	182				
Does your mother (or female guardian) smoke cigarettes?					
Yes	339	1,405	1.34	1.15- 1.57	0.00
No	652	3,419			
Invalid response	213				
Does your father (or male guardian) smoke cigarettes?					
Yes	455	2,130	1.08	0.94- 1.25	0.23
No	524	2,626			
Invalid response	281				
How many people living in your house smoke cigarettes?					
0	278	1,399			
1	251	1,308	0.95	0.78- 1.16	0.65
2	200	901	1.15	0.93- 1.41	0.17
3	102	429	1.25	0.96- 1.63	0.08
=4	109	447	1.30	0.99- 1.68	0.04
Invalid response	553				
Do you smoke?					
Yes	126	433	1.67	1.33- 2.10	0.00
No	868	4,417			
Invalid response	187				
Is your house wet inside?					
Yes	93	507	0.85	0.66- 1.08	0.19
No	896	4,305			
Invalid response	225				
Has anyone in your household ever had TB?					

Yes	133	691	0.91	0.74- 1.12	0.39
No	854	4,133			
Invalid response	213				
Have you ever been treated for TB?					
Yes	71	325	1.11	0.83- 1.46	0.44
No	893	4,447			
Invalid response	265				
How many adults live in your household?					
0- 1	93	425			
2	484	2,263	0.97	0.75- 1.26	0.81
3	175	823	0.96	0.71- 1.29	0.80
=4	204	1,101	0.81	0.61- 1.08	0.13
99	425				
How many children live in your household?					
0- 1	107	509			
2	315	1,298	1.20	0.93- 1.55	0.14
3	248	1,233	0.94	0.72- 1.23	0.66
=4	275	1,541	0.81	0.63- 1.05	0.11
Invalid response	456				
Do you have taps in your house?					
Yes	836	3,861	1.52	1.25- 1.86	0.00
No	143	933			
Invalid response	243				
Do you have electricity in your house?					
Yes	964	4,666	1.55	1.01- 2.46	0.03
No	26	181			
Invalid response	190				
Do you have a TV in your house?					
Yes	932	4,504	1.295594	0.96- 1.76	0.08
No	58	346			
Invalid response	187				
What type of dwelling do you live in?					
House	836	3,936			
Flat	53	263	0.93	0.67- 1.28	0.67
Shack	86	573	0.65	0.50- 0.83	0.00
Other	12	60	0.92	0.44- 1.78	0.81
Invalid response	205				
How many people in your household are working?					
0	46	289			
1	282	1,549	1.17	0.83- 1.69	0.35
2	388	1,707	1.55	1.10- 2.22	0.00
3	129	598	1.45	0.99- 2.15	0.04
=4	80	352	1.55	1.02- 2.37	0.03
Invalid response	542				
How many people in your household are working?					
0	408	1,652			
1	282	1,507	0.70	0.58- 0.83	0.00
2	114	724	0.56	0.44- 0.71	0.00

3	42	251	0.61	0.42- 0.87	0.00
= 4	30	150	0.76	0.48- 1.16	0.19
Invalid response	753				
How many people in your household are NOT working					
0	300	1,201			
1	257	1,285	0.75	0.61- 0.91	0.00
2	207	1,078	0.71	0.58- 0.87	0.00
3	101	544	0.68	0.52- 0.88	0.00
= 4	61	417	0.51	0.37- 0.70	0.00
Invalid response	512				