1.0 INTRODUCTION

Asthma is a multifactorial disease that results from interactions between a genetically determined predisposition to allergic diseases and environmental factors which serve to enhance allergic inflammation of the lower airway.[1] According to the South African Childhood Asthma Working Group (SACAWG), a sub-committee of the Allergy Society of South Africa (ALLSA), Asthma should be diagnosed in a child with chronic/recurrent wheeze with or without cough (owing to bronchoconstriction) triggered by multiple factors including viral infections, allergens, irritants (pollution), exercise and sudden emotional changes (e.g. crying, laughing) and which responds to an inhaled bronchodilator.[2]

The disease remains a common chronic illness in childhood worldwide with an increasing prevalence in the past 20 years.[3] Asthma in children contributes significantly to school absenteeism, sleep disturbance, limitation in play activities and parental anxiety. It also accounts for a loss of 10 million school days per year in the United States of America.[4]

In South Africa, it is the third most common cause of hospital admission in children, after pneumonia and gastroenteritis.[5] Prevalence of asthma in South Africa according to the global burden of asthma report is 8.1% with South Africa ranking 25th in the world.[5] However, a South African based study (ISAAC study) showed prevalence of wheeze in children aged 13-14 years old to be 20.3% with only 14.4% of these children actually diagnosed to be having asthma.[6]

Managing asthma is problematic; hence the current emphasis is on evolving institutional and possible national treatment guidelines. Appropriate asthma care can help prevent most

episodes of acute exacerbations and ensure freedom from troublesome day and night symptoms, as well as sustain physical activity in asthmatic patients.[7]

International guidelines for asthma management indicate that the primary goal of therapy should be optimum asthma control. Asthma control refers to the degree to which the manifestations of the disease (symptoms, functional impairments, and risks of untoward events) are minimized and the goals of therapy met.[2] Control is generally accepted as a dynamic classification factor, critical to guiding treatment. In assessing severity and control, a distinction between current impairment and future risk is proposed by National Asthma Education and Prevention Program (NAEPP) and Global Initiative for Asthma (GINA).[8] Components of asthma control include current impairment (symptoms, need for rescue medication, limitation of activities, lung function in children >5 years) and future risk (exacerbations, medication side effects). The most severe impairment or risk defines the level of asthma control.[8]

Control should be maintained for prolonged periods taking into account the safety of treatment, potential for adverse effects and cost of treatment required. When control is achieved, it means the asthmatic patient is able to lead a normal and physically active life.

Asthma control ranges from 'well controlled', in which the patient is totally unimpaired and unlimited (this may be achieved either spontaneously, as in seasonal asthma, or by the use of medications) to ‘extremely poorly controlled’, which is a ‘life-threatening’ state.[9]

Several asthma control questionnaires have been validated which have various categorisation of levels of control.

There are many factors associated with poor asthma control ranging from concomitant rhinitis and co morbidities[10] to poor adherence with medications or inappropriate inhaler technique[10,11] in addition to home or environmental factors. Presence of infections may cause asthma exacerbations which may consequently give rise to poor asthma control.[12]

Several factors around the home of asthmatic patients contribute to poor asthma control which include factors such as parental smoking or smoking by other relatives within the home, biomass fuel exposure especially cooking with open flame and the child is around the mother, aeroallergen exposure and parental/ caregiver occupations or hobbies contribute to failure to achieve control despite adequate drug therapy.

2.0 LITERATURE REVIEW

2.1 ASTHMA DEFINITION

The exact definition for asthma has been difficult for clinicians for more than three decades. This is partly because of the inherent difficulty of differentiating asthma from other causes of the major clinical manifestations of the disease like recurrent cough, wheeze and breathlessness. These symptoms can occur singly or in combination. Indeed, some of these specific complaints are also found in varying degrees in other cardio respiratory disorders like bronchiolitis, pneumonia, pertussis and congenital heart disease[13]. Hence asthma is either misdiagnosed or under diagnosed with the corresponding propensity for undertreatment.[14,15]

Asthma is currently defined according to the International Consensus on pediatric asthma as ‘‘chronic inflammatory disorder associated with variable airflow obstruction and bronchial hyperresponsiveness (BHR). It presents with recurrent episodes of wheeze, cough, shortness of breath, and chest tightness.’’[8]

It is noteworthy to observe that in the 1950s, asthma was defined as a disease characterized by reversible airflow obstruction that could resolve spontaneously or with treatment.[3] This definition gave way to a subsequent one in the 1960s which, viewed asthma as an episodic disease in which airflow obstruction was caused by bronchial hyperresponsiveness.[3] The next decade witnessed the 1975 World Health Organization (WHO) definition of asthma as ‘‘a chronic condition characterized by recurrent bronchospasm resulting from a tendency

to develop reversible narrowing of the airway lumen in response to stimuli of a level or intensity not capable of inducing such narrowing in most individuals.''[13]

In 1989, the British Asthma Consensus Group defined asthma as ''a condition characterized by episodic wheeze and or cough in a clinical setting where asthma is most likely and rarer conditions associated with same symptoms have been excluded.''[16]

In South Africa, according to the SACAWG[2] published in the 2009 update the disease is defined as chronic/recurrent wheeze with or without cough (owing to bronchoconstriction) triggered by multiple factors including viral infections, allergens, irritants (pollution), exercise and sudden emotional changes (e.g. crying, laughing) and which responds to an inhaled bronchodilator.[2]

2.2 EPIDEMIOLOGY OF ASTHMA

With about 300 million individuals currently affected, the prevalence of asthma is reportedly on the increase worldwide.[5] This increase in asthma prevalence can hardly be ascribed to the current depth of knowledge on several aspects of the causation of the disease. The current surge in the disease burden may be associated with a corresponding increase in atopic sensitization, an observation that appears to be corroborated by a similar increase in the prevalence of other allergic disorders i.e. eczema and rhinitis.[5]

The prevalence of asthma in the developed world is eight to ten times higher than the corresponding values in third world countries,[4] but the disease burden appears to increase in urban communities and with the adoption of western life styles. It is projected that the proportion of the world's population that is urbanized will increase from 45% to 59% by 2025. The expectation therefore is that there is likely to be a marked increase in the number of asthmatics worldwide over the next two decades. It is estimated that there may be an additional 100 million persons with asthma by 2025.[5]

In the USA, an estimated 0.69 in 10 children had asthma,[17] while in UK about one in 10 children are affected by the disease.[18] In general, the highest prevalence of asthma symptoms are found in the UK, New Zealand and Australia[19-23] with 15.3%, 15.1% and 14.7% respectively.

On the other hand, African countries have recorded variable prevalence rates of asthma with 0%, 3.8%, and 4.3% reported from the Gambia,[13] Morocco[5] and Tunisia[5] respectively. In South Africa, it is the third most common cause of hospital admission in children, after pneumonia and gastroenteritis.[5] The prevalence of asthma in South Africa according to the global burden of asthma report is 8.1% with South Africa ranking 25th in the world.[5] However, a South African based study showed the prevalence of wheeze in children 13-14 years old to be 20.3% with only 14.4% of these children actually diagnosed with asthma.[6]

The prevalence of asthma varies from region to region, country to country and indeed within individual countries. It has been suggested that some of the reasons why developed

countries have higher disease prevalence of asthma include good living conditions with better insulated homes and fitted- carpets leading to an increase in house dust mite.[24] In addition, the hygiene hypothesis has also been proffered as a possible explanation in the rural urban differences of asthma prevalence. This hypothesis is premised on the observation that children raised on farms or in households where hygiene may not be meticulous tend to have lower rates of asthma.[24]

However, the modified hygiene hypothesis which is a counter regulatory model of allergy causation suggests that regulatory T cells (Tregs) inhibit both T helper cells type 1 (Th1) and T helper cells type 2 (Th2).[25] This mechanism of suppression by Treg is mediated through production of inhibitory or anti-inflammatory cytokines, such as IL-10 and transforming growth factor β. Tregs selectively express several toll-like receptors (TLRs), a family of proteins with a critical role in the detection of and response to pathogens, and can suppress both Th1 and Th2 responses.[25,26] Bacterial endotoxins and lipo polysaccharied enhance the suppressive effect of Treg.

The reason for the different rates of paediatric asthma in developing countries especially in Africa may be attributed to the fact that children in different parts of Africa are not exposed to adverse environmental precipitating factors such as atmospheric air pollution and other allergens in the same way and the same ages as those in developed countries. Another possible explanation may be the difficulty in differentiating bronchial asthma from other forms of chronic respiratory diseases affecting African children.

With regard to the age at first presentation, approximately 50% of asthmatic children are expected to present with symptoms by the age of three years [19,27] and indeed, 80% by the sixth year of life. However of all children who experience recurrent wheezing, only a minority will go on to have persistent asthma in later childhood.[28]

In general boys are three times more likely to get asthma than girls; but during adolescence, the prevalence becomes equal between the genders.[4] In adults however, the prevalence is higher in women than men.[4,19] Motika et al[29] conducted population-based studies of asthma and atopy in the Hutterites of South Dakota and observed similar increase asthma among females.

2.3 AETIOLOGY AND RISK FACTORS OF ASTHMA

The expression of asthma is a complex, interactive process that depends on the interplay between two major factors- host factors (particularly the genes) and environmental factors that occur at a crucial time in the development of the immune system.[27] No single agent or factor has yet been defined as the cause of asthma.[30] The important asthma related environmental variables include several respiratory viral infections, chemicals and aeroallergens exposure, as well as non biological air- pollutants such as tobacco and culinary smoke.

In the predisposed host, immune responses to exposure to these common environmental agents can be a stimulus for a prolonged and pathogenic inflammation as well as an aberrant repair of injured airways tissues. When these occur in the growing lung during

early life, airway growth and differentiation are affected, with subsequent long term pathologic consequences.[31] This sequences of events constitute the induction or sensitization phase. Once asthma has developed, ongoing or continuing exposures to trigger agents or inciters appear to worsen it. This constitutes the driving force for the persistence of the disease as well as increasing the risk of severe exacerbations.

a. Genetics

More than 22 loci on 15 autosomes have been linked to asthma,[28] although genetic linkages to asthma have sometimes differed between cohorts. Asthma has been consistently linked with loci containing pro-allergic, proinflammatory genes controlling Immunoglobulin E (IgE)-(the interleukin [IL]–4 gene cluster on chromosome 5).[28] Other genes include a disintegrin and metalloproteinase 33 super family gene (ADAM-33),[32] the gene for the prostanoid DP receptor, and genes located on chromosome 5q31 (possibly IL-12), chromosome 6, 11q13, 12 and 13 as documented earlier by Weiss & Raby[33] in addition to Cookson & co-workers.[34] Recently, Koppelman and Sayers[35] indicated that certain single nucleotide polymorphisms spanning ADAM33, ESR1, PLAUR, and VEGF have been found to be associated with an excess decrease in lung function in asthmatic subjects that carry the rare alleles.

Genetic predisposition to atopy constitutes the strongest host factor in developed countries but in South Africa <50% of asthmatic children are associated with atopy.[36] Airway hyper responsiveness, male gender and race/ethnicity have also been identified in earlier reports.[4,37]

Boys suffer more from asthma than girls,[4,19] it is not clear when exactly this change occurs. The mechanism of the changing gender ratio appears to be a late incidence of asthma among girls because the latter constitute a considerable part of adult asthma cases.[30] Furthermore, the link between sex or sex hormones and predisposition to asthma has not been established, but it has been suggested that this gender skewing may contribute to the onset or persistence of the disease.[37]

The prevalence of asthma is high in U.S in minority groups (blacks 5-8 %, Hispanics 15%), but generally, higher prevalence data have been recorded in white children.[33]

b. Viruses

Several reports[38-41] have suggested that recurrent wheezing in early childhood is usually associated with the common respiratory viruses like respiratory syncytial virus, rhinovirus (RV), influenza virus, parainfluenza virus and human metapneumovirus. Guilbert et al[41] determined the relationship of virus specific wheezing illness and lung function in a longitudinal cohort study of children at risk for asthma. They concluded that viral wheezing illnesses in early life that was caused by rhinovirus were the most significant predictors of decreased lung function up to 8 years in a high-risk birth cohort. It is not clear whether the low lung function is a cause, effect, or both of rhinovirus-induced wheezing illnesses.[41] White reported that virus- induced wheezing in infancy has been found to be associated with an increased risk for recurrent wheezing as children grow older.[39]

Rhinovirus is likely to cause disease by subversion of key elements of the host tissue immune response, particularly innate immune responses. It is now clear that RV may cause asthma exacerbations through excessive virus replication in patients following initial infection. This augmented virus replication is probably the result of both host and pathogen factors.[42]

Mechanisms by which RV causes asthma exacerbation include direct infection of the lower respiratory tract, induction of inflammatory responses to the virus itself, reduction in lung function, exacerbation of bronchial reactivity, and up regulation of surface intercellular adhesion molecule 1 (ICAM-1) expression in bronchial epithelium.[39]

This implies that host features affecting immunologic host defense, inflammation, and the extent of airways injury from ubiquitous viral pathogens may account for this susceptibility to recurrent wheezing in early childhood.[40-43] Furthermore, injurious viral infections of the airways causing severe bronchiolitis requiring hospitalization have also been identified as a possible risk factor for persistent symptoms of asthma in childhood.[4,14,44]

The prolonged morbidity associated with virus-induced airway inflammation and BHR in asthmatic children is reportedly more severe in subjects with significant pre-existing airway disease.[30,45]

c. Allergens

i Aeroallergen

In sensitized individuals, exposure to several domestic aeroallergens and pollutants (e.g. house dust mite and culinary smoke) have also been reported to initiate airway inflammation, hyper reactivity, and hence disease severity and persistence.[14,44] Indoor allergens like house dust mites, animal danders, cockroach, fungi, yeasts and several outdoor allergens like pollens have been implicated. The role of allergens in the pathogenesis of asthma is not fully defined. It is however agreed that sensitization following a long term exposure to house dust mite and cockroach allergens are important inducers of the disease.[46]

ii Food allergen

Food allergy is often one of the earliest manifestations of atopy, and sensitization to food is a risk factor for the subsequent appearance of respiratory allergy and asthma. Despite numerous studies of the effects of dietary restrictions on the prevention of allergy and asthma,[30] a firm conclusion can hardly be drawn in view of inadequate controls, length of follow-up, and/or sample size.[30]

d. Environment

Environmental exposure to tobacco smoke and air pollutants like ozone and sulfur dioxide can also aggravate airway inflammation and increase asthma severity.[14,44] Cold dry air and strong odours e.g. perfume can irritate the airways and trigger bronchoconstriction in sensitized individuals.

Passive tobacco smoke inhalation, especially from maternal smoking, (as against active smoking) is a more common environmental inciter of asthma in children than in adults. Maternal smoking during pregnancy has been shown to increase the likelihood of a genetically predisposed baby to asthma, presumably on account of the propensity for developing smaller airways.[4,30] Numerous studies have shown that maternal smoking during pregnancy results in a persistent deficit in lung function of children, most commonly due to reduced flow in the small airways. It is likely that nicotine, which readily crosses the placenta, plays a major role in causing these effects.

Maternal smoking during pregnancy has been found to be an independent risk factor for reduced lung function.[47] Altered alveolarisation and airway developmental abnormalities have been found after gestational exposure to nicotine.[48] Maternal smoking during the neonatal period may also help increase sensitization of the infant's lungs to allergens thereby increasing risk of asthma later in life.[4] It is also associated with increasing incidence of wheezing up to age six years.[49]

Maternal smoking predisposes to intrauterine growth restriction (IUGR) which is an established risk factor for respiratory complications in both term and preterm neonates. These neonatal problems are not likely to be a result of surfactant deficiency, but are more likely as a result of delayed clearance of lung liquid or structural immaturity of lung tissue. IUGR has been associated with reduced lung function in infants and children indicating that it can program the lung for altered function throughout life.[47] Children exposed to second hand smoke have been found to be at increased risk for severe asthma exacerbations.[50]

2.4 PATHOPHYSIOLOGY

The pathophysiological mechanisms of asthma are variable.[3,9] Interactions between environmental and hereditary factors result in relentless airway inflammation, a corresponding airflow limitation, mucosal oedema, mucus plugs and bronchospasm. Airways inflammation is linked to hypersensitivity of airways smooth muscle to numerous provocative exposures that act as triggers.[4]

a. *Asthma Triggers*

Several agents have been found to act as triggers of the disease. These include common viral infections of the respiratory tract, aeroallergens, animal dander, house dust mite, cockroaches, moulds and pollens from trees, grasses or weeds. Air pollutants like tobacco and culinary smoke, sulphur dioxide and house dust have been implicated.[38-41] Strong or noxious odour or fumes, perfumes, hair sprays, cleaning agents and paint fumes are also common triggers. Exposures to cold air or dry air, exercise and emotions such as crying or laughter have also been shown to trigger an attack. Other triggers include co-morbid conditions like rhinitis, sinusitis and gastro esophageal reflux.[2,21,51]

Following exposure to trigger factors, mucosal oedema and mucus hyper secretion results.[51,52] Consequently, there is resultant bronchoconstriction with a corresponding deprivation of the respiratory unit of the much needed oxygen and a subsequent decrease in oxygen saturation to less than 92% during an asthmatic attack.[4] Other effects include atelectasis, as a result of check-valve obstruction from mucus plugs, and varying degrees of abnormal lung function test parameters. The consequences of the airway obstruction

and other flow limiting events include hyperinflation (following a ball-valve obstruction and an increase in the dead space), hyperventilation with a decrease in lung compliance, alveolar hypoventilation, pulmonary vasoconstriction and decreased surfactant.[13] If the obstruction persists for long, hypercapnea, acidosis, respiratory failure and death may occur. During acute exacerbation of asthma, clinical signs often reflect evidence of ball-valve obstruction phenomenon like barrel chest, while in those with severe chronic asthma, there may be evidence of loss of lung volume.[13,28]

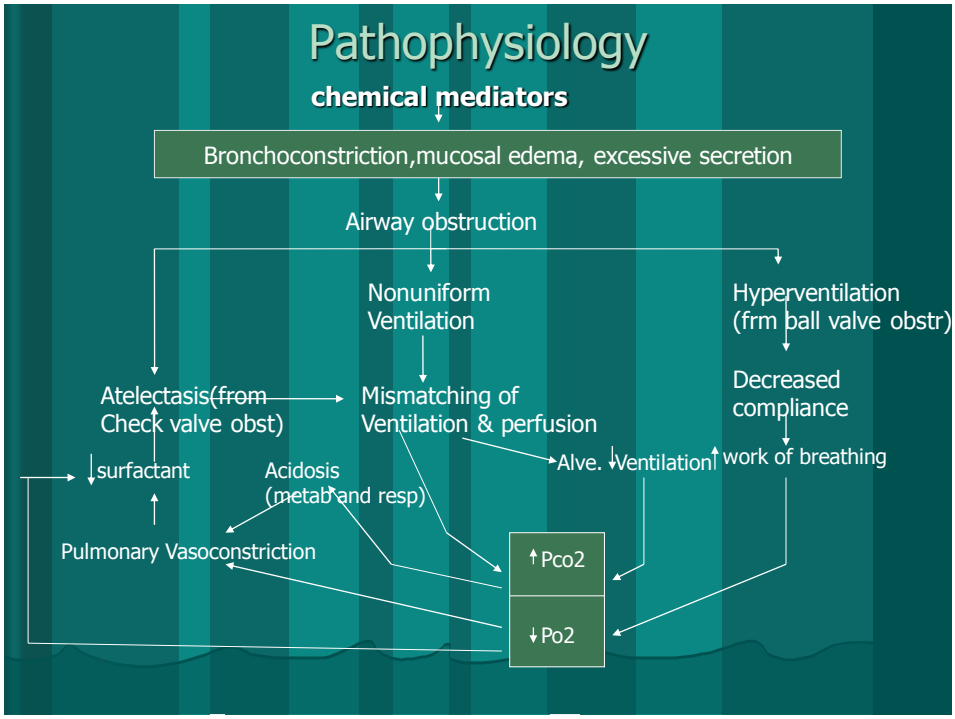

Figure 2.1- Pathophysiology of asthma. (PO_2 partial pressure of oxygen, PCO_2 partial pressure of carbon dioxide.) (Modified from Liu AH,Spahn JD, Leung DYM. Asthma. In: Behrman RE, Kliegman RM, Jensen HB(ed): Nelson textbook of paediatrics 16th edition. Philadelphia, WB Saunders company 2000: Chapter 145).

2.5 CLINICAL FEATURES

The common recurrent symptoms of asthma include episodic cough (paroxysmal and usually unproductive), wheeze, chest tightness and shortness of breath. Often the only symptom is nocturnal or early morning cough especially in pre-school children. Nocturnal symptoms are typically worse during prolonged exacerbations triggered by respiratory infections or inhaled allergen exposure.[53,54]

Other symptoms in children can be subtle, and these include limitation of physical activities/exercise, general fatigue, insomnia, abdominal pain and skin rash. About 50% of patients have other atopic diatheses like atopic dermatitis, allergic rhinitis, vernal conjunctivitis and urticaria.[54,55]

In the mildest form, bronchial asthma- related wheezing is only end-expiratory. As severity increases, wheezing lasts throughout expiration. In a more severe asthmatic episode, a bi-phasic wheeze (inspiratory and expiratory) is heard. However, during the most severe episode, wheezing may be absent because of the marked limitation of airflow associated with airway narrowing and respiratory muscle fatigue. Also, asthma may occur without wheezing when obstruction involves predominantly the small airways.[4] Majority of these non wheezing asthmatics would present with chronic cough (cough-type asthma). Thus, while wheezing is not necessarily a sine- qua-non of the diagnosis of asthma, it is indisputably one of the commonest clinical indicators.

Physical findings vary with the severity of asthma. Symptoms may follow viral URTIs or an antecedent scenario of massive allergen exposure or may indeed be exercise- induced. During an outpatient visit, it is not uncommon for a patient with mild intermittent asthma to have normal chest findings on physical examination.[4] In those patients with more severe asthma signs of chronic respiratory distress and hyperinflation may be evident. The anteroposterior diameter of the chest may be increased because of hyperinflation. Hyperinflation may also cause an abdominal breathing pattern. The auscultatory findings in those with acute or residual symptoms include prolongation of the expiratory phase, expiratory wheezing, coarse crepitations, or unequal intensity of breath sounds.[4]

Signs of concomitant atopy may include those of allergic rhinitis, such as conjunctival congestion/periorbital darkening (allergic shiners), Dennie's lines (a nasal crease on the nose due to constant rubbing), pale violaceous nasal mucosa and constant rubbing related absence of the medial eye lashes.[4]

Features of allergic rhinitis like mouth breathing as a result of partially blocked nostrils may also be evident, while the sclera may appear brownish with concomitant itching and excessive lacrimation (vernal conjunctivitis). The physical findings during an acute episode may reveal different findings in mild, moderately severe, and severe episodes and in one with life threatening features and imminent respiratory arrest.

In mild episode, the respiratory rate is increased but the accessory muscles of respiration are not used. The heart rate is usually less than 100 beats per minute and there is no pulsus

paradoxus. Auscultation of the chest reveals moderately loud polyphonic, expiratory wheezing. The oxygen saturation in room air is greater than 95%.[4]

In children with moderately severe episode of bronchospasm, there is tachypnoea with active use of the accessory muscles of respiration with the corresponding intercostal and sub-costal retractions. Infrequently, there is also suprasternal retraction. The heart rate is 100-120 beats per minute and pulsus paradoxus may be present (10-20 mm Hg). A loud expiratory wheeze may be heard. Oxygen saturation in room air is 91-95%.[4]

In a severe episode, the respiratory rate is often greater than 30 breaths per minute. Accessory muscles of respiration are usually used with suprasternal retractions. The heart rate is more than 120 beats per minute. Loud biphasic (expiratory and inspiratory) wheeze may also be heard. Pulsus paradoxus is often present (20-40 mm Hg) and the oxygen saturation with room air is less than 91%.[4]

With regard to the most severe category, namely severe acute asthma with life threatening features and imminent respiratory failure, the child presents with paradoxical thoraco-abdominal movement. The absence of wheezing suggests a severe airway obstruction. Severe hypoxemia may manifest as bradycardia and the child may also be tachypneic with a respiratory rate of 40 and above. Pulsus paradoxus noted earlier may be absent at this stage, a finding suggesting respiratory muscle fatigue.[4]

2.6 DIAGNOSIS

In view of the propensity for a delayed diagnosis or misdiagnosis of asthma, the need for a high index of suspicion cannot be over emphasized, especially when there are persistent or recurrent respiratory symptoms.

In establishing a diagnosis of asthma, a good history is often helpful. Most infant wheezers have a positive family history of atopy, and can identify a specific exposure or circumstance that triggers the symptoms. Some additional screening questions that may prove useful in the diagnostic pursuit of asthma had been highlighted by earlier workers.[16,21]

Asthma should be diagnosed in a child with chronic/recurrent wheeze with or without cough (owing to bronchoconstriction) that is triggered by multiple factors including viral infections, allergens, irritants, exercise and sudden emotional changes and which responds to an inhaled bronchodilator. Features supporting the diagnosis include a family or personal history of atopy, nocturnal cough, exercise-induced cough and/or wheeze and seasonal variation in symptoms.[2] In children, allergy is often the main trigger that determines the severity of the disease. Early sensitisation, severe atopy and synergistic interaction between atopy and infections are risk factors for persistent asthma. Cough variant asthma is a rare form of asthma which presents with cough but no wheeze and no evidence of airway obstruction on spirometry.[2]

According to the South African chronic asthma management working group[2], diagnosis of asthma depends on the age of the child.

a. Children older than 5 years

In diagnosing asthma in older children; careful history and physical examination, in addition to objective evidence of reversible airflow obstruction after administration of a short-acting β2-agonist (SABA) (an increase in forced expiratory volume in 1 second (FEV_1) >12% or in peak expiratory flow rate (PEFR) >15% after 10 minutes), will confirm the diagnosis in most instances. Monitoring symptoms and PEFR using a diary card is also useful for making the diagnosis; diurnal PEFR variability of >20% is highly suggestive of asthma.[2]

b. Children 5 years and younger

Diagnosis of asthma in early childhood is challenging and based largely on clinical judgement (assessment of symptoms and physical findings). Asthma should be distinguished from other causes of persistent and recurrent wheeze since the use of the label 'asthma' for wheezing in children has important clinical implications.[2]

Castro et al[56] proposed a clinical index (asthma predictive index) which is based on the presence of wheeze before the age of three, and the presence of 1 major risk factor (parental history of asthma or eczema) or 2 of 3 minor risk factors (eosinophilia, wheezing without colds, and allergic rhinitis). This has been shown to predict the occurrence of childhood asthma in developed countries but not in African children, who have less atopy.[2]

Cough and episodic wheezing are very common even in children who do not have asthma, and especially in those < 3 years old. Martinez et al[57] described three categories of wheezing in children namely transient early wheezing, persistent early-onset wheezing, and late-onset wheezing.

Brand[58] categorised wheeze in young children into 2 broad groups: episodic (viral) wheeze and multi-trigger wheeze. Those children found to have multi-trigger wheeze have symptoms precipitated by factors other than viral infections (such as allergens and exercise) and are likely to be asthmatic.

2.7 DIFFERENTIAL DIAGNOSIS OF CHILDHOOD ASTHMA

Clinical entities that may be confused with or co-exist with bronchial asthma in childhood are shown the tables below.

Table 2.1: Differential diagnosis of asthma in children 5 years and older

Hyperventilation syndrome and panic attacks
Vocal cord dysfunction
Upper airway obstruction and inhaled foreign bodies
Other forms of obstructive lung disease
Non-obstructive forms of lung disease (e.g. diffuse parenchymal lung disease)
Non-respiratory causes of symptoms (e.g. left ventricular failure)

Adapted from Motala C, Green RJ, Manjra AI, Potter PC, Zar HJ for the South African Childhood Asthma Working Group. Guideline for the management of chronic asthma in children-2009 update. S Afr Med J 2009;4:255-69.

Table 2.2: Differential diagnosis of asthma in children 5 years and younger

Infections
Recurrent respiratory tract infections
Chronic rhino-sinusitis
Tuberculosis
HIV disease
Congenital problems
Tracheomalacia
Cystic fibrosis
Bronchopulmonary dysplasia
Congenital malformation causing narrowing of the intrathoracic airways
Primary ciliary dyskinesia syndrome
Immune deficiency
Congenital heart disease
Mechanical problems
Foreign body aspiration
Gastro-oesophageal reflux

Adapted from Motala C, Green RJ, Manjra AI, Potter PC, Zar HJ for the South African Childhood Asthma Working Group. Guideline for the management of chronic asthma in children-2009 update. S Afr Med J 2009;4:255-69.

2.8 ASTHMA MANAGEMENT AND CONTROL

2.8.1 Factors affecting asthma control

Achieving asthma control remains an elusive goal for the majority of patients worldwide. Correct diagnosis of asthma is the first and most important step in assessing poor asthma control. A number of factors may contribute to sub-optimal asthma control.

There are factors associated with poor asthma control ranging from concomitant rhinitis (a common co-pathology and contributor to poor control)[2,10] to poor compliance with medications [10,11,59,60] or inappropriate inhaler technique[10,11] in addition to home/ environmental factors.

Once coexistent airway disease has been excluded, other explanations for lack of control include regular or excessive use of inhaled β2-agonist, which can worsen asthma control, co morbid conditions such as uncontrolled sinusitis, untreated gastroesophageal reflux, obesity and psychogenic problems (psychogenic dyspnoea, anxiety-hyperventilation, paradoxical vocal cord function, and factitious asthma). [10,60,61]

Presence of infections may cause asthma exacerbation which may consequently give rise to poor asthma control.[62] Viral respiratory infections represent the most common cause of asthma exacerbations and, hence, contribute to a loss of asthma control.[61]

Several factors around the home of asthmatic patients contribute to failure to achieve optimal asthma control. These include parental smoking or smoking by other relatives within the home, biomass fuel exposure especially cooking with open flame, aeroallergen exposure and parental/ caregiver occupations or hobbies.

Green[63] reported on asthma control in South Africa following a review on asthma morbidity from around the world (five studies in all) by Rabe[11] who commented on the disappointing lack of asthma control as reflected by ongoing asthma morbidity. Many surveys of asthma care have been published from around the world which suggests that in total only 5% of asthmatics are meeting the 'Goals of asthma management' as set out in Guidelines.[63]

Rabe[11] listed 3 important reasons for lack of control which include:

1. Asthma is a subtle disease

2. Patients have low expectations and accept limitation

3. Patient and doctors consistently under-estimate severity & control

However, Green[63] believes that 2 additional reasons for poor asthma control include:

1. Patients are often non-adherent to chronic long-term therapy

2. Patients ability to use metered dose inhaler (MDI) is usually limited

An additional reason for such poor quality asthma control in South Africa is the apparent lack of use of adequate anti-inflammatory therapy for this chronic condition. There is published evidence that asthma therapy is dominated by the use of short acting reliever medication in South Africa and that SAβA prescriptions in the respiratory market outweigh inhaled corticosteroid.[63]

Furthermore, there is mounting evidence that a compounding factor to poor asthma control is under-diagnosis of the condition. Many surveys from South Africa have suggested delay in asthma diagnosis.[64] Green also suggested another reason for poor asthma control to be the fact that patients and doctors consistently over-estimate control.[65]

Deger et al[62] conducted a cross-sectional population-based study using data from a respiratory health survey of Montreal children aged 6 months to 12 years in 2006 which comprises of 7980 respondents. Asthma control was assessed in 980 asthmatics using an adaptation of the Canadian asthma consensus report clinical parameters. Subjects with acceptable asthma control were compared with those with inadequate disease control.[62]

Of 980 children with active asthma in the year prior to the survey, 36% met at least one of the five criteria as to poor control of their disease. The population's characteristics that were found to be related with a lack of asthma control were younger age, history of parental atopy, low maternal education level, foreign-born mothers, and tenant occupancy.[62]

Two cross-sectional surveys assessing asthma control status were conducted by Stanford et

al[12] in 2008, among adult and paediatric patients with asthma in the United States. Participants completed a self-administered questionnaire including demographics, medical history, and current asthma medication use. In addition, they also completed either the asthma control test (ACT) or childhood asthma control test (C-ACT). One study enrolled 2238 adults (aged ≥ 18 years) and the other 2429 children (aged 4-17 years) with asthma. The patients were visiting their health care provider for a scheduled appointment for any reason.

The overall prevalence of uncontrolled asthma was 58% and 46% in adult and paediatric patients, respectively.[12,66] Predictors of uncontrolled asthma in both adults and children in the study included self-reported asthma severity, lack of adherence, and recent history of cold, flu, or sinus infection. The predictors of uncontrolled asthma seen only in children were female aged 12-17 years, caregiver unemployment and history of asthma exacerbation.[66] The finding of uncontrolled asthma in 46% of children was consistent with previously reported rates of uncontrolled asthma in children in primary care settings which range between 37%-64%.[67,68]

2.8.2 Home circumstances associated with poor asthma control

a. Smoking

Children are more vulnerable to environmental tobacco smoke (ETS) than adults, since the respiratory and immune systems are not fully developed; additionally, children spend more time at home.[69] Many studies[69,70] have shown ETS to be associated with respiratory symptoms in children.

Passive tobacco smoke inhalation (as against active smoking) in children is a more common environmental inciter of asthma in children. In 2002, Finkelstein et al[71] reported household smokers to be 30%. Smoking by parents of asthmatic children can be as high as 86% regardless of asthma severity even though parents know the effects of passive smoking.[72] Among children with established asthma, parental smoking was associated with more severe disease. Substantial benefits to children would arise if parents stopped smoking after birth, even if the mother smoked during pregnancy.[70]

A cross sectional study done by Mc Ghan et al on 153 children in Edmonton, Albarta assessing asthma control in children aged 5-13 years found 75% of children were rated as having poorly controlled asthma. Overall, 44% of children had exposure to tobacco smoke in the home. Of those with poor control, 51% had household tobacco smoke exposure.[73]

In a multi centre study conducted by Halterman et al[68] in United States, 15.5% of children were exposed to smoke in the home. Based on asthma control, 20.9% had inadequate asthma control while 10.7% had suboptimal asthma control.[68] A literature review done by Mc Leish et al on smoking and asthma revealed that smoking was associated with decreased asthma control and increased risk of mortality and asthma exacerbations.[74] Smoking is also associated with accelerated decline in baseline lung function over time. Exposure to environmental tobacco smoke also impacts asthma control in children and adults. It also attenuates the therapeutic response to inhaled and oral corticosteroids.[61]

b. Biomass fuel

About 3 billion people in the world use solid fuels, 2.4 billion use biomass fuels and the remainder utilize coal for the majority of their household energy needs. Biomass fuel is any material derived from plants or animals which is deliberately burnt by humans. Wood is the most common example, but the use of charcoal, animal dung and crop residues are also widespread.[75]

Use of solid fuels in homes is the most widespread source of indoor air pollution worldwide. They are extensively used for cooking and home heating in developing countries, especially in rural areas.[76] China, South Africa and some other countries also use coal extensively for domestic needs.[76]

The percentage of people using solid fuels varies widely among countries and regions, ranging from 77% in sub-Saharan Africa, 74% South-East Asia, and74% in the Western Pacific Region to 36% in the Eastern Mediterranean Region, and 16% in Latin America, the Caribbean and Central and Eastern Europe. In the majority of industrialized countries, solid fuel use falls below the <5% mark.[77]

In developing countries, studies on biomass smoke in relation to asthma in children and adults have yielded mixed findings.[77] Exposure to solid fuel smoke may act as an asthma trigger, additionally exposure to biomass smoke has been associated with an increased prevalence of asthma[75] which may also serve as a compounder to effective asthma control.

Wood is often collected by women, and women and small children also have largest exposure to indoor air pollution from cooking; exposure from heating may be similar in men and women.[78] Cooking and heating with biomass fuel can be as high as 90% in rural households in sub Saharan Africa,[79] which has been shown to be associated with increase in prevalence of asthma[80] and possible poor outcome. In another study, 20.5% of all asthmatic children were exposed to a fireplace or wood stove, 24.7% were found to belong to the group with inadequate asthma control, while 15.6% belonged to the suboptimal asthma control group.[68]

In 2001, almost 60% of households in Limpopo, a predominantly rural province, used wood as the main source of energy for cooking (almost 3 times the national average), while in the more developed province of Gauteng less than 1% of households used wood for cooking. [78] In 2011, 13% of South Africans used wood for cooking and less than 1% used coal and animal dung for cooking.[81] While 15% used wood for heating, less than 3% of South Africans used animal dung and coal for heating.[81] Limpopo still had the highest number of people using wood for heating purpose in the country. The use of animal dung for heating and cooking was found to be highest in the Eastern Cape and most common in blacks.[81] Mpumalanga has the highest number of people using coal for cooking and heating in their homes also commoner in blacks.[81]

Limited ventilation of homes is common in many developing countries and this increases exposure, particularly for women and young children who spend much of their time indoors.[78]

c. Kerosene (paraffin)

It was reported that in South Africa 1 in 5 households used paraffin for cooking and heating in 2001,[82] this was reduced to 9% in 2011 census.[81] Azizi et al[83] conducted a case-control study of children aged between 1 month and 5 years who were hospitalized with asthma in Kuala Lumpur found that the use of kerosene was not associated with asthma.

d. Pets/poultry

Presence of pets or poultry in homes also compound to poor asthma control. Studies have implicated furry pets contributing as triggers of asthma attack hence leading to poor asthma control. In a multicentre study conducted by Finkelstein et al[71] in United States, they reported 59.0% of households had furry pets including 32.0% with cats and 39.0% with dogs. Rosenstreich et al[84] found a frequency of allergy to cat dander to be only 10.0% of the homes in their study had cats. Presence of indoor pets accounted for 43.0% of homes of asthmatic children in a study done by Halterman et al.[68] They found 39.6% of children with inadequate asthma control have pets at home and 45.9% of those with suboptimal asthma control.

e. Carpets

Carpets are known to harbour house dust mites and removal of carpets from bedrooms or homes completely have been recommended by several studies and guidelines.[2,58] Finkelstein et al[71] reported 78% of households in United States had bedroom carpeting.

f. Cockroaches

Cockroach allergy is widespread in South Africa. Cockroaches may be a cause of ongoing airway inflammation, and sensitivity to cockroaches is a risk factor for more severe asthma.[2] Two previous South African studies reported that cockroach sensitivity was found to be up to 40% in allergic children.[85,86] Lopata et al[87] also demonstrated high level of sensitisation to three types of cockroaches in allergic children and adults living in Pretoria, Cape town and Durban, however it was not mentioned whether the patients were asthmatic or not. Seedat et al[88] reported 38% of patients with allergic rhinitis had sensitisation to cockroach in Free state.

Finkelstein et al[71] reported presence of household pests (including cockroaches and rodents) in United States to be a problem for 18% of families, including 6% who reported exposure to cockroaches. Halterman et al[68] reported presence of cockroaches inside homes of American asthmatic children to be 16.9%. This was seen in 20.4% of homes of children with inadequate asthma control and 13.8% of homes of those with suboptimal asthma control.

2.8.3 Measures of asthma control

Asthma control is a central focus of the updated version of the GINA Guidelines, in which clinicians are encouraged to concentrate on assessment of control, defined by symptoms, lung function and the presence or history of exacerbations.[89] The main question, of course, is whether guideline-defined asthma control is achievable.

The Asthma Insights and Reality surveys of over 10,000 adults and children with asthma[11] revealed a shortfall in the current level of asthma control worldwide, compared with guideline-defined goals of asthma care. While the majority of patients can achieve control of their asthma under strict research study conditions, as demonstrated in the recent Gaining Optimal Asthma Control (GOAL) study, a significant minority cannot.[90] Furthermore, the level of control achieved and time taken to do so also depends upon asthma measures utilised with more time required to attain control using composite measures.[91]

Managing asthma is problematic; hence the current emphasis is on evolving institutional and possible national treatment guidelines. Appropriate asthma care can help prevent most episodes of acute exacerbations and ensure freedom from troublesome day and night symptoms, as well as sustain physical activity in asthmatic patients.[7]

Achieving and maintaining optimal asthma control is a major asthma management goal advocated by GINA. Recent evidence suggests that asthma control is clearly achievable in most asthmatics.[92]

The definition of asthma control is difficult as physicians, patients and regulatory bodies have different perceptions. The challenge therefore remains as to how best to assess asthma control and define management strategies to ensure that this control is achieved and maintained.

International guidelines for asthma management indicate that the primary goal of therapy should be optimum asthma control. Control refers to the degree to which the manifestations of asthma (symptoms, functional impairments, and risks of untoward events) are minimized and the goals of therapy are met.[2] Control should be maintained for prolonged periods with regards to the safety of treatment, potential for adverse effects and cost of treatment required.

When control is achieved, it means the asthmatic patient is able to lead a normal and physically active life. The criteria for normal life are:[27]

1. to be completely free from any symptoms, i.e. cough, wheeze and breathlessness.

2. to attend school regularly and participate fully in all school activities, including sports.

3. to sleep restfully free from night time cough and /or wheeze.

4. to grow and develop normally.

5. to minimise the number of attacks of acute asthma and avoid hospitalization.

6. to avoid or minimize medication related side effects.

Asthma control is difficult to measure and reproduce, but despite these limitations, the GINA guidelines (as follows) are widely used. These include absence or minimization of chronic symptoms; reduction of exacerbations; avoidance of asthma-related visits to emergency health care facilities; minimal or no requirement for as-needed (quick-relief), short-acting β_2-agonist medication; no asthma-related limitation of normal physical

activity; near-normal lung function; and minimal or no adverse effects of asthma medications.[89]

Assessment of asthma control has been put forward as a more valuable measure than assessment of asthma severity. Assessment of asthma severity has limited reproducibility among both generalists and specialists. It has not been validated clinically, especially in children, and asthma is a dynamic disease where severity changes over time.[93]

Although assessments of asthma control may be desirable, they too fail to incorporate patient-specific goals of treatment and therefore the desired level of control is seldom reached. Literature review in respect of asthma control assessment in children reveals many inconsistencies and recommendations based on, at best, weak scientific principles. The GINA Guideline is a working scheme that is based on current opinion and has not been validated.[93]

According to the SACAWG which use the GINA recommendations, asthma control may be assessed clinically (symptoms on history, physical findings, reliever use), and by measurement of lung function and fractional exhaled nitric oxide (FE_{NO}) in certain situations.[2] Patient -centred questionnaires are also useful for identifying children who are uncontrolled. Levels of asthma control recommended by GINA are shown in the table 2.3.

Table 2.3: Levels of asthma control according to GINA

Characteristics	Controlled (all of the following)	Partly controlled (any measure present in any week)	Uncontrolled (≥ 3 features of partly controlled asthma in any week)
Daytime symptoms: wheezing, cough, difficult breathing	< 2/week	> 2/ week	> 2/week
Limitation of activities	None	Any	Any
Nocturnal symptoms/awakening	None	Any	Any
Need for reliever/rescue treatment	< 2/week	> 2/week	> 2/week
Lung function* (PEF/FEV_1) predicted or personal best (if known)	Normal	< 80%	< 80%

*Applicable to children older than 5 years.

Adapted from Motala C, Green RJ, Manjra AI, Potter PC, Zar HJ for the South African Childhood Asthma Working Group. Guideline for the management of chronic asthma in children-2009 update. S Afr Med J 2009;4:255-69.

a. History taking and clinical assessment

Clinical assessment includes taking a good history including the frequency of daytime and nocturnal symptoms, extent of limitation of activities, and need for reliever treatment, followed by a thorough clinical examination of the entire respiratory system including the ear, nose and throat.

b. Spirometry

Spirometry can only be performed reliably in children > 5 years old and commonly used parameters derived from the volume/time plot are forced expired volume in 1 second (FEV_1) and the forced vital capacity (FVC). The most commonly used parameters derived from the flow/volume plot are peak expiratory flow rate (PEFR) and the maximum mid-expiratory flow rate (MMEF).[2] The FEV_1 and PEFR are most frequently utilised for assessing asthma control. Peak expiratory flow changes do not always reflect changes in lung function and are generally late indicators of loss of asthma control. [2]

c. Fraction of Exhaled nitric oxide (FE_{NO})

FE_{NO} is not a routine test of assessing asthma control and mostly in children; it offers no benefit over clinical monitoring, however there may be value in certain circumstances such as a child with difficult-to-control asthma.[2]

Levels of FE_{NO} have also been shown to increase before the onset of symptoms or loss of control and therefore monitoring may be used to predict loss of control.[2] It has also been found to be a useful tool in identifying persistent atopic non-smoking asthmatics.[50]

d. Asthma control questionnaires

Several asthma control questionnaires have been developed; some have been validated while others were not, all have different ways of categorising levels of asthma control.

i. Childhood Asthma Control Test (C-ACT)

The C-ACT was published in 2007 and aims to overcome some of the problems in history taking. It is now promoted as a validated measure and is widely used in clinical settings and research studies. However, in the validation study itself the questionnaire only achieved a specificity of 74% and sensitivity of 68% against a specialist's rating of asthma control. Positive predictive value of 52% with a negative predictive value of 85%.[94] In addition, studies utilising this test have failed to match test scores to other objective measures of asthma control.[95]

The C-ACT was developed to assess asthma control in children 4-11 years of age for use in the clinic and at home. It was designed to be self-administered, to incorporate input from parent and child, to capture the multidimensional nature of asthma control, and to demonstrate good predictive properties for assessing asthma control.[96]

For the development of C-ACT, the children were asked about the present, because children 4-6 years of age had difficulty recalling beyond 1 day. Also such children tended to use more extreme responses and had difficulties understanding a neutral state, so a 4-point scale was chosen.[97]

Seven items were selected from regression analyses of the development sample to comprise the C-ACT. The seven-item questionnaire asks about asthma symptoms; four questions are answered by the child while the remaining three are answered by the parent regarding symptoms in the past 4 weeks.

The scores of each item were summed for a total score (0-27), scores of >19 were

associated with well controlled asthma, score of 27 is totally controlled'' asthma, scores of <16 were considered ''poorly controlled'' or ''not controlled at all,'' and scores of 16-19 corresponded to ''somewhat controlled'' asthma.[94]

The C-ACT can be valuable in clinical practice and research based on its validation, ease of use, input from the child and caregiver, and alignment with asthma guidelines.[96]

ii. Asthma Control Test (ACT)

Four primary care clinicians and seven asthma specialists specified the essential components of asthma control and defined a criterion measure of asthma control which was published in 2004.[98]

Each survey item asked the respondent to consider the last 4 weeks, a total of 407 respondents, aged 12-94 years participated in the survey. The asthma specialist interviewed and examined the patient and rated the level of asthma control on a National Heart Lung and Blood Institute (NHLBI) guideline-based 5-point scale:

1 Not controlled at all

2 Poorly controlled

3 Somewhat controlled

4 Well controlled

5 Completely controlled

Forward stepwise logistic regression analyses showed 5 items correlating with specialist assessment, these include[98]:

Shortness of breath, patient's rating of asthma control, use of rescue medication, role limitations due to asthma and nocturnal asthma symptoms.

Each item includes 5 response options corresponding to a 5-point Likert-type rating scale. In scoring the ACT, responses for each of the 5 items are summed to yield a score ranging from 5 (poor control of asthma) to 25 (complete control of asthma).[94]

The cut off point for well-controlled asthma is > 19, with a score of 25 signifying total asthma control. Uncontrolled asthma is any score ≤ 19, with poorly controlled asthma being < 16 and scores of 16-19 is somewhat controlled asthma. The higher the ACT scores on the range of 5 to 25, the better the asthma control.[67] Values ≤19 predicting uncontrolled asthma had a sensitivity of 69.2%, specificity of 76.2%, positive predictive value of 56.1% and negative predictive value of 84.9%.[97]

iii. Asthma Control Questionnaire (ACQ)

The authors of Asthma Control Questionnaire (ACQ) which was published in 1999 defined asthma control as: "the full range of clinical impairment that patients with asthma may experience as a result of their disease. The range is from 'well controlled', in which the patient is totally unimpaired and unlimited to 'extremely poorly controlled', which is a 'life-threatening state'.[9]

Five highest scoring symptoms used to assess asthma control were selected for the ACQ. In addition, there was a question on β2-agonist use and another on airway calibre (total questions were 7).[9] The drawback is the questionnaire was developed using only 50 asthmatic individuals in a homogeneous Caucasian population, variations due to ethnic diversity or population size may affect applicability.[97] The ACQ has also been validated in children and published in 2010.[99] This was however carried out on 35 asthmatic children.

The scoring of the questionnaire is based on 7 responses ranging from 0 signifying well controlled asthma to 6 signifying extremely poorly controlled asthma with score of 1-5 as being in between. Final score is the mean of the scores for the 7 items.[97]

Value less than or equal to 0.75 is well-controlled while value of greater than or equal to 1.50 is not well-controlled.[97] This makes values of 0.76-1.49 to be indeterminate which is another drawback of the questionnaire.

iv. Asthma Therapy Assessment Questionnaire (ATAQ) for children and adolescents

This was developed in 2004 to assist clinicians and health plans to identify children at risk for adverse outcomes of asthma.[100] ATAQ is a brief, 20-item parent-completed questionnaire that generates indicators of potential care problems in several categories, including symptom control, behaviour and attitude barriers, self-efficacy barriers, and communication gaps. For its development, cross-sectional mail survey with telephone follow-up was conducted with parents of 434 children aged 5-17 years being treated for asthma and enrolled in three managed care organizations in the Midwestern and North

eastern United States.[100] ATAQ scales were found to correlate with measures of physical health, psychosocial health, resource use, and family impact.

The ATAQ is very simple to use and has a good validity data. But the drawback is its smaller scale makes degrees of change difficult to assess. It is less reported in clinical practice and trials; because it consists of 20 questions this makes it difficult to use in office setting.[100]

v. Test for Respiratory and Asthma Control in Kids (TRACK)

In the TRACK study reported in 2009,[101] a 33-item questionnaire that included asthma impairment and risk items was administered to 486 caregivers of children aged younger than 5 years with a current, recent, or past history of respiratory symptoms. Reliability, validity, and ability to screen for respiratory control problems were tested for.

Five items were selected which included the frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night time awakenings in the past 4 weeks; use of rescue medication in the past 3 months and the use of oral corticosteroid in the previous year.[101] Each item was scored on a 5-point scale; the total score was the sum of individual scores on each item. These scores were then transformed to a 0- to 100-point scale for the final TRACK instrument (0, 5, 10, 15, or 20 points for each item response), where higher scores indicated better respiratory control. Asthma control is classified here as well controlled, not well controlled and very poorly controlled. A TRACK score of less than 80 suggest poor asthma control. The questionnaire was found to be a valid, easy-to-

administer, caregiver completed questionnaire of asthma control in preschool aged children.[101]

vi. Asthma Quiz for kids

Six clinical criteria of asthma control were used as questions and response options.[102] A cross-sectional study reported in 2004, was conducted in children one to 17 years of age. Children that were nine years of age or older and their parents were asked to complete the questionnaire separately, and then together, before their medical visit. Parents of younger children completed the questionnaire with their child. Physicians were not informed of the results of the quiz. A score of at least 2 out of 6 had 73% sensitivity and 59% specificity for identifying poor control.[102]

There are fundamental challenges when assessing asthma control in children, including selecting meaningful measures to assess asthma symptoms and determining the most reliable source of the information (parent/caregiver, child, and/or health care provider).

Developmental issues may influence the accuracy of a young child's symptom reporting. For example, some children may have difficulty associating time with asthma events and may be reluctant to acknowledge their asthma symptoms, because they do not recognize abnormal symptoms or they want to be perceived as ''normal.'' As a result, caregivers are often asked to assess their child's symptoms.[96]

However, numerous studies have demonstrated poor correlations between the symptom reports of children and those of their parents.[103,104] Indeed, some studies suggest that child symptom reporting should not be discounted or ignored. In a study by Lara et al[103] assessing the validity of exercise-related symptom reporting by children with asthma compared with their parents; child-reported coughing and wheezing correlated with FEV_1 and observed symptoms due to exercise; in contrast, parent reported symptoms did not correlate.

Guyatt et al[104] observed in younger children (age < 11 years) that their symptom reports correlated strongly with changes in quality- of-life measures, although parents' ratings of asthma symptoms showed moderate correlations with FEV_1 and asthma control but not quality-of-life measures. They concluded that, in younger children, clinicians are likely to obtain important and complementary information from children and their parents. Owing to these challenges, there is a need for a simple yet reliable measurement tool to assess asthma control in children to help them achieve the goals of asthma care.[105]

Four instruments have established cut off values for uncontrolled versus controlled asthma: ACQ score of 1.5 or greater[9] ACT score of 19 or less,[94] ATAQ score of 1 or greater[100] and C-ACT score of 19 or less.[96] These cut offs have been defined in populations, generally on the basis of optimizing the balance between sensitivity and specificity, but may not always be accurate for individual patients. The distributions of scores for the various instruments vary by study population.[106]

Some instruments have been developed for patients of all ages (Royal College of Physicians ‘‘3 Questions’’)[107], but others have been developed and validated specifically for patients aged 0 to 4 years e.g. TRACK,[101] in older children such as (Asthma Quiz for kids,[102] ATAQ for Children and Adolescents[100] and C-ACT[96]), patients aged 12 years and older (ACQ[9] and ACT,[94]) or those aged 18 years and older such as Asthma Control Scoring System (ACSS),[107] Seattle Asthma Severity and Control Questionnaire.[109]

2.9 REVIEW OF ASTHMA CONTROL STUDIES

Previous reviews of surveys assessing asthma prevalence and control across the world have concluded that the majority of patients with asthma do not achieve adequate asthma control and underuse controller medication, but these studies have included a majority of adult subjects.[11,110] Various instruments have been used with varying definitions of suboptimal/inadequate asthma control depending on measure of asthma control used and population studied.

In a review done by Green in 2006,[63] a random sample of asthmatics was identified by practitioners in South Africa. Patients completed an ACT and provided a list of medications currently being taken. The doctor also provided an assessment of control which was summarised into the categories - 'not controlled' and 'controlled' and listed all medications prescribed.

Half of the patients classified themselves as being ‘not controlled’ (ACT score < 20, category 1), while doctors classified only 33% of patients as being ‘not controlled’.

Although only 7% of patients disagreed with the doctor's classification of 'not controlled', 29% disagreed with the doctor's assessment of being 'controlled'. This study suggests that asthma still appears to be relatively poorly controlled in South Africa, although levels of patient control appear to have improved compared to previous surveys, and confirms that physicians and patients differ in their assessments of asthma control.[65] Green concluded that South Africa is still far from achieving asthma control despite the availability of medications for treatment.

A prospective sequential sample of atopic asthmatic children aged 4 to 11 years was carried out by Green et al to describe agreement among different measures of asthma control in children. Patients were assessed using FE_{NO}, spirometry, C-ACT and conventional clinical assessment by a paediatrician.[111]

They found that mean FE_{NO} in paediatrician-judged uncontrolled asthma was double that of controlled asthma. There was disagreement among common measures of asthma control especially for FE_{NO} and C-ACT. However, clinical assessment by the paediatrician and the C-ACT agreed with each other. They have demonstrated that different measures of assessing asthma control showed lack of agreement for all comparisons.[111]

A worldwide survey on severity and control of asthma - Asthma Insight and Reality survey (AIR) done between 1998 to 2001 in 29 countries within North America, Europe and Asia (five regions) showed all the regions performing poorly against the different GINA goals.[11] All the regions showed most of the patients experiencing moderate to severe symptoms

believed their asthma to be well or completely controlled, however Africa was not included in the survey.

The AIR surveys found that the current level of asthma control in children is poor and falls far short of the goals set out in the GINA guidelines.[11] For example, only one in 20 children with asthma in Western Europe (5.8%) met all the GINA criteria for asthma control [110] Other recent surveys determining asthma control based on GINA guidelines have found high levels of inadequate asthma control: in the Patient Outcomes Management Survey (POMS) in New Zealand, 90% of children had sub optimally controlled asthma [112] and 31% of children in the Hunair Study had moderate or poor asthma control.[113] Good asthma control was only present in 25.7% of asthmatic children in a Switzerland study.[114]

A cross sectional survey done at the Asia- Pacific region comprising of 8 countries (China, Hong Kong, Korea, Malaysia, The Philippines, Singapore, Taiwan and Vietnam) was reported in 2003 using a population sample of 3207 with physician-diagnosed asthma identified by screening 108,360 households.[115] Daytime asthma symptoms were reported by 51.4% of respondents and 44.3% reported sleep disturbance caused by asthma in the preceding 4 weeks. At least 2 in every 5 respondents (43.6%) had been hospitalized, attended a hospital emergency department, or made unscheduled emergency visits to other health care facilities for treatment of asthma during the previous 12 months.[115]

Overall, 15.3% reported requiring hospital admission for asthma treatment. Severity of asthma correlated with the frequencies of hospitalizations and emergency visits for asthma

in the past year. Even patients with severe persistent asthma, 34.3% regarded their disease as being well or completely controlled. Current use of an inhaled corticosteroid was reported by only 13.6% while only 6.3% reported use of quick-relief bronchodilators. Absence from school and work in the past year was reported by 36.5% of children and 26.5% of adults. As reported for other regions, current levels of asthma control in the Asia-Pacific region fall markedly short of goals specified in international guidelines for asthma management.[115]

Adachi et al[116] conducted the AIR survey in Japan in 2000 which aimed to assess the current status of asthma treatment and management in Japan. The detailed survey on asthma management was conducted among 803 of households, 401 adults and 402 children. More than half had experienced a daytime asthma attack during the previous month while more than one third had experienced an asthma attack at night during that same period. About 70% of adults and 60% of the children with asthma reported some limitation on activities of daily life.[116]

Pulmonary function tests had never been done in about 50% of adults and 80% of children. There was a large gap between subjective perception of asthma control and objective findings in patients with severe asthma. Many Japanese asthmatics as in other studies tended to underestimate the severity of their condition. The study revealed only 5% of asthmatics met the GINA goals of asthma control which suggests asthma management in Japan falls far short of goals stated in the guideline.[116]

2.10 STUDY OBJECTIVES

1. To determine the level of asthma control in children seen at the Asthma and Allergy clinic of Charlotte Maxeke Johannesburg Academic Hospital.

2. To document the home circumstances that contributes to poor asthma control in children attending the clinic.

3.0 MATERIALS AND METHODS

This study was carried out from July to October 2012. The protocol for this study was approved by the Human Ethics Committee of the University of the Witwatersrand; ethics clearance certificate number M120633 (APPENDIX A).

3.1 Study population

3.1.1 Sample size

The sample size was calculated based on the prevalence of asthma in South Africa according to GINA which was 8.1%.[5] The sample size was calculated based on recommendation of the statisticians of the University of Witwatersrand as follows:-

$$n = \frac{z^2 pq}{d^2}$$

Where

n= minimum sample size.

z= standard normal deviate corresponding to a 95% confidence interval obtained from a Normal distribution table =1.96.

p= prevalence of asthma (8.1%).

q= complementary probability to p i.e. (1-p).

d= desired precision =0.05 or 5%.

A minimum sample size of 112 was calculated and was rounded up to 115 patients.

3.1.2 Study site

The study was conducted at the Paediatric Asthma and Allergy clinic of the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Johannesburg; a tertiary care teaching and referral hospital in Gauteng, South Africa.

3.1.3 Inclusion criteria

All children age 5years to 18 years 11months diagnosed with asthma attending the Paediatric Asthma and Allergy clinic of the Charlotte Maxeke Johannesburg Academic Hospital.

3.1.4 Exclusion criteria

1 Legal guardian/patient refusal for study enrolment.

2 Newly diagnosed asthmatics patients that are not on any asthma treatment.

3.1.5 Study design

This was a prospective cross sectional study. Every patient that fulfilled the inclusion criteria was given the opportunity to participate in the study.

3.2 Methods

Patients were recruited from the Paediatric Asthma and Allergy Clinic using convenience sampling. Consent was obtained from legal guardian in children < 7 years of age (APPENDIX B). Children ≥ 7 years signed their own assent form while their legal guardian also gave consent (APPENDIX C).

The diagnosis of asthma was confirmed by a history of recurrent cough/wheeze, supported by one or more of the following:

1. A positive family history of asthma and/ atopy in first degree relative.
2. Presence of clinical features suggestive of atopy.
3. The demonstration of reversible airway obstruction either on peak expiratory flow rate or spirometry.
4. A positive therapeutic response to anti-asthma medications.

3.2.1 Questionnaires

A validated childhood asthma control test[92] (C-ACT) detailing asthma symptoms was completed by the legal guardian and children less than 12 years (APPENDIX D). The C-ACT is a seven-item questionnaire about symptoms; four questions are answered by the child in relation to symptoms, and three are answered by the parent regarding symptoms in the past 4 weeks. Children more than 12years filled the validated asthma control test (ACT - APPENDIX E).[93]

The scores of each item were summed for a total score (0-27) in C-ACT.

- Scores of 27—total/complete asthma control
- ≥ 19—well controlled asthma
- ≤ 19 indicates uncontrolled asthma
- 16-19—somewhat controlled asthma
- < 16—poorly controlled asthma

For those children that used ACT, scores of each item were summed for a total score (0-25).

- Scores of 25—total/complete asthma control
- ≥ 19—well controlled asthma
- ≤ 19 indicates uncontrolled asthma
- 16-19—somewhat controlled asthma
- < 16—poorly controlled asthma

For this study, scores of >19 using both questionnaires are considered controlled asthma (merging well controlled and total control).

Another questionnaire relating to home circumstances was filled by the legal guardian and patient (APPENDIX F). Factors such as the presence of a smoker at home, presence of pets, cockroaches and use of biomass fuel as well as about the child's sleeping environment including carpet and soft toys in the bedroom were asked.

For those legal guardians/patients who were unable to read, the questionnaire was read to them and they were asked to choose the most appropriate answer. There were no legal guardians/patients that did not understand English amongst the participants, however there was a translator that was familiar with the questionnaire and knew what was being asked in case there was need for translation into the major South African languages.

3.2.2. Examination

a. The patient's variables were recorded i.e. age (as at last birthday), sex, weight and height; and each patient was assigned an identification number on the clinical information sheet (APPENDIX G).

The weight was measured using a digital scale by SECA to the nearest 0.1 kilogram. Height was measured using a tape by Levita attached to the wall which measures up to two metres. Each patient stood as erect as possible with the heels, buttocks and occiput against the wall bare footed and arms supinated by the side. The readings were taken to the nearest 0.1 centimetre.

b. Compliance with medications was assessed by the researcher who asked each patient or legal guardian how many times he/she uses the medications per day and compared it with what has been prescribed by the doctor in the file.

c. Use of inhaler technique was assessed by the researcher who asked the patient to demonstrate how he/she uses the inhaler. Patients that had a poor inhaler technique were corrected.

d. A full medical examination relevant to allergy and asthma was conducted on all study participants by the researcher i.e general examination, skin, ear, nose and throat and respiratory. Specifically features of atopy were looked for such as presence of allergic shiners, Dennie Morgans lines and swollen turbinates.

e. A lung function test was carried out on each patient by the researcher using a spirometer manufactured by Erich Jaeger GMbH 97204, Hoechberg. 1992-2003.

The procedure was explained to each patient and also demonstrated to each patient. The patients usually stand during the procedure and a nose clip was attached to prevent air leakage through the nasal passages. Each patient was asked to take a deep inhalation before the mouthpiece was placed in the mouth between the teeth. The lips were sealed tightly around the mouthpiece to prevent air leakage during maximal forced exhalation. During each exhalation, the patient was loudly prompted to blow out the air into the spirometer as fast and as hard as he/she could. Exhalation was encouraged to last at least 6 seconds.

The patients were allowed to rest for several seconds and the procedure was repeated. Usually, three manoeuvres were performed; although additional tests may have been necessary if one or more of the curves were unacceptable.[116]

4.0 RESULTS

4.1 DEMOGRAPHIC CHARACTERISTICS

In this cross sectional study, 115 asthmatic children were enrolled for the study comprising of 59 males (51.3%) and 56 females (48.7%) giving a male to female ratio of 1.05:1.

There were 99 Blacks (86.1%), 7 Coloured (6.1%), 5 Whites (4.3%) and 4 Asians (3.5%).

The mean age ± SD of the study population was 11.69 ±3.42 years with a range of 5.10 years to 18.90 years. Table 4.1 shows mean age ± SD according to gender and race.

Table 4.1: Mean age ± SD according to gender and race.

		Black	White	Asian	Coloured
Gender	M	11.31±3.43	10.37±1.94	12.96±0.22	11.37±0.25
	F	11.80±3.64	12.35±5.02	14.25±2.05	14.38±2.86

4.2 ASTHMA CONTROL

Level of asthma control was determined using C-ACT in 59 patients (51.3%) and in 56 (48.7%) ACT was used to determine the level of asthma control. More than half of the asthmatic children had controlled asthma. Of the patients with controlled asthma, total asthma control was seen in 3 patients (2.6%) while 61 (53.1%) had well controlled asthma.

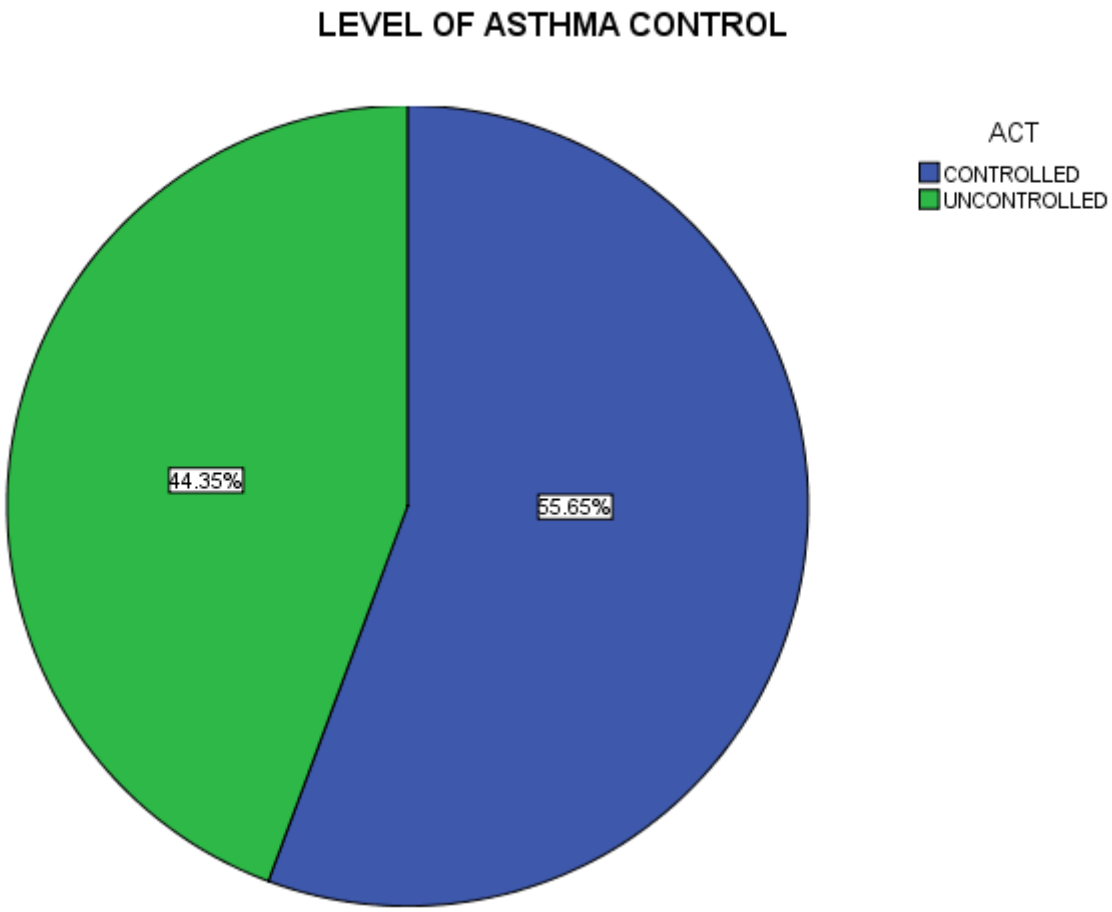

Figure 4.1: Pie chart showing level of asthma control.

The mean±SD of C-ACT was 19.86±4.49 with a minimum score of 9 and maximum of 26 while mean±SD of ACT was 19.00±3.62 with a minimum score of 11 and maximum of 25.

Nocturnal awakening was seen in a small percentage of asthmatic patients with controlled asthma as shown in table 4.2. This was significantly associated with asthma control. Presence of daytime symptoms was seen more frequently in patients with poor asthma

control as shown in table 4.2. Daytime asthma symptoms was also significantly associated with asthma control

Table 4.2: Asthma control symptoms.

Asthma control	Controlled Frequency (%)	Uncontrolled Frequency (%)	Total Frequency (%)
Nocturnal awakening	19(30.1)	44(69.9)	63(100)
Day time symptoms	27(38.0)	44(62.0)	71(100)

Nocturnal awakening - $\chi 2$=36.689, df=1, p=0.0001.

Day time symptoms - $\chi 2$=23.354, df=1, p=0.0001.

Males were not better controlled than females as shown in table 4.3. When gender was compared with asthma control, there was no significant association seen.

Table 4.3: Association between asthma control and gender.

Gender	Controlled n(%)	Uncontrolled n(%)	Total n(%)
Male	34(57.6)	25(42.4)	59(100)
Female	30(53.6)	26(46.4)	56(100)

n= number, %= percent $\chi 2$ = 0.191, df=1, p=0.662.

Most of the patients were black of which 53 (46.1%) were well controlled asthma and 3 had total asthma control as shown in table 4.4.

Table 4.4: Asthma control and race.

Asthma control	Total control n(%)	Well control n(%)	Uncontrolled n(%)	Total n(%)
Black	3(3.0)	53(53.6)	43(43.4)	99(100)
White	0(0.0)	4(80.0)	1(20.0)	5(100)
Coloured	0(0.0)	3(42.9)	4(57.1)	7(100)
Asian	0(0.0)	1(25.0)	3(75.0)	4(100)

There was however no statistically significant difference between asthma control and race.

$\chi 2=3.22$, df=3, p=0.359.

Twenty nine children aged 10-14 years had controlled asthma while only 12 children aged 15-18 years were controlled as shown in table 4.5. There was no significant difference between asthma control and age.

Table 4.5: Asthma control and age.

Age (years)	Controlled n(%)	Uncontrolled n(%)	Total n(%)
5-9	23(60.5)	15(39.5)	38(100)
10-14	29(53.7)	25(46.3)	54(100)
15-18	12(52.2)	11(47.8)	23(100)

$\chi 2=0.562$, df=2, p=0.755.

4.3 HISTORY

Majority of the patients presented with history of cough, family history of atopy in first degree relatives and responded to bronchodilator therapy as shown in the table 4.6. Good adherence with medications was seen in 82.6% of patients while good inhaler technique was seen in74.8% of patients.

Table 4.6: Questions on Asthma diagnosis and management

	Frequency (n)	Percentage (%)
Cough	114	99.1
Family history of atopy	112	97.4
Family history asthma	51	44.3
Response to bronchodilator	114	99.1
Adherence to medications	95	82.6
Good inhaler technique	86	74.8

Good inhaler technique was seen in 45 (52.3%) of patients with controlled asthma and 41 (47.7%) of patients with uncontrolled asthma. This was not statistically significant ($\chi 2=1.529$, df=1, p=0.216). Good adherence to medications was seen in 59 (62.1%) of patients with controlled while in those patients with uncontrolled asthma it was seen in 36 (37.9%). Asthma control was significantly associated with adherence to medications ($\chi 2=0.217$, df=1, p=0.002).

4.4 HOME CIRCUMSTANCES

Use of biomass fuel was not common in this study only five homes were found to be using biomass fuel; two homes use kerosene while no home was found to use animal dung. These were seen in 6 homes of asthmatics with controlled asthma and home of one asthmatic with uncontrolled asthma. There was no association between use of biomass fuel and asthma control ($\chi 2=6.202$, df=4, p=0.185).

When home circumstances were compared with the level of asthma control, there was no statistically significant association seen as shown in the table 4.7.

Table 4.7: Association between home circumstances and asthma control.

Home factor	Frequency	%	Controlled	Uncontrolled	χ^2	p value
Dust	46	40.0	25	21	0.053	0.818
Cockroach	39	34.0	19	20	1.150	0.284
Carpet	38	33.0	17	21	2.740	0.098
Pets	26	22.6	15	11	0.057	0.812
Toys on bed	20	17.0	9	11	1.113	0.291
Smoking	13	11.3	6	7	0.536	0.464

Twenty two (19.1%) patients own a dog as pet in their homes, another patient had a cat (0.87%), another had a bird (0.87%) and one (0.87%) patient had both a cat and a dog at home.

4.5 CLINICAL FEATURES

Most of the patients that were enrolled were stable; hence few patients were seen with features of concurrent infection or acute asthma as shown in table 4.8.

Table 4.8: Examination findings

	Frequency (n)	Percentage (%)
Infection	8	7.0
Fever	1	0.9
Hyperinflation	27	23.5
Tachypnoea	7	6.1
Wheeze	12	10.4

4.6 CLINICAL FEATURES OF ATOPY

Fifty four patients (55.7%) had multiple atopic features. Ninety nine patients had swollen turbinates (86.0%), 56 had allergic shiners (48.7%), 28 had Dennie Morgan's lines (24.3%) and while 19 had eczema (16.5%).

4.7 SPIROMETRY

The mean ± SD PEFR for the study population was 87.03 ± 22.94 L/min and mean ± SD FEV_1 was 84.78 ± 16.48, the FEV_1/FVC of the study population was 95.29±16.21.

4.7.1 Asthma control and FEV_1

The FEV_1 percentage of predicted was categorised as <60%, 60-80% and ≥80%. Forty seven percent of patients had good asthma control with FEV_1 of ≥80% while only 2.6% of patients with good asthma control had FEV_1 of <60% as shown in table 4.9.

Table 4.9: Level of asthma control and FEV_1

Asthma control	FEV_1 n(%)			Total
	<60%	60-80%	≥80%	
Controlled	3(4.7)	7(10.9)	54(84.4)	64(100)
Uncontrolled	8(15.7)	17(33.3)	26(51.0)	51(100)

n= number, %= percent

When asthma control was compared with FEV_1, there was statistically significant difference as shown in table 4.10.

Table 4.10: Comparism of asthma control with FEV_1

FEV1	< 60%			60-80%			≥ 80%		
	T	df	p	t	df	p	t	df	p
CACT	4.70	3	0.018	14.98	12	0.0001	37.94	41	0.0001
ACT	15.47	6	0.0001	15.66	10	0.0001	31.81	37	0.0001

Normal FEV1 which is ≥ 80% of predicted was seen in 33.0% of patients with nocturnal symptoms and 38.3% of patients with day time asthma symptoms as shown in table 4.11. Both nocturnal and daytime asthma symptoms were significantly associated with FEV1.

Table 4.11: Asthma control symptoms and FEV_1

FEV_1 % predicted	≥ 80% Frequency (%)	< 80% Frequency (%)	Total Frequency (%)
Nocturnal awakening	38(33.1)	25(21.7)	63(54.8)
Day time symptoms	44(38.3)	27(23.5)	71(61.8)

Nocturnal awakening $\chi 2=5.628$, df=1,p=0.018.

Day time symptoms $\chi 2=5.054$, df=1, p=0.025.

4.7.2 Comparism of controlled and uncontrolled asthmatics with FEV_1 and PEFR

There was a statistically significant difference when FEV_1 was compared between controlled and uncontrolled asthmatics; t = 55.173, df= 114, p=0.0001 similarly this difference was seen when PEFR was compared between controlled and uncontrolled asthmatics, t=40.683, df= 114, p= 0.0001.

5.0 DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 DISCUSSION

Asthma control is a central focus of the updated version of the GINA Guidelines, in which clinicians are encouraged to concentrate on assessment of control, defined by symptoms, lung function and the presence or history of exacerbations.[89] Control is of critical importance in asthma and is now more important than the actual level of severity. Measures of asthma control do not necessarily perform well and all of them need to be looked at as a whole as studies have shown.[111]

Previous reviews of surveys assessing asthma prevalence and control across the world have concluded that the majority of patients with asthma do not achieve adequate asthma control and underuse controller medication, but these studies have included a majority of adult subjects.[10,110] South African studies that looked at asthma control showed different measures to assess asthma control disagree with each other[111] and most patients assessed were found to have poor asthma control.[63,111]

Previous studies revealed a lack of agreement between C-ACT and specialist assessment of asthma control[96] and a conflicting association has been observed between C-ACT and spirometry[95] for the assessment of asthma control.

Disparity exists between what is recommended about the treatment of asthma and what occurs in practice in the community. The present study was undertaken to examine the

level of asthma control in children at the Paediatric Asthma and Allergy Clinic, Charlotte Maxeke Johannesburg Academic Hospital and to investigate home circumstances associated with poor asthma control. This cross sectional study is the first in South Africa to assess asthma control in relation to home circumstances. Although cross-sectional surveys only provide a 'snapshot' of the current level of asthma control, which can vary over time, they are helpful in identifying several factors associated with poor asthma control in children.

The high prevalence of asthma in the world and the impact of morbidity warrant the need to ensure patients are well controlled. Home circumstances that constitute part of the environmental triggers of asthma need to be identified and intervention offered so that asthma control can be fully achieved which is the goal of asthma therapy.

Many factors have been found to be associated with poor asthma control ranging from concomitant rhinitis and co morbidities[10] to poor compliance with medications or inappropriate inhaler technique[10,11] in addition to home or environmental factors. Presence of infections may cause asthma exacerbations which may give rise to poor asthma control.[12]

Several factors around the home of asthmatic patients contribute to poor asthma control which includes parental smoking or smoking by other relatives within the home, biomass fuel exposure, exposure to aeroallergens and animal danders contribute to failure to achieve control despite adequate drug therapy.

The AIR surveys found that the current level of asthma control in children was poor and falls far short of the goals set out in the GINA guidelines.[10] Other recent surveys determining asthma control based on GINA guidelines have found high levels of inadequate asthma control in United States,[11] Canada,[62] New Zealand,[112] Hungary,[113] and Switzerland.[114]

There were more males than females in this study; this conforms to the fact that asthma in childhood is commoner in males.[4,18] The male preponderance for asthma before adolescence appears to be a universal finding as similar observations were made by other workers.[4,36] Reason for the male preponderance is not exactly clear, but may be partly due to the fact that males are more adventurous and more likely to come in contact with trigger factors.[52] However there was no association between gender and asthma control.

This study showed that majority of the patients had good asthma control which is higher than 50% obtained in a South African study[63], similarly higher than that obtained by the New Zealand,[112] Hunair,[113] Switzerland[114] and Japan[116] studies. Reason for this difference may be due to difference in methodology. Previous studies used different instruments and definitions to determine poorly controlled asthma.

The mean ACT of 19 in patients with controlled asthma in this study seems very similar to 20.7 obtained by Greenblatt et al[65] but higher than 12.8 obtained in those with uncontrolled asthma. Reason for the higher rate in patients with controlled asthma may be due to

improved asthma management and care. Other reasons are due to good inhaler technique and adherence to medications. Patients seen in our hospital which is a tertiary referral centre are mostly those with moderate to severe persistent asthma that require specialist care.

Patients with day time and nocturnal symptoms were higher than 51.4% and 44.3% respectively obtained by Lai et al.[114] Reason for the disparity may be because asthma symptoms both during the day and at night significantly correlated with poor control, this shows that simply taking a thorough history is very effective.

Blacks constituted the majority of study participants this is in contrast to that found by Smith et al [13] where Hispanics were found to be more than blacks and whites. This is due to the fact that they constitute 79.4% of South African population.[118] They are also more likely to patronise the South African public hospitals as fewer black families access private care. Lack of significance between asthma control and race may be attributable to small number of patients in other races as compared to the Blacks.

Males were not better controlled than females, no significant association was seen between asthma control and gender which is similar to what was obtained by Kuehni et al[119] and in contrast to what was observed by Greenblatt et al[65] where they found significant difference between the sexes. Reason for the lack of significance cannot be explained.

Majority of the patients had good adherence (82.6%) and good inhaler technique (74.8%), reason for the good adherence in our study may be due to the fact that patients are taught regularly on how to use inhalers and adherence assessed at each clinic visit. Rate of non adherence in our study is higher than what was reported by Kuehni et al[119] where the rate of non-adherence was the same (28%) in children with well controlled and poorly controlled asthma. However, significant association was observed between adherence and asthma control which was in contrast to that observed by Kuehni et al,[119] and Ho et al.[120] Other studies have reported poor adherence to asthma management guidelines, even for children who have been hospitalised for their asthma[120,121] which is probably an important factor influencing asthma control. Technical difficulties with inhalation therapy are also likely to be more common in younger children, although few problems were reported by parents in our study.

Most of our study patients had swollen turbinates (86%) which suggests presence of allergic rhinitis. This may be due to the fact that allergic rhinitis co exist with asthma in about 80% of patients.[122] Concomitant rhinitis has been found to contribute to poor asthma control[2,10,123] however in this study majority of the patients had good asthma control despite presence of swollen turbinates.

Use of biomass fuel was not common in the present study; probably because Gauteng is a more developed province where less than 1% of households use wood for cooking.[77] No significance was observed between biomass fuel use and asthma control which is similar to observation by Azizi et al[83] but in contrast to reports by Halterman et al.[67] Reason for this dissimilarity may be attributable to the number of respondents.

Presence of furry toys on bed (17.4%), cats (0.8%) and dogs (19.1%) was found to be lower than that in other studies and not significantly associated with asthma control.[67,70,82,119] Prevalence of cockroach (33.9%) was higher than that found by Finkelstein[70] and Halterman et al,[67] this may be responsible for the widespread cockroach allergy in South Africa.[7] Presence of carpeting in homes of asthmatic patients was found to be lower than that reported by Finkelstein et al[71] and similar to 33% obtained by Kuehni et al.[119] Reason for the dissimilarity may be due to increase in the usage of floor tiles and removal of carpets in homes of asthmatics as a form of allergen avoidance in asthma management. However, despite the high prevalence of cockroaches and use of carpets which harbour house dust mites in the homes of our patients, it was not found to affect asthma control probably due to the fact that not all patients are sensitised to cockroach or house dust mite allergen which can worsen asthma symptoms and lead to poor control.

Exposure to smoking (11.3%) was similar to what was reported by Halterman et al.[68] However, smoking was not found to be associated with poor asthma control in this study which is in contrast to earlier studies,[70,71,73] this may be due to the small number of patients that had smokers in their homes. However none of these home circumstances was found to be significantly associated with asthma control probably due to the relatively small size of respondent in our study compared to other studies.

Most of the children had experience with performance of lung function. The mean PEFR predicted was similar to 84.1% obtained in the study done by Hammer et al.[68] FEV_1 was significantly associated with asthma control; this conforms to the recommendation by

GINA guidelines. Lower ACT and C-ACT was associated with lower FEV_1 percent predicted which is similar to that obtained by Friedlander et al.[95]

Patients with normal FEV1 were higher than 42% obtained in the Switzerland study, however similar to 11% seen in patients with low FEV1 (<60%).[114]

5.2 CONCLUSION

1. This study results demonstrates that most of the asthmatic patients attending the paediatric Charlotte Maxeke Johannesburg asthma and allergy clinic had well controlled asthma.

2. There was no association seen between home circumstances and asthma control.

3. The majority of the patients were blacks.

4. Good adherence and inhaler techniques were associated with asthma control.

5. The history of nocturnal and daytime asthma symptoms was significantly associated with poor asthma control.

6. The use of biomass fuel was uncommon in this study.

7. There was a significant association seen between asthma control and $FEV_{1.}$

5.3 RECOMMENDATIONS

1. The results from this study need confirmation in a representative population study.

2. Further longitudinal study is required to see if home circumstances may affect asthma control in patients that had controlled asthma.

APPENDIX A: ETHICS

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Dr Bilkisu G Illah

CLEARANCE CERTIFICATE	M120633
PROJECT	Do Home Ciorcumstances Affect Asthma Control in Children from a Developing Country
INVESTIGATORS	Dr Bilkisu G Illah.
DEPARTMENT	Dept of Paediatrics/Paediatric Pulmonology
DATE CONSIDERED	29/06/2012
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 29/06/2012 CHAIRPERSON .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof D Ballot

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX B

INFORMATION LEAFLET AND CONSENT FORM

Do home circumstances affect asthma control in children from a developing country?

Hello,

My name is Bilkisu Garba and I am a doctor at the Charlotte Maxeke Johannesburg Academic Hospital. I would like to invite you to consider taking part in a research study. Before agreeing to join the study, it is important that you read and understand the following explanation about the study.

PURPOSE OF THE STUDY

Home circumstances affect the way asthma is controlled. This study will look at

1 How many of the asthmatic children have their asthma well controlled (i.e. no cough, wheeze or shortness of breath).

2 What are the home factors that contribute to lack of good asthma control.

PROCEDURES

If you and your child agree to participate, you would both be asked to fill in a form about how you feel about your child's asthma which will be used to assess asthma control and also about your home, which will only take a few minutes. The doctor will assess your child's inhaler technique and how he/she uses the medications. Your child will be examined and then he/she would blow as hard and as fast as he/she can, few times into the lung function machine which is a machine that records amount of air your child can breathe out.

There is no risk involved in the study.

BENEFITS OF THE STUDY

It will improve our understanding of the extent of control in our asthmatic patients and the home factors that worsen asthma in our patients. We can give advice on what to avoid which may improve your child's asthma control.

VOLUNTARY PARTICIPATION

You can choose to allow your child to be part of this study or not and if you refuse, your child's care will not be affected in any way.

ETHICAL APPROVAL

This clinical study protocol has been submitted to the University of Witswatersrand Human Research Ethics Committee.

CONFIDENTIALITY

All the information on your child, your home and lung function result will be kept a secret.

INFORMED CONSENT FOR PARENTS/ LEGAL GUARDIANS

Bilkisu Garba has given me a copy of the Information leaflet and consent form regarding this study and has fully explained to me the meaning of the study.

She has given me a chance to ask any question about the study.

She has explained to me that I am free to refuse to join the study, and my child's future care will not be affected in any way.

I have understood everything that has been explained to me.

I, ----------, the parent/legal guardian of ----------

----------(name of child) consent for my child to participate in this study.

Parent/ legal guardian's signature or thumb print Date and time

---

Researchers signature Date and time

Witness Date and time

APPENDIX C

INFORMATION LEAFLET AND ASSENT FORM

Do home circumstances affect asthma control in children from a developing country?

Hello,

My name is Bilkisu Garba and I am a doctor at the Charlotte Maxeke Johannesburg Academic Hospital. I would like to invite you to consider taking part in a research study. Before agreeing to join the study, it is important that you read and understand the following explanation about the study.

PURPOSE OF THE STUDY

Home circumstances affect the way asthma is controlled. This study will look at

1 How many of the asthmatic children have their asthma well controlled (i.e. no cough, wheeze or shortness of breath).

2 What are the home factors that contribute to lack of good asthma control.

PROCEDURES

If you agree to help me, you would be asked to fill in a form on how you feel about your asthma which will be used to know about your asthma control and also about your home, which will only take a few minutes. If you are < 12 years, your parent will answer some of the questions. The doctor will look at how you use your inhalers and ask about your medications. You will be examine d and then blow as hard and as fast as you can few times into the lung function machine which is a machine that will record the air that you will blowout.

There is no risk involved in the study.

BENEFITS OF THE STUDY

It will improve our understanding of the extent of control in our asthmatic patients and the home factors that worsen asthma in our patients. We can give advice on what to avoid which may improve your asthma control.

VOLUNTARY PARTICIPATION

You can choose to be part of this study or not and if you refuse, your care will not be affected in any way.

ETHICAL APPROVAL

This clinical study protocol has been submitted to the University of Witswatersrand Human Research Ethics Committee.

CONFIDENTIALITY

All the information on you and lung function result will be kept a secret.

PARTICIPANT ASSENT(Children seven years and older)

Bilkisu Garba has told me all about the study.

She has given me a chance to ask any question about the study.

She has explained to me that I can choose to take part or not. This will not change the way I am looked after.

I have understood everything that has been explained to me.

I, ---------- (name of participant) want to take part.

Participants signature or thumb print Date and time

Researchers signature Date and time

Witness Date and time

APPENDIX D

PARENT/PATIENT QUESTIONNAIRE (<12 YEARS)

CHILDHOOD ASTHMA CONTROL TEST

Have your child complete these questions.

1.How is your asthma today?				
 Very Bad 0	 Bad 1	 Good 2	 Very Good 3	
2.How much of a problem is your asthma when you run, exercise or play sports?				
 It's a big problem, I can't do what I want to do. 0	 It's a problem and I don't like it. 1	 It's a little problem but it's okay 2	 It's not a problem. 3	
3. Do you cough because of your asthma?				
 Yes, all of the time. 0	 Yes, most of the time. 1	 Yes, some of the time. 2	 No, none of the time. 3	
4.Do you wake up during the night because of your asthma?				
 Yes, all of the time. 0	 Yes, most of the time. 1	 Yes, some of the time. 2	 No, none of the time. 3	

Please complete the following questions on your own.

5.During the last 4 weeks, how many days did your child have any daytime asthma symptoms?					
Not at all 5	1-3 days 4	4-10 days 3	11-18 days 2	19-24 days 1	Everyday 0
6.During the last 4 weeks, how many days did your child wheeze during the day because of asthma?					
Not at all 5	1-3 days 4	4-10 days 3	11-18 days 2	19-24 days 1	Everyday 0
7.During the last 4 weeks, how many days did your child wake up during the night because of asthma?					
Not at all 5	1-3 days 4	4-10 days 3	11-18 days 2	19-24 days 1	Everyday 0

Liu AH, Zeiger R, Sorkness C, Mahn T, Ostan N, Burgess S et al. Development and cross sectional validation of the childhood asthma control test. J Allergy Clin Immunol 2007;119:817-25.

APPENDIX E

PATIENT'S QUESTIONNAIRE (>12 YEARS)

ASTHMA CONTROL TEST

1.In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at school or home?					
All of the time	Most of the time	Some of the time	A little of the time	None of the time	
2.During the past 4 weeks, how often have you had shortness of breath?					
More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all	
3.During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning.					
4 or more nights a week	2 to 3 nights a week	Once a week	Once or twice	Not at all	
4.During the past 4 weeks, how often have you used your rescue inhaler or nebuliser medication (such as asthavent)?					
3 or more times /day	1 to 2 times /day	2 to 3 times a week	Once a week or less	Not at all	
5.How would you rate your asthma control during the past 4 weeks?					
Not at all	Poorly controlled	Somewhat controlled	Well controlled	Completely controlled	

Nathan AR, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P. Development of the asthma control test: a survey for assessment of asthma control. J Allergy Clin Immunol 2004;113(1):59-65.

APPENDIX F

DATA SHEET 1

HOME CIRCUMSTANCES, Please circle the appropriate answer.

TO BE COMPLETED BY ALL PATIENTS/PARENTS

1. Type of home	House	Flat	RDP	Shack
2. Smoking in home	Yes	No		
3. Pets in home	Yes	No		
If Yes	Dog	Cat	Hamster	Bird
4.Open flame cooking	Yes	No		
If Yes	Wood Paraffin Coal Dung Grass Crop residue			
5. Dust in home	Yes	No		
6.Carpet in bedroom	Yes	No		
7.Soft toys on bed	Yes	No		
8. Do you see` cockroaches	Yes	No		
9.Parental occupation/hobby				

APPENDIX G

DATA SHEET 2

CLINICAL INFORMATION

TO BE COMPLETED BY DOCTOR FOR ALL PATIENTS

Study No			Age		
Sex			Race		
Address					
Diagnosis of asthma					
History of recurrent cough/wheeze +					
1 Family hx of asthma			2 Presence of features suggestive of atopy		
3Reversible airway obstruction on spirometry or PEFR			4 Positive response to bronchodilators		
Compliance with medications and technique					
Correct inhaler technique	Yes	No	Adherence with medications	Yes	No
List of medications					
Dose of medications					
Examination					
Height(cm) centile			Weight(kg) centile		
Features of atopy					
Evidence of infection	Yes	No	Febrile	Yes	No
Distressed	Yes	No	Tachypnoeic	Yes	No
Hyperinflated	Yes	No	Wheeze	Yes	No
Lung Function test result					
PEF predicted	FEV_1 predicted		FEV_1/FVC predicted		

REFERENCES

1. Gern JE, Lemanske RF Jr. Infectious triggers of pediatric asthma. Pediatr Clin N Am 2003;50:555-575.

2. Motala C, Green RJ, Manjra AI, Potter PC, Zar HJ. For the South African Childhood Asthma Working Group. Guideline for the management of chronic asthma in children-2009 update. S Afr Med J 2009;4:255-269.

3. Guilbert T, Krawiec M. Natural history of asthma. Pediatr Clin N Am 2003;50:523-538.

4. Sharma GD, Gupta P. Asthma (PED). eMedicine. 2009. Available from http://www.medscape.com>. Accessed 21/02/2009.

5. Masoli M, Fabian D, Holt S, Beasley R. Global Burden of Asthma Report. In: Global Initiative for Asthma (GINA) 2004. Available from <http://www.ginasthma.org>. Accessed 17/07/2005.

6. Zar HJ, Ehrlich RI, Workman L, Weinberg EG. The changing prevalence of asthma,allergic rhinitis and atopic eczema in African adolescents from 1995 to 2002. Pediatr Allergy Immunol 2007;18;560-565.

7. Bush A, Saglani S. Management of severe asthma in children. Lancet 2010;376:814-825.

8. Papadopoulos NG, Arakawa H, Carlsen K-H, Custovic A, Gern J, Lemanske R et al. International consensus on (ICON) pediatric asthma. Allergy 2012;67:976–997.

9. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. Eur Respir J 1999;14:902-907.

10. Haughwey J, Price D, Kaplan A, Chrystyn H, Horne R, May N et al. Achieving asthma control in practice: understanding the reason for poor asthma control. Resp Med 2008;102(12):1681-1693.

11. Rabe KF, Adachi M, Lai CKW, Soriano JB, Vermeire PA, Weiss KB et al. Worldwide severity and control of asthma in children and adults: The global asthma insights and reality surveys. J Allergy Clin Immunol 2004;114:40-47.

12. Stanford RH, Gilsen AW, Ziemiecki R, Zhou X, Lincourt WR. Predictors of uncontrolled asthma in adult and pediatric patients: analysis of the Asthma Control Characteristics and Prevalence Survey Studies (ACCESS). J Asthma 2010;47(3):257-262.

13. Oviawe O. Asthma in children. In: Azubike JC, Nkanginieme KEO. Paediatrics and Child Health in a tropical region. 2nd ed. Owerri: African Educational Services; 2007 p.460-468.

14. Barnes PJ. Pathogenesis of asthma: a review. J R Soc Med 1983;76(7):580-586.

15. Okoromah CN, Oviawe O. Is childhood asthma under diagnosed and undertreated? Nig Postgrad Med J 2002;9(4):221-225.

16. Expert Panel Report: Guidelines for the diagnosis and management of asthma. NIH Publication No. 91-3642. Bethesda, MD: U.S. Department of

Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute National Asthma Education and Prevention Program. 1991. Available from< http://www.nhlbi.nih. gov/guidelines /asthma/asthgdln.pdf>. Accessed 5/02/2009.

17. Centre for disease control and prevention, asthma mortality and hospitalization among children and young adults: US 1980-1993. Morb and Mortal Wkly Rep 1996;45:350-353.

18. Campbell MJ, Cogman GR, Holgate ST, Johnston SL. Age specific trends in asthma mortality in England and Wales, 1983-95; results of an observational study. BM J 1997;314:1439-1441.

19. Wilmott R. In: Polin RA, Ditmar MF. Pediatric Secrets.4th ed. Philadelphia: Elsevier mosby; 2005. p .576-581.

20. Beasley R, Ellwood P, Asher I. International patterns of the prevalence of paediatric asthma. The ISAAC program. Pediatr Clin N Am 2003;50:539-553.

21. GINA pocket guide for asthma management and prevention in children. 2004. cited 2005 Jul 17. Available from http://www.ginasthma.org.

22. Guill MF. Asthma Update: Epidemiology and pathophysiology. Pediatr Rev 2004;25:299-305.

23. ISAAC steering committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjuctivitis and atopic eczema. Lancet 1998;351:1225-33.

24. Cookson WOC, Moffat MF. Asthma – an epidemic in the absence of an infection? Science. 1997;275(5296):41-42.

25. Obihara CC. Infection and atopic disease burden in African countries: key to solving the 'hygiene hypothesis'?. Curr Allergy Clin Immunol 2007;20(4):178-183.

26. Prescott SL. Promoting tolerance in early life: pathways and pitfalls. Curr Allergy Clin Immunol 2008;21(2):64-69.

27. Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. NIH publication no. 07-4051. Bethesda, MD: US. Department of Health and Human Services; National institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program. 2007. cited 2008 Nov 4. Available from http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.

28. Liu AH, Covar RA, Spahn JD, Leung DYM. Childhood asthma. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF. Nelson textbook of Paediatrics. 18th ed. Philadelphia: Saunders Elsevier; 2007. p.953-570

29. Motika CA, Papachristou C, Abney M, Lester LA, Ober C. Rising prevalence of asthma is sex specific in a US farming population. J Allergy Clin Immunol 2011;128:774-779.

30. Miller, RL. Breathing freely: the need for asthma research on gene environmental interactions. Am J Pub Hlth 1999;89(6):819-821.

31. Gern JE, Lemanske RF Jr, Busse WN. Early life origins of asthma. J Clin Invest 1999;104(7):837-843.

32. Van Eerdewegh P, Little RD, Dupuis J, Del Mastro RG, Falls K, Simon J et al. Association of ADAM 33 gene with asthma and bronchial hyperresponsiveness. Nature 2002;418:426-430.

33. Weis ST, Raby BA. Asthma Genetics 2003. Human Mol Genetics 2004;13(R1):R83-89.

34. Cookson WOC. Asthma Genetics. Chest 2002;121:75-135.

35. Koppelman GH, Sayers I. Evidence of a genetic contribution to lung function decline in asthma. J Allergy Clin Immunol 2011;128:479-484.

36. Els C, Boozaaier L, Green RJ. Atopy in asthmatic children attending a tertiary hospital in Pretoria. Curr Allergy Clin Immunol 2010;23(4):180-182.

37. Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. Pediatr 1985;75(5):859-868.

38. Carlsen KH, Orstarik I, Leegaard J. Respiratory virus infections and aeroallergens in acute bronchial asthma. Arch Dis Child 1984;59:310-315.

39. White DA. Asthma exacerbations – allergens or viruses? S Afr Respir J 2011;17(1):12-16.

40. Pattemore PK, Johnston SL, Bardin PG. Viruses as precipitants of asthma symptoms 1. Epidermiology. Clin Exp Allergy 1992;22:325-336.

41. Guilbert TW, Singh AM, Danov Z, Evans MD, Jackson DJ, Burton R, et al. Decreased lung function after preschool wheezing rhinovirus illnesses in

children at risk to develop asthma. J Allergy Clin Immunol 2011;128:532-538.

42. Thomas B, McDonald M, Ghildyal R, Bardin PG. Rhinovirus, allergy and asthma – what are some of the key questions. Curr Allergy Clin Immunol 2009;22(4):162-165.

43. Wark PAB, Gibson PG. Asthma exacerbations.3: pathogenesis. Thorax 2006;61:909-915.

44. Kelly WF, Oppenheimer JJ, Argyros GJ. Allergic and environmental asthma. eMedicine. 2009. cited 2009 May 2. Available from http://www.medscape.com.

45. Bardin PG, Johnston SL, Pattermore PK. Viruses as precipitants of asthma symptoms II (physiology and mechanism). Clin Exper Allergy 1992;22(9):809-822.

46. Huss K, Adkinson NF Jr, Eggleston PA, Dawson C, Van Natta ML, Hamilton RG. House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the childhood Asthma management programme. J Allergy Clin Immunol 2001;107(1):48-54.

47. Hylkema MN, Blacquiere MJ. Intrauterine effects of maternal smoking on sensitization, asthma and chronic obstructive pulmonary disease. Proc Am Thorac Soc 2009;6:660-662.

48. Harding R, Snibson K, O'Reiley M, Martin G. Early environmental influences on lung development: implication for lung function and respiratory health throughout life. In: Newnham JP, Ross MG. Early life

origins of human health and disease. Los Angeles. Basel, Karger. 2009.p.78-88.

49. Strachen DP, Cook DG. Parental smoking and childhood asthma: longitudinal and case control studies. Thorax 1998;53:204-212.

50. Szefler SJ. Advances in pediatric asthma in 2011: moving forward. J Allergy Clin Immunol 2012;129:60-68.

51. National Asthma Council Australia. Asthma management handbook. 2006. cited 2007 Jul 19; [1-157]. Available from http://www.nationalasthma.org.au.

52. Strachan D, Warner J, Pickup J, Schweigher M, Pennington H, Jones M et al. Are we too clean? Health and Hygiene Supplement 2003;3:1-12.

53. Hill M, Szelfer SJ, Larsen GL. Asthma pathogenesis and the implications for therapy in children. Pediatr Clin N Am 1992;39:1205-1223.

54. Kelly HW. The assessment of childhood asthma. Pediatr Clin N Am 2003;50:593-608.

55. Barnes PJ. Pathophysiology of asthma. Br J Clin Pharmacol 1996;42:3-10.

56. Castro-Rodriguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. Am J Respir Crit Care Med 2000;162:1403-1406.

57. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ and the group health medical associates. Asthma and wheezing in the first six years of life. NEJM 1995;332(3):133-138.

58. Brand PLP, Baraldi E, Bisgaard H. Definition, assessment and treatment of wheezing disorders in preschool children:an evidence based approach. Eur Respir J 2008;32:1096-1110.

59. Cockroft DW, Swystun VA. Asthma control versus asthma severity. J Allergy Clin Immunol 1996;98:1016-1018.

60. Gustafsson PM, Watson L, Davis KJ, Rabe KF. Poor asthma control in children: evidence from epidemiological surveys and implications for clinical practice. Int J Clin Pract 2006;60(3):321–334.

61. Humbert M, Holgate S, Boulet LP, Bousquet J. Asthma control or severity: that is the question. Allergy 2007;62:95–101.

62. Değer L, Plante C, Goudreau S, Smargiassi A, Perron S, Robert L et al. Home environmental factors associated with poor asthma control in Montreal children: A population-based study. J Asthma 2010;47(5):513-520.

63. Green RJ. Asthma control- is there a problem. S Afr Fam Pract 2006;48(4):32-36.

64. Green RJ, Luyt DK. Clinical characteristics of childhood asthmatics in Johannesburg. S Afr Med J 1997;87:878-882.

65. Greenblatt M, Galpin JS, Hill C, Feldman C, Green RJ. Comparison of doctor and patient assessments of asthma control. Respir Medicine 2010;104(3):356-361.

66. Liu AH, Gilsenan AW, Stanford RH, Lincourt W, Ziemiecki R, Ortega HJ. Status of Asthma Control in Pediatric Primary Care: Results from the

Pediatric Asthma Control Characteristics and Prevalence Survey Study (ACCESS). J Pediatr 2010;157:276-281.

67. Hammer SC, Robroeks CMHHT, van Rij C, Heynens J, Droog R, Jo¨ bsis Q et al. Actual asthma control in a paediatric outpatient clinic population: Do patients perceive their actual level of control? Pediatr Allergy Immunol 2008; 19:626–633.
68. Halterman JS, Auinger P, Conn KM, Lynch K, BA, Yoos HL, Szilagyi PG. Inadequate Therapy and Poor Symptom Control among Children with Asthma: Findings from a Multistate Sample. Ambulatory Pediatrics 2007;7:153–159.
69. Larsson ML, Frisk M, Hallström J, Kiviloog J and Lundbäck B. Environmental Tobacco Smoke Exposure During Childhood Is Associated With Increased Prevalence of Asthma in Adults. Chest 2001;120(3):711-717.
70. Cook DG, Strachan DP. Summary of effects of parental smoking on the respiratory health of children and implications for research. Thorax 1999;54:357–366.
71. Finkelstein JA, Fuhlbrigge A, Lozano P, Grant EN, Shulruff R, Arduino KE et al. Parent reported environmental exposures and environmental control measures for children with asthma. Arch Pediatr Adolesc Med 2002;156:258-264.
72. Kamenov SP, Kamenov A, Kamenov.B. Parental knowledge and education, key factors in childhood asthma control. Oral presentation, 4437. 16/09/2009. Cited 02/02/13.

73. McGhan SL, MacDonald C, James DE, Naidu P, Wong E and Hessel PA. Factors associated with poor asthma control in children aged five to 13 years. Can Respir J. 2006;13(1):23–29.

74. Mc Leish AC, Zvolensky MJ. Asthma and cigarette smoking: A review of the empirical literature. J Asthma 2010;47(4):345-361.

75. Perez-Padilla R, Schilmann A, Riojas-Rodriguez H. Respiratory health effects of indoor air pollution. Int J Tuberc Lung Dis 2010;14(9):1079-1086.

76. Bruce N, Perez-Padilla R, Albalak R. Indoor air pollution in developing countries: a major environmental and public health challenge. Bull World Health Organ 2000;78:1078-1092.

77. Rehfuess E, Mehta S, Pruss-Ustun A. Assessing household solid fuel use: multiple implications for the Millennium Development Goals. Environ Health Perspect 2006;114:373–378.

78. Norman R, Barnes B, Mathee A, Bradshaw D. Estimating the burden of disease attributable to indoor air pollution from household use of solid fuels in South Africa in 2000 and the South African Comparative Risk Assessment Collaborating Group. SAMJ 2007;97(8):769-771.

79. Gemert F, Van der Molen T, Rupert J, Chavannes N. The impact of asthma and COPD in sub-saharan Africa. Prim Care Respir J 2011;20(3):240-248.

80. Mishra V. Effect of indoor air pollution from biomass combustion on prevalence of asthma in elderly. Environmental Health Perspectives 2003;111:71-77.

81. Census 2011. Census in brief. Statistics South Africa. Pretoria: Statistics South Africa, 2011. Available from <http//www.ststsa.gov.za>. [Accessed 02/02/2013].

82. Census 2001. Census in brief. Statistics South Africa. Pretoria: Statistics South Africa, 2003. Available from <http//www.statssa.gov.za>. [Accessed 03/08/2012].

83. Azizi BH, Zulkifli HI, Kasim S. Indoor air pollution and asthma in hospitalized children in a tropical environment. J Asthma 1995;32(6):413-418.

84. Rosenstreich DL, Eggleston P, Kattan M, Baker D, Slavin RG, Gergen P et al for the National Cooperative Inner-City Asthma Study. N Engl J Med 1997;336:1356-1363.

85. Potter PC, Lee S, Roodt L. Cockroach allergy in South Africa; coastal vs inland. Curr Allergy Clin Immunol 1998;16-17.

86. Manjra A, Prescott R, Potter PC. Cockroach allergy in Durban. Curr Allergy Clin Immunol 1995;8:3-7.

87. Lopata AL, Jeebhay MF, Groenewald M, Manjra A, du Toit G, Sibanda EN et al. Sensitisation to three cockroach species in Souther Africa. Curr Allergy Clin Immunol 2005;18(2);62-66.

88. Seedat RY, Claassen J,Claassen AJ, Joubert G. Mite and cockroach sensitisation in patients with allergic rhinitis in Free state. S Afr Med J 2010,100:160-163.

89. Bateman ED, Hurd SS, Barnes PJ, et al. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 2008;31:143–178.

90. Bateman ED, Boushey HA, Bousquet J, et al. Can guideline-defined asthma control be achieved? The gaining optimal asthma control study. Am J Respir Crit Care Med 2004;170:836–844.

91. Bateman ED, Clark TJH, Frith L, Bousquet J, Busse WW, Pedersen SE. Rate of response of individual asthma control measures varies and may overestimate asthma control: an analysis of the goal study. J Asthma 2007;44:667–673.

92. Dahl R, Lundback B. Assessment of asthma control and its impact on optimal treatment strategy. Allergy 2007;62:611-9.

93. Green RJ, Klein M. What is meant by control of childhood asthma? CME 2010;28(9):408-410.

94. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: Reliability, validity and responsiveness in patients not previously followed by asthma specialists. J Allergy Clin Immunol 2006;117:549-556.

95. Friedlander J, Williams AR, Portnoy J, Lynch DA, Sherman A, Dinakar C. Association of ACT and Childhood ACT Scores with FEV1 in Primary and Specialty Clinics using the Asthma Control Tracker _ Web-Based Registry. J Allergy Clin Immunol 2009;123(Suppl 2):S48.

96. Liu AH, Zeiger R, Sorkness C, Mahn T, Ostan N, Burgess S et al. Development and cross sectional validation of the childhood asthma control test. J Allergy Clin Immunol 2007;119:817-825.

97. Donnell A. Measuring Asthma Control with Patient-Completed Questionnaires. Chicago Family Asthma & Allergy, SC Children's

Community Physicians Association Member. 09/09/2009. Cited 06/02/2012.

98. Nathan AR, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P. Development of the asthma control test: a survey for assessment of asthma control. J Allergy Clin Immunol 2004;113(1):59-65.

99. Juniper EF, Guffydd-Jones K, Ward S, Svensson K. Asthma control questionnaire in children: validation, measurement properties, interpretation. Eur Respir J 2010;36:1410-1416.

100. Skinner EA, Diette GB, Algatt-Bergstrom PJ, Nguyen TTH, Clark RD, Markson LE et al. The Asthma Therapy Assessment Questionnaire (ATAQ) for children and adolescents. Dis Manage 2004;7(4):305-313.

101. Murphy KR, Zeiger RS, Kosinski M, Chipps B, Mellon M, S Michael et al. Test for Respiratory and Asthma Control in Kids (TRACK): A caregiver-completed questionnaire for preschool-aged Children. J Allergy Clin Immunol 2009;123:833-839.

102. Ducharme FM, Davis GM, Noya F, Rich H Ernst P. The Asthma Quiz for Kidz: a validated tool to appreciate the level of asthma control in children. Can Respi J 2004;11(8):541-546.

103. Lara M, Duan N, Sherbourne C, Lewis M, Landon C, Halfon N et al. Differences between child and parent reports of symptoms among latino children with asthma. Pediatrics 1998;102:68.

104. Guyatt GH, Juniper EF, Griffith LE, Feeny DH, Ferrie PJ. Children and adult perceptions of childhood asthma. Pediatrics 1997;99:165-168.

105. Yawn BP, Brenneman SK, Allen-Ramey FC, Cabana MD, Leona E. Markson, Assessment of Asthma Severity and Asthma Control in Children Pediatrics 2006;118(1):322-329.

106. Cloutier MM, Schatz, M, Castro M, Clark N, Kelly HW, Mangione-Smith R, et al. Asthma outcomes: Composite scores of asthma control J Allergy Clin Immunol 2012;129:S24-33.

107. Thomas M, Gruffydd-Jones K, Stonhame C, Ward S, Macfarlaneg T. Assessing asthma control in routine clinical practice: use of the Royal College of Physicians '3 Questions.' Primary Care Respiratory Journal 2009;18(2): 83-88.

108. LeBlanc A, Robichaud P, Lacasse Y, Boulet LP. Quantification of asthma control: validation of the Asthma Control Scoring System. Allergy 2007:62:120–125.

109. Hallstrand TS, LoGerfo JP, Williams BL, Hummel JP, Martin DP. Initial test of the Seattle Asthma Severity and Control Questionnaire: a multidimensional assessment of asthma severity and control. Ann Allergy Asth Immunol 2009;103(3):225-232.

110. Rabe KF, Vermeire PA, Soriano JB, Maier WC. Clinical management of asthma in 1999: the Asthma Insights Reality in Europe (AIRE) study. Eur Respir J 2000;16:802-807.

111. Green RJ, Klein M, Becker P, Halkas A, Lewis H, Kitchin O et al. Disagreement Among Common Measures of Asthma Control in Children. Chest 2013;143(1):117-122.

112. Holt S, Klijakovic M, Reid J for the POMS steering committee. Asthma morbidity, control and treatment in New Zealand: results of the

Patients Outcomes Management Survey (POMS) 2001. N Z Med J 2003;116: U436.

113. Herjavecz I, Nagy GB, Gyurkovits K, Magyar P, Dobos K, Alemao et al. Cost, morbidity, and control of asthma in Hungary: the Hunair study. J Asthma 2003;40:673–681.

114. Moeller A, Steurer-Stey C, Suter H, Hofer M, Peter M, Brooks-Wildhaber J et al. Disease control in asthmatic children seen in private practice in Switzerland. Current Med Opin Research 2006;22(7):1295-1306.

115. Lai CKW, de Guia TS, Kim Y, Kuo SH, Mukhopadhyay A, Soriano JB. Asthma control in the Asia-Pacific region: The asthma insights and reality in Asia-Pacific study. J Allergy Clin Immunol 2003;111(2):263-268.

116. Adachi M, Morikawa A, Ishihara K. Asthma insights and relity in Japan (ARIJ). Arerugi 2002;51:411-420.

117. Enright PL, Stoller JK, Hollingsworth H. Office spirometry. Up to date. Last updated Jan 23, 2012. Cited 20/02/2012.

118. Demographics of South Africa. Wikepedia the free encyclopedia. Available from <http//www.wikepedia.org>. [Accessed 02/20/2013].

119. Kuehni CE, Frey U. Age-related differences in perceived asthma control in childhood: guidelines and reality. Eur Respir J 2002;20:880-889.

120. Ho J, Bender BG, Gavin LA, O'Connor SL, Wamboldt MZ, Wambolt FJ. Relations among asthma knowledge, treatment adherence and outcome. J Allergy Clin Immunol 2003;111:498-502.

121. Smith LA, Bokhour B, Hohman KH, Miroshnik I, Cohn E, Kleinman KP et al. Modifiable Risk Factors for Suboptimal Control and Controller

Medication Underuse Among Children with Asthma. Pediatrics 2008;122:760–769.

122. Bosquet J and the ARIA workshop group. Management or allergic rhinitis and its impact on asthma (ARIA) pocket guide. A pocket guide for physicians and nurses 2001. J Allergy Clin Immunol 2001;108(5):S147-S330.

123. De Groot EP, Nijkamp A, Duiverman EJ, Bard PLP. Allergic rhinitis is associated with poor asthma control in children with asthma. Thorax 2012;67(7):582-587.