SELECTED SOCIODEMOGRAPHIC AND DRUG ADHERENCE FACTORS ASSOCIATED WITH UNCONTROLLED ASTHMA AT CHEST CLINIC, KENYATTA NATIONAL HOSPITAL.

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE AT THE UNIVERSITY OF NAIROBI

BY

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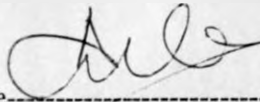SCHOOL OF MEDICINE, UNIVERSITY OF NAIROBI

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DECLARATION

DECLARATION BY THE CANDIDATE.

I hereby declare that this dissertation is my original work and has not been presented for a degree or research in any other university or institution.

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LIST OF ABBREVIATIONS.

A&E	Accident and Emergency
AAFB	Acid-alcohol-fast bacilli
ACQ	Asthma Control Questionnaire
ACSS	Asthma Control Scoring System
ACT	Asthma Control Test
AHR	Antihyaluronidase Reaction.
AIDS	Acquired Immunodeficiency syndrome
AIRE	Asthma Insights and Reality in Europe.
ATAQ	Asthma Therapy Assessment Questionnaire
BMI	Body Mass Index
CBA	Chocolate blood agar
COPD	Chronic Obstructive Airways Disease.
ECRHS	European Community Respiratory Health Survey
ENFUMOSA	European Network for Understanding Mechanisms of Severe Asthma.
ENHWS	European National Health and Wellness Survey
FeNO	Fraction of Exhaled Nitric Oxide
FEV_1	Forced Expiratory Volume in one second.
FVC	Forced Vital Capacity
GINA	Global initiative for Asthma
GOAL	Gaining Optimal Asthma Control
HDU	High Dependency Unit
HIV	Human Immunodeficiency Virus
ICS	Inhalational Corticosteroid
ICU	Intensive Care Unit
INSPIRE	Investigating New Standards for Prophylaxis in Reduction of Exacerbations
KNH	Kenyatta National Hospital
LABA	Long-Acting B_2 agonist.
LJ	Lowenstein-Jensen
MAQOL	Mini asthma Quality of life Questionnaire

NAEPP	National Asthma Education and Prevention Program.
NHLBI	The National Heart, Lung, and Blood Institute.
NO	Nitrous Oxide
PAF	Platelet-Activating Factor.
PEFR	Peak Expiratory Flow Rate
PFTs	Pulmonary Function Tests.
PGL	Prostaglandin
PI	Principal Investigator
RBS	Random blood sugar
REACT	Real-world Evaluation of Asthma Control and Treatment
SABA	Short-Acting B_2 agonist.
TB	Tuberculosis
TC	Total Control
WC	Well Controlled
WHO	World Health Organization

ABSTRACT.

Background: Factors influencing asthma control include patient adherence with prescribed medications and sociodemographic characteristics. The prevalence of uncontrolled asthma and factors that affect asthma control have not been explored at Kenyatta National Hospital (KNH).

Study Objectives: To determine the level of asthma control in adults at KNH chest clinic and determine selected sociodemographic and drug adherence factors associated with the level (s) of control achieved.

Study Design: A descriptive cross-sectional study.

Study site: KNH Chest Clinic.

Patients: Asthmatic patients aged more than 13 years, on follow up for asthma for more than 6 months prior to study commencement.

Materials and Methods: Patients' clinical data, asthma control and treatment modalities data were collected using a standard validated Asthma Control Questionnaire and a proforma.

Primary outcome: A composite value of the rates and profile of subjects with either well-controlled or poorly controlled asthma.

Secondary outcomes: The factors associated with either well-controlled or poorly controlled asthma among the study subjects and the drug treatment modalities used for asthma control.

Data analysis: Was done using SPSS version 16.0. Qualitative variables were summarized with numbers and frequency distributions. Quantitative variables were summarized with means, standard error, median, minimum and maximum. A multivariate analysis was performed (logistic regression including the following factors in the model: age, sex, education level, asthma control, drug adherence status, and number of drugs at inclusion.

Results: Three hundred and sixty asthma patients with a mean age of 44.9 years (17.7 years SD); ranging from 13 to 100 years. Majority were female (75.3%) and with secondary level of education (39.2%). Most patients were uncontrolled for their disease (64.7%) and there were no statistically significant differences between the socio-demographic characteristics (sex, age and educational level) and asthma control. Eighty five point eight percent (85.8%) of the patients were adherent to the drugs prescribed and patients that did not adhere to the prescribed medications cited lack of money (83.7%) and forgetfulness (67.4%) as the commonest reasons for their non-adherence. The commonest drug used was inhalational corticosteroid (budesonide)

(94.7%) followed by short-acting B_2-agonist inhaler (92.5%). A greater part of the patients were on combination therapies of 2 (58.5%) and 3 (25.8%) drugs with the commonest drug combinations being inhalational corticosteroid with short-acting B_2 –agonist. Patient adherence to the treatments given and the number of drug combination regimens the patient was taking were the key determinants of overall asthma control on this clinic (p-value=0.004 and 0.005 respectively).

Conclusion: Most patients with asthma at KNH chest clinic were uncontrolled. Majority of the sufferers who were uncontrolled were aged between 30-60 years and more likely to use multiple drugs (combination therapy of two or three drugs). More than 84% of them were adherent to their drugs. The two chief predictors of poor asthma control were the number of drugs the individual patient was taking and the drug adherence status.

CHAPTER ONE.

1.0 INTRODUCTION AND BACKGROUND.

Asthma is a chronic inflammatory disease of airways that is characterized by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli (1). Asthma affects 5 to 6 % of the world's population and people of all ages are affected (1). When uncontrolled, asthma can place severe limits on daily life, and sometimes cause permanent lung damage (1, 2). It is a complex disease because its presence as well as control is influenced by a large number of genetic factors (3) as well as a wide range of both allergic and nonallergic factors (4, 5, and 6). The final expression of a patient's asthma symptoms, as well as their severity, may be affected not only by their genetic predisposition, but also by the timing and intensity of their environmental exposures to certain triggers as well as the presence or absence of certain co-morbidities (4, 5, and 6).

Uncontrolled asthma is common and an under-recognized health problem that has significant impact on patients and their families (2, 7). This is because uncontrolled asthma results in missed school days and missed work, more emergency room visits, more hospitalizations, and life-threatening asthma attacks. However, this is a problem that can be overcome through sound application of pharmacologic and nonpharmacologic intervention strategies (2, 7).

In 1993, the Global Initiative for Asthma (GINA) was formed. Its goals and objectives were described in a 1995 National Heart, Lung, and Blood Institute and World Health organization (NHLBI/WHO) Workshop Report, Global Strategy for Asthma Management and Prevention. In January 2004, the GINA Executive Committee recommended that the Global Strategy for Asthma Management and Prevention be revised to emphasize asthma management based on clinical control, rather than classification of the patient by severity (2, 8). This shift in the pattern for asthma care reflects the progress that has been made in the care of asthma patients. The role of the health care professional in these new guidelines is to establish each patient's current level of treatment and control, and then adjust treatment to gain and maintain control. This means that asthma patients should experience no or minimal symptoms (including night awakening), have no limitations on their activities (including physical exercise), have no (or minimal) requirement

for rescue medications, have near normal lung function, and experience only very infrequent exacerbations (2, 8).

Since the publication of the GINA guidelines on asthma control, epidemiologic studies have repeatedly proven that the natural history and control of asthma is in some ways predictable through examination of the associated risk factors (5, 9). Major factors that can influence the severity and persistence of asthma are genetics, atopy, environmental pollution, tobacco smoke, gastroesophageal reflux, use of non-steroidal anti-inflammatory drugs (NSAIDS) or aspirin, Body Mass Index (BMI), rhino sinusitis and respiratory infections, among others. Early identification of patients at risk for persistent asthma, combined with early institution of pharmacologic and nonpharmacologic intervention strategies, has resulted in better outcomes (5, 9).

Another major factor associated with poor control of asthma has been identified as non adherence to drugs plus other treatment regimens which could either be due to difficulties with inhaler devices, awkward regimes (e.g., four times daily inhalations or multiple drugs), side effects of the drugs, cost of medication, dislike of medication, lack of appropriate drugs in pharmacies, stigmatization due cultural or religious issues, forgetfulness or complacency and improper inhalational techniques (10). Improving adherence to asthma medications has resulted in better outcomes in asthma control (5, 9, and 10).

Some studies have further shown that if airway remodeling is related to duration of asthma, then when matched for disease control, the airways of older adults should show greater alterations than the airways of younger adults, hence poor asthma control in adults but this has not been evaluated in our set up (11).

To evaluate asthma control, a number of tools have been designed, validated and applied in different settings. Some of these instruments include the Asthma Control Questionnaire (ACQ) (*Appendix 2*) (*2, 12, and 13*). It is a 7-item questionnaire, but a 6-item shorter version is also available, and has been validated to measure the goals of asthma management as defined by international guidelines for asthma control: (minimization of day- and night-time symptoms,

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minimization of activity limitation, minimization of beta$_2$-agonist use and minimization of bronchoconstriction and wheezing). The final item on this questionnaire is on lung function test (FEV$_1$ or PEFR). Responses on the ACQ are given on a 7-point scale and the overall score is the mean of the responses (0=totally controlled, 6=severely uncontrolled) (*2, 12, 13*).

Despite the shift in asthma management, the Kenyan guidelines have not changed to reflect these new guidelines in asthma management. It is not easy therefore to tell the level of asthma control at Kenyatta National Hospital (KNH) chest clinic in Nairobi Kenya because no study has ever been done to show this. This is why this study was designed to document the level of asthma control at KNH and determine pharmacologic and sociodemographic factors associated with the poorly controlled asthmatics.

CHAPTER TWO.

2.0 LITERATURE REVIEW.
21. A. INTRODUCTION.

Asthma is a chronic inflammatory disease of the airways with widespread but variable airflow obstruction in response to a variety of stimuli (1, 15, and 16). Airflow obstruction in asthma is usually reversible, either spontaneously or with treatment, though remodeling may lead to irreversible structural changes of the airways in the long run (1, 17).

Since the publication of the GINA guidelines on asthma management in 2002, clinical trials show that asthma can be controlled in the majority of patients, but poorly controlled asthma still imposes a considerable burden *(2, 12)*. Control of asthma is dependent on a number of factors which broadly revolve around the behavior of both healthcare professionals and patients. A key confront for healthcare professionals is to help patients to employ self-management behaviors with optimal adherence to appropriate treatment, whereas patients are expected to comply with the treatment given as well as avoid the triggers for asthma *(2, 10)*.

Clinical factors involved in asthma control not only include exposure to environmental triggers, but also adherence to drugs given, treatment of concomitant morbidities such as rhino sinusitis, obesity, gastro esophageal reflux disease (GERD), emotional stress and other atopic diseases affecting the respiratory tract all of which are important *(15, 16, 17)*. These patient factors if not addressed reduce the efficacy of treatment. Perceptual barriers to adherence include being skeptical about the need for treatment when symptoms are absent and concerns about adverse effects of drugs or not being able to use the inhalational medicines properly. Under-treatment may also be related to patients' underestimation of the significance of symptoms, and lack of knowledge of achievable control or lack of money to purchase the correct medications *(15, 16, and 17)*.

B. PREVALENCE AND AETIOLOGY OF UNCONTROLLED ASTHMA.

PREVALENCE.

Uncontrolled asthma affects an estimated 300 million people worldwide and the burden is likely to rise substantially in the next few decades (2, 18). Estimates of the prevalence of uncontrolled asthma range from 7% in France and Germany to 11% in the USA and 15-18% in the United Kingdom. Approximately 20% of these patients have severe asthma and it is well known that patients with inadequately controlled severe persistent asthma are at a particularly high risk of exacerbations, hospitalization and death, and often have severely impaired quality of life (10, 18, 19). There are no studies conducted so far to show the prevalence of uncontrolled asthma in Kenya.

AETIOLOGY AND PATHOGENESIS OF UNCONTROLLED ASTHMA.

Asthma is a heterogeneous disease and genetic (atopic) and environmental factors, such as viruses, occupational exposures, and other allergens, contribute to its initiation and continuance (1, 5, 20). Atopy is the single largest risk factor for the development of asthma (5). Allergic asthma is often associated with a personal and/or family history of allergic diseases such as rhinitis, urticaria, and eczema; with positive wheal-and-flare skin reactions to intradermal injection of extracts of airborne antigens; with increased levels of IgE in the serum; and/or with a positive response to provocation tests involving the inhalation of specific antigen (5).

A significant fraction of patients with asthma however, present with no personal or family history of allergy, with negative skin tests, and with normal serum levels of IgE, and therefore have disease that cannot be classified on the basis of currently defined immunologic mechanisms. These patients are said to have idiosyncratic asthma or nonatopic asthma. Other patients have disease that does not fit clearly into either of the preceding categories but instead fall into a mixed group with features of each. In general, asthma that has its onset in early life tends to have a strong allergic component, whereas asthma that develops late tends to be nonallergic or to have a mixed etiology (17, 18, and 20).

The pathogenesis of uncontrolled asthma results from a status of persistent sub-acute inflammation of the airways. Even in asymptomatic patients, the airways can be edematous and

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infiltrated with eosinophils, neutrophils, and lymphocytes, with or without a rise in the collagen content of the epithelial basement membrane. These changes may persist despite treatment and time and again do not relate to the severity of the disease (1, 12, 18). Thus, the physiologic and clinical features of asthma derive from an interaction among the resident and infiltrating inflammatory cells in the airway surface epithelium, inflammatory mediators, and cytokines (1, 8, and 20). The cells thought to play important parts in the inflammatory response are mast cells, eosinophils, lymphocytes, and airway epithelial cells. Each of the major cell types can contribute mediators and cytokines to initiate and amplify both acute inflammation and the long-term pathologic changes (1, 8, and 20).

The mediators released by the cells produce an intense, immediate inflammatory reaction involving bronchoconstriction, vascular congestion, edema formation, increased mucus production, and impaired mucociliary transport. This results in airway narrowing and causes symptoms such as wheezing, shortness of breath, chest tightness, and coughing. The airway constriction responds to bronchodilators and the degree of airway narrowing as well as the response to therapy can be measured by peak expiratory flow (PEF) and spirometry (1, 8, and 20). Other elaborated chemotactic factors (eosinophil and neutrophil chemotactic factors of anaphylaxis and leukotriene B_4) also bring eosinophils, platelets, and polymorphonuclear leukocytes to the site of the reaction. Thus the airway epithelium is both the target of, and a contributor to, the inflammatory cascade and this tissue both amplifies bronchoconstriction and promotes vasodilatation through the release of compounds such as cytokines, growth factors, nitric oxide (NO), prostaglandins (PGLs) and endothelin-1 (8,20). The intense local event that occurs could then be followed by a more chronic one leading to chronic asthma (8, 20).

Asthma control therefore refers to control of the manifestations of disease through reduction of inflammation and bronchoconstriction. Ideally, this should apply not only to reduction in the clinical manifestations of the disease, but also to laboratory markers of inflammation (such as sputum eosinophils and fraction of exhaled nitric oxide, FeNO) and pathophysiological features of the disease as well (8, 17, 18, 21 and 22). There is as a consequence enough evidence that reducing inflammation with controller therapy achieves clinical control, but because of the cost and/or general unavailability of tests such as endobronchial biopsy and measurement of sputum

eosinophils and exhaled nitric oxide **(8, 17, 21, 22),** it is recommended that treatment be aimed at controlling the clinical features of disease; including lung function abnormalities **(25).** *Table 1* **below** provides the characteristics of controlled and uncontrolled asthma as defined by the GINA guidelines **(2).**

COMMON CAUSES OF POOR ASTHMA CONTROL.

There are many reasons why asthma may be poorly controlled, and these can be broadly grouped into clinical and behavioral. Important clinical factors include the genetic and sociodemographic characteristics of the individual, type of asthma (allergic or nonallergic), co-morbidity (e.g. dysfunctional breathing, allergic rhinitis) **(24, 25).** The behavior of both clinicians and patients is also a key determinant of the level of asthma control achieved.

The behavior of clinicians is not only useful in making an accurate diagnosis and prescribing the best treatment but also in carrying out appropriate review of progress and subsequent control **(25, 26).** Healthcare professionals may have limited awareness of symptom prevalence. In the AIRE (Asthma Insights in Real Life) study, general practitioners substantially underestimated the prevalence of asthma symptoms **(25, 27).** Furthermore, healthcare professionals may have difficulties estimating levels of asthma control **(28, 29).** Clearly, there is a need for healthcare professionals to appreciate the widespread occurrence of poor asthma control **(29).**

Patient behaviors affect the level of asthma control by influencing adherence to treatment and other self-management behaviors such as smoking, **(26, 27, and 30).** Patients' may also fail to consult their doctor as reported in one UK survey in which found that 10% of asthmatic patients had seen no health professional about asthma in the previous 3 years **(30).**

Among all these factors that influence asthma control, drug adherence is a major factor that can be addressed through proper patient education **(30).** International recommendations recognize patient adherence to prescribed treatment as an important aspect of a treatment's evaluation, but this issue is little assessed **(31).** Lack of adherence to prescribed medications is common among asthma patients and the common reasons for non-adherence include forgetfulness, prescription not collected or not dispensed, purpose of treatment not clear, perceived lack of effect, real or perceived side-effects, instructions for administration not clear (e.g. poor inhalation techniques), physical difficulty in complying (e.g. opening medicine containers, handling small tablets,

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swallowing difficulties, travel to place of treatment), unattractive formulation, such as unpleasant taste, complicated regimen (such as 4-hourly regimens) and cost of drugs.

Patient adherence to asthma treatments as a major factor in asthma control.

Patient adherence to the treatments given is a key determinant of asthma control (31, 32). Poor adherence means that patients may not take the medications they have been prescribed, contributing to poor disease control and this can happen regardless of age, gender and socioeconomic status of patients, and type and severity of disease. Non-adherence rates of over 30% have consistently been noted across chronic asthma and with even higher rates of nonadherence to inhaled corticosteroids (33, 33). Non-adherence may be lower for more complex regimens, but significant non-adherence remains even when the frequency of dosing is reduced (33, 34). Furthermore, providing clear information – although essential – is not enough to guarantee adherence (34).

Nonadherence to any drug is consequently best thought of as a variable action, rather than a mannerism characteristic: most people are nonadherent some of the time and nonadherence can have both intentional and unintentional causes (10, 35, and 36). Unintentional nonadherence arises from capacity and resource limitations that prevent patients from implementing their decisions to follow treatment recommendations and involves individual constraints (e.g. poor inhaler technique, problems remembering doses etc) and aspects of their environment (e.g. problems of accessing prescriptions, cost, competing demands etc). Intentional nonadherence arises from the beliefs, attitudes and expectations that influence patients' motivation to begin and persist with the treatment regimen (34, 35, and 36).

This failure of patients to adhere to physician-prescribed regimens, either pharmacologic or behavioral, has been well documented as a common cause of poorly controlled asthma (36). Medication regimens for asthma care are particularly vulnerable to adherence problems because of their duration of use, the use of multiple medications, and the periods of symptom remission and inhalational medications are likely to be missed than oral drugs. As reported in one study, adherence to preventive therapy, like inhaled corticosteroids, is especially problematic since the patients do not notice an immediate effect of taking the drugs (34, 38, and 39). The clinical effects of nonadherence by asthmatic patients include treatment failure, unnecessary and

dangerous intensification of therapy, and costly diagnostic procedures, complications, and hospitalizations (37, 38, and 39).

Although the measurement of adherence is an important component of both medical and behavioral interventions to control asthma, relatively little research has directly addressed this issue when assessing asthma control (37, 38, and 39), and in Kenya, there are no studies done so far to show the level of disease control and the associated factors.

C. DIAGNOSING UNCONTROLLED ASTHMA.

The diagnostic tools used to determine if a patient's asthma is well or poorly controlled include history, physical examination, pulmonary function testing, and other laboratory evaluations that evaluate the degree of lower airway inflammation (41, 42).

1. HISTORY.

Asthma may develop at any age, although new-onset asthma is less frequent in the elderly compared to other age groups. Asthma is diagnosed before the age of seven years in approximately 75 percent of cases (1, 41). The historical information that is relevant to disease control includes the following:

Characteristic symptoms — History of respiratory symptoms such as daytime symptoms (twice or more/week), limitations of activities (e.g. missed school or work days), nocturnal symptoms/awakening at night, need for reliever/rescue treatment and severe acute exacerbations requiring admission to hospital all indicate poorly controlled disease (1, 41). Personal history of nonadherence and frequent side-effects from drugs is also a pointer to poorly controlled asthma (1, 41, and 42).

2. PULMONARY FUNCTION TESTING.

Pulmonary function tests are critical tools in the diagnosis and monitoring of asthma. Measurement of peak expiratory flow rate and spirometry are the two pulmonary function tests most often used in the diagnosis and monitoring of asthma control (44, 45).

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I. Peak expiratory flow rate — the peak expiratory flow rate (PEFR) is measured during a brief, forceful exhalation. The patient can be taught to monitor PEFR routinely at home. However, the resulting measurements are highly dependent upon the patient's expiratory effort and technique. Thus, it is important that the physician assess the patient's use of the monitor and effort level and correct any mistakes (**44, 45**). The PEFR maneuver can be performed sitting or standing. Proper technique involves taking a maximally large breath in, putting the peak flow meter quickly to the mouth and sealing the lips around the mouthpiece, and blowing as hard and fast as possible into the meter. For PEFR, the effort does not need to be sustained beyond one to two seconds. The patient should perform the maneuver three times and record the highest of the three measurements (**44, 45**).

Interpretation of PEFR variability — there is some variability inherent in measurements of peak flow. This may be as much as 15 to 20 percent with repeated measurements, even in individuals without asthma. PEFR results that vary little over time (less than 20 percent of the maximal value) argue against the diagnosis of asthma, particularly if reported symptoms are associated with unchanging peak flow measurements. In contrast, peak flow values that repeatedly fall by 20 percent when symptoms are present and return to baseline as symptoms resolve are consistent with asthma (**44, 45**).

A single peak flow determination made in the doctor's office at the time that a patient is experiencing respiratory symptoms, if reduced from the normal predicted value, is suggestive of asthma. However, it is not diagnostic, because a reduced peak flow is not specific for airflow obstruction and can be seen with other pulmonary processes. A reduced peak flow that improves by more than 20 percent approximately 10 minutes after administration of a quick-acting bronchodilator (e.g., inhaled albuterol) is also confirmatory evidence favoring the diagnosis of asthma. Normal values for men and women are based upon height and age (**44, 45**).

II. Spirometry — Spirometry, which includes measurement of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), provides additional information that is useful in

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the diagnosis of asthma. Spirometry can be completed in 10 to 15 minutes with virtually no risk to the patient (44, 45).

The results of spirometry can be used to determine the following: Distinguish normal from abnormal lung function, Categorize abnormalities into obstructive or restrictive patterns, Characterize the severity of the abnormality, Assess the reversibility of the obstructive abnormality if the testing is repeated after administration of a bronchodilator agent (45).

Variable airflow obstruction is the hallmark characteristic of asthma. A non-smoker with cough, shortness of breath, and/or wheezing who has expiratory airflow obstruction that reverses to normal with treatment or over time almost certainly has asthma. In contrast, the person with cough and chest congestion who has consistently normal spirometry probably does not have asthma, and alternative explanations (e.g., recurrent bronchitis) should be sought (45).

An obstructive pattern on spirometry is identified numerically by a reduction in the ratio of FEV1 to FVC. When FEV1/FVC is reduced below normal (best defined by 95 percent confidence intervals around the normal values, determined electronically by modern computerized spirometers), airflow obstruction is present. When the FEV1/FVC ratio is normal or increased, there is no expiratory airflow obstruction (44, 45).

Having identified the presence of airflow obstruction by a reduction in FEV1/FVC, then the severity of airflow obstruction is best defined by the degree of reduction of the FEV1 below normal. By convention, the severity of airflow obstruction based on spirometry is graded as mild, moderate, severe, and very severe according to the following categories (Note: these are categories used for pulmonary function interpretation and are NOT the same as categories used to stage asthma severity): FEV1 80 to 99 percent: mild obstruction FEV1 51 to 79 percent: moderate obstruction FEV1 36 to 50 percent: severe obstruction FEV_1 less than 35 percent: very severe obstruction (44, 45).

Bronchodilator response in asthma — acute reversibility of airflow obstruction is tested by administering a quick-acting bronchodilator such as albuterol and repeating spirometry 10 to 15

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minutes later. The variability of the measurement is such that an increase of less than 12 percent may occur simply due to making repeated measurements. However, an increase in FEV1 of 12 percent or more, accompanied by an absolute increase in FEV1 of 200 mL, can be attributed to bronchodilator responsiveness with 95 percent certainty (44, 45).

3. EXHALED NITRIC OXIDE

This is a novel technique currently being used for the diagnosis of asthma. It involves measurement of the concentration of nitric oxide in a patient's exhaled breath. As part of bronchial inflammation, persons with asthma have up-regulation of nitric oxide synthase in their respiratory mucosal epithelium and generate increased amounts of nitric oxide in their exhaled breath. Low levels of nitric oxide are present in normal individuals. Preliminary results have suggested a sensitivity and specificity similar to methacholine bronchoprovocative testing. The simplicity of the testing procedure and its usefulness even in the absence of airflow obstruction make the concept highly appealing. However, additional testing is required to confirm the validity of exhaled nitric oxide as a diagnostic test for asthma, particularly among persons with other, potentially confounding respiratory diseases. In addition, although equipment is commercially available to measure the exhaled nitric oxide concentration in parts per billion and to remove any nitric oxide from the ambient air, it is still prohibitively expensive (46, 47).

Measurements can be obtained in almost all adults and children over 5 years. There is reasonably close relationship between FeNO and eosinophilic airway inflammation, which is independent of gender, age, atopy and inhaled corticosteroid use but the relationship is lost in smokers. Normal range <25 ppb at exhaled flow of 50 ml/sec and a 95% range for repeat measure 4 ppb. When the value is >50 ppb, it is highly predictive of eosinophilic airway inflammation where as <25 ppb is highly predictive of its absence. Raised FeNO (>50 ppb) very predictive of a positive response to corticosteroids and the use of FeNO to guide corticosteroid treatment has been shown to result in a non-significant 25% reduction in exacerbations with 40% less corticosteroid. Low FeNO (<25 ppb) may be of particular value in identifying patients who can step down corticosteroid treatment safely. Protocols for diagnosis and monitoring have not been well defined and experience with the technique is limited (47, 48, 49).

4. *SPUTUM EOSINOPHILS.*

This is another marker of airway inflammation and can be used to assess asthma control. In one study, sputum eosinophils appeared to correlate with disease severity, lung function, and bronchial hyperreactivity. The disadvantage with this marker in asthma control is that it is not disease- specific, not easy to perform and is expensive **(50, 51, 52)**. It is only available in specialist centres although the technology is widely available nowadays. Sputum eosinophil count is not closely related to other measures of asthma morbidity. Normal range is <2% (95% range for repeat measure +/- 2-3 fold). Here is close relationship between raised sputum eosinophil count and corticosteroid responsiveness and use of sputum eosinophil count to guide corticosteroid therapy has been consistently shown to result in better outcome for the same exposure to corticosteroids. Benefits are greater in patients with more severe disease **(50, 51, and 52)**.

D. MEASURING ASTHMA CONTROL.

The first release of GINA guidelines that stressed the importance of disease control in asthma management was in 2002 *(Table 1) (52, 53)*. Subsequently, two other editions of GINA guidelines have maintained this classification system **(54)** and it is also expected that the guidelines to be released in 2010 will focus heavily on asthma control as well.

A major difference between control and severity is the duration of the assessment period: Severity is assessed over the preceding six months to one year, whereas control refers to the preceding weeks (one week to three months). Thus, while the level of control has to be evaluated at each visit and may change from one visit to another, reclassification of severity should be envisaged only when a stable level of control has been obtained and maintained during several (e.g., at least three) months, allowing to decrease the "therapeutic pressure"**(55, 56).**

To date, there has been no definitive study contrasting or comparing these two disease management principles of severity versus control, and it is possible that a mixture of control and severity may improve asthma management. The ability to measure and quantify asthma control appears easier to operationalize in real world, clinical practice than disease severity **(57).** Asthma control is best measured by routine clinical review or by use of biochemical tests.

The factors that should be monitored and recorded include symptomatic asthma control: best assessed using directive questions such as the Asthma Control Questionnaire or Asthma Control Test questions *(see appendix 2)*. Since broad non-specific questions may underestimate symptoms lung function, assessed by spirometry or by PEF and biochemical markers of FeNO and sputum eosinophils is necessary (56, 57). Reduced lung function compared to previously recorded values may indicate current bronchoconstriction or a long term decline in lung function and should prompt detailed assessment of oral corticosteroid use and time off work or school since last assessment. inhaler technique, and drug compliance which can be assessed by reviewing prescription refill. frequency of bronchodilator reliance which can be assessed by reviewing prescription possession (56, 57).

Since the introduction of GINA guidelines on asthma management and especially the guidelines released in 2002. presentations and studies by various groups on different aspects of asthma control have resulted in a wide ranging discussion that has crystallized around two key questions.

1. What levels of asthma control are patients currently achieving?

2. What are the common causes of poor asthma control?

Contemporary levels of asthma control.

The common causes of uncontrolled asthma have been covered in section B above. Studies have shown that a substantial proportion of patients with asthma experience suboptimal levels of asthma control. The AIRE (Asthma Insights and Reality in Europe) study, involving over 2,800 people with asthma in France, Germany, Italy, Netherlands, Spain, Sweden and UK, is one such study which found that asthma symptoms are part of everyday life for many patients in Europe despite treatment (25). More than half (56%) of the respondents (identified by telephone interviews of randomly selected households) in the AIRE study suffered daytime symptoms in the previous 4 weeks. and around one in three respondents experienced sleep disruption due to asthma at least once a week. Among the 753 children (<16 years) surveyed in this study, 28% suffered night time symptoms in the previous month, with 61% needing to use their rescue medication.

Similar findings consistent with the AIRE study have been reported from the INSPIRE (INternational aSthma Patient Insight REsearch) study (26). This study, conducted in eleven

countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, Sweden, UK, USA), included 3,415 adults with asthma treated with inhaled corticosteroids, recruited via their physicians and interviewed by telephone. Nearly three-quarters of the patients (74%) used a short-acting bronchodilator every day and half of all patients (51%) had at least one exacerbation requiring medical intervention in the past year. The mean number of asthma worsenings was 16 in those patients with uncontrolled asthma, compared with 6 in patients with well-controlled asthma (26).

E. TOOLS FOR ASSESSING ASTHMA CONTROL.

Asthma control is assessed using a number of instruments. Monitoring asthma control with these validated instruments better assesses disease outcomes and medication regimens for both short- and long-term management. These instruments for assessing clinical control of asthma score goals have been applied in different settings. Examples of such validated instruments include:

1. The Asthma Control Test (ACT) (60, 61, 62, 63).
2. The Asthma Control Questionnaire (ACQ) (12, 13, 60, 63).
3. The Asthma Therapy Assessment Questionnaire (ATAQ) (60, 63).
4. The Asthma Control Scoring System (60, 63).
5. The Mini Asthma Quality of Life (MAQOL) questionnaire (60, 63, 64).

Not all of these instruments include a measure of lung function or biomarker of asthma control. Therefore, sometimes, studies will combine two instruments (such as ACQ and ATAQ) to measure clinical and pathophysiological asthma control and hence arrive at the intended study outcomes. The questions are usually translated into a language suitable for the individual patient prior to or during the data collection or at the clinic visit. These study instruments have been reported in literature to have the potential to improve the assessment of asthma control, providing a reproducible objective measure that may be charted over time (week by week or month by month) and representing an improvement in communication between patient and health care professional (44, 60, 63). The choice of questionnaire should depend on the task at hand. All the tools describe the impact of asthma on daily activities, sleep disrupted by asthma, and the need for rescue albuterol.

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Asthma Control Test (ACT).

The **Asthma Control Test** is either five- or seven-item question assessments of asthma control completed by the asthmatic (12 years of age or greater) or the child and parent/caregiver (four to 11 years of age), respectively. The ACT is designed to identify patients whose asthma is inadequately controlled and is available many languages. It is a simple method for assessing asthma control without lung function testing or lung inflammation markers **(61, 62, 63)**. It is good tool in a busy clinic practice with limited time and resources where there is need for a simple method for assessing asthma control without the need for lung function testing.

It is a self-administered survey questionnaire designed with a clinical working group to provide a broader assessment of asthma control at the individual patient level. The ACT yields precise and scientifically valid scores across a wide range of asthma control that are easy for both patients and clinicians to interpret. While proving the benefit of treatment beyond any one indicator, the ACT is fast to complete and easily scored, and can be completed in a clinical practice setting, at home, or other locations **(61, 62, 63)**.

The National Heart, Lung, and Blood Institute has recognized ACT as a validated instrument for the assessment and monitoring of asthma in its Guidelines for the Diagnosis and Management of Asthma **(60, 63)**.

It has five questions, three related to symptoms, one to medication use and one on overall control. On a 5 point response score: Well controlled <19. Within subject intraclass correlation coefficient of 0.77 and a 95% range for repeat measure and minimally clinically important difference not defined. Could be used to assess response to longer term treatment trials, particularly in those with normal or near normal spirometric values. 95% range for repeat measure and minimally clinically important difference need to be defined **(61, 62, and 63)**.

Asthma Control Scoring System (ACSS).

This is the most recent instrument in the literature and assesses three types of parameters in asthma control **(64)** namely:

- Clinical (diurnal and nocturnal symptoms, rescue beta agonist use, activities)
- Physiological (FEV1 and/or peak expiratory flows [PEF] and/or PEF circadian variations)

- Lower airway inflammation (induced sputum eosinophilia).

The Asthma Therapy Assessment Questionnaire (ATAQ).

The Asthma Therapy Assessment Questionnaire (ATAQ) was developed as a disease management (DM) tool to identify individuals whose asthma management may be suboptimal. This brief, self-administered questionnaire generates a five-level measure of asthma control (0 = no control problems to 4 = four control problems). In addition, the ATAQ is used to identify possible barriers to good disease management. It has been used in a study describing the distribution and properties of the ATAQ control score among members of a large health maintenance organization (HMO) in the Pacific Northwest who have asthma with good results **(60, 62, and 65).**

The Mini Asthma Quality of Life (MAQOL) questionnaire.

The Mini Asthma Quality of Life Questionnaire is a questionnaire designed for patients with asthma to assess their quality of life in respect to the level of disease control **(66, 67, 72).** Although the MAQLQ(S) has been highly successful and used in a large number of clinical studies around the world, it takes 4-5 minutes to complete hence may not be good in big clinical trials. The validated MiniAQLQ has 15 questions in the same domains as the original questionnaire (symptoms, activities, emotions and environment) and has very good reliability, cross-sectional validity, responsiveness and longitudinal validity. However, as might be expected with a shorter questionnaire, none of these properties are quite as good as those of the original AQLQ. For purposes of analysis, a change in score of greater than 0.5 can be considered clinically important in analyzing responses from MAQOLQ **(66, 67, and 72).**

The MiniAQLQ has been tested in a 9-week observational study of 40 adults with symptomatic asthma. Patients completed the MiniAQLQ, the AQLQ, the Short Form (SF)-36, the Asthma Control Questionnaire and spirometry at baseline, 1, 5 and 9 weeks. In patients whose asthma was stable between clinic visits, reliability was very acceptable for the MiniAQLQ (intraclass correlation coefficient (ICC) =0.83), but not quite as good as for the AQLQ (ICC=0.95). Similarly, responsiveness in the MiniAQLQ (p=0.0007) was good but not quite as good as for the AQLQ (p<0.0001). Construct validity (correlation with other indices of health status) was strong for both the MiniAQLQ and the AQLQ. Criterion validity showed that there was no bias

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between the instruments (p=0.61) and the correlation between them was high (r=0.90). Following these findings, it was concluded that the Mini Asthma Quality of Life Questionnaire has good measurement properties but they are not quite as strong as those of the original Asthma Quality of Life Questionnaire (AQLQ) **(65, 66, and 72).**

It has 15 questions in 4 domains (symptoms, activity limitations, emotional function and environmental stimuli). Responses are usually assessed over the preceding week. It is closely related to larger 32-item asthma quality of life questionnaire. 95% range for repeat measure +/- 0.36. Minimal important difference 0.5. Well validated quality of life questionnaire. Could be used to assess response to longer term treatment trials (**(65, 66, and 67).**

The Asthma Control Questionnaire (ACQ).

It has seven questions, five relating to symptoms, one to rescue treatment use and one to FEV_1. Responses are usually assessed over the preceding one to four weeks. Shortened, five question symptom only questionnaire is just as valid. Cut offs for well controlled disease is ≤0.75 and inadequately controlled ≥1.5. 95% range for repeat measure +/- 0.36.

Minimal important difference 0.5. Well validated composite scoring system with a strong bias to symptoms. Could be used to assess response to longer term treatment trials. Shortened five-point questionnaire is probably best for those with normal or near normal FEV_1.

The *Asthma Control Questionnaire (ACQ)* can be used to discriminate between asthma patients with well- and suboptimally controlled asthma symptoms. It is the most widely applied in clinical research **(12, 13, 53, and 68).** The control criteria used in ACQ are based on definitions of asthma control guidelines published in the Global Initiative for Asthma **(53)** and applied in several studies including the Gaining Optimal Asthma control (GOAL) study, among others **(14,66,67).** The GOAL study specified two target levels of control (Total Control, TC and Well Controlled, WC) because, while suggesting that complete absence of symptoms of asthma was possible (TC), the GINA guidelines suggest that 'minimal' daytime symptoms and β_2-agonist use are acceptable in 'controlled asthma' (WC)**(14).** The two new guideline-based composite measures of control (well-controlled and uncontrolled based on the AQC criteria, as provided for in the GINA GUIDELINES 2006 and used in the Gaining Optimal Asthma control (GOAL) study, will be applied in this study **(14).** In this study, the ACQ was only be used to differentiate controlled from the uncontrolled asthma cases irrespective of disease severity state at initiation

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of therapy or entry into the study plus whether the FEV_1 was included or not. The questionnaire can either include a question on pulmonary function or not, and omission of that question has not been shown to influence the validity of the ACQ *(63, 65, 66) (Table 1)*.

Table 1: Levels of Asthma Control

Characteristic	Controlled (All of the following)	Uncontrolled (Any measure present in any week)
Daytime symptoms	None (twice or less/week)	More than twice/week
Limitations of activities	None	Any
Nocturnal symptoms/awakening	None	Any
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/week
Lung function (PEF or FEV1)‡	Normal	< 80% predicted or personal best (if known)
Exacerbations	None	One or more/year*
Wheezing	None	Any

*Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡ Lung function is not a reliable test for children 5 years and younger.

SOURCE: Modified from Global Initiative for Asthma web site. Global strategy for asthma management and prevention, 2006.

2.2 STUDY JUSTIFICATION.

According to the GINA (*Global Strategy for Asthma Management and Prevention*) report of 2007. more than 300 million people around the world have uncontrolled asthma. The disease imposes a heavy burden on individuals, families. and societies. Patients with inadequately controlled asthma are at high risk of exacerbations. hospitalizations and death, and often have severely impaired quality of life.

Nonadherence in asthma treatment is a major factor in disease control and is associated with increasing mortality, morbidity, and increasing treatment costs. There is also close linkage between drug adherence and sociodemographic factors (such as young age. male gender. etc). The exact prevalence of uncontrolled asthma and the risk factors associated with uncontrolled disease at KNH chest clinic is not known and no study has ever been done to establish this. Therefore, it is not easy to design interventional plus preventive measures; hence the need for this study to which was planned to document the prevalence. drug adherence and sociodemographic risk factors for poorly controlled asthma at KNH. Understanding treatment barriers to comply with asthma treatment is important in developing programs to promote treatment adherence.

The findings of this study will not only form a baseline for future studies on asthma control in Kenyatta hospital, but also help develop guidelines for future management of asthma patients attending KNH chest clinic.

2.3 OBJECTIVES OF THE STUDY.

MAIN OBJECTIVE.

The general objective was to establish the level of asthma control among patients attending KNH chest clinic and determine selected sociodemographic and drug adherence factors associated with the level (s) of control achieved.

Primary Objectives:

1. To determine the prevalence of uncontrolled asthma at KNH chest clinic.

2. To determine the sociodemographic factors (age. gender and level of education) associated with the uncontrolled asthmatic patients at KNH chest clinic.

3. To determine drug adherence level and its association with asthma control among asthmatic patients at KNH chest clinic.

Secondary Objectives

1. To document the common drugs used to achieve the levels of asthma control ascribed.

3.0 CHAPTER THREE.

STUDY METHODS

Study Design and Study Site.

The study was a descriptive, cross-sectional study conducted at the chest clinic of the Kenyatta National Hospital (KNH).

Study Population.

Asthmatic patients aged thirteen years or more with a diagnosis of chronic asthma with proven use of inhaled, oral or combination of corticosteroid and beta2-agonists or any other drug combinations at recommended doses which were stable for at least six months (without major drug switches in the previous four to six months before visit). Subjects were to be without changes in usual asthma treatment from any other health facility other than KNH.

Study period.

February 2009 to May 2009.

Sampling and Sample size

Large population-based studies, varying in methodology and funding, suggest that prevalence of poorly controlled asthma ranges between 28-96% in different parts of the world **(62, 63)**. Therefore, taking the median of the two as 62%, the formula below was used to calculate the sample size.

$$\frac{Z^2 PQ}{D^2} \quad = \frac{1.962 \times 0.62 \times 0.38}{0.0025} \quad = 362$$

Whereby;

Z=1.96

P=0.62

Q=0.38

 D=0.05

Total number of patients interviewed was 360.

Case Definitions.

1. *An asthmatic* was defined as any patient who presented with an episode of cough, dyspnoea and a wheeze with PEFR or FEV_1 of less than 80% of predicted and PEFR or FEV_1 variability less that 25% and/or demonstrable variability in symptoms following inhalation of beta agonist. The diagnosis should have been confirmed by a chest physician.

2. *Well controlled asthma* was defined as all of the following in the previous one month:-

    1) No (or absent) daytime or nocturnal chronic symptoms,

    2) No (or absent) exacerbations.

    3) No limitation on activities,

    4) No absences from school or work.

    5) Maintenance of normal or near-normal pulmonary functions,

    6) The minimal use of short-acting β_2-agonists (< once per day, <1 canister/month), and

    7) Normal or near-normal pulmonary function test (FEV_1).

3. *Poorly controlled asthma* being defined as any three or more features of the well controlled asthma above present in any given month.

Drug Nonadherence was defined as estimated > 20% of the number of doses missed within the defined period (previous six months) **(69)**. Self-reported adherence to the asthma medications was enquired qualitatively. Estimated total dose (s) of the drug (s) missed for the past 6 months was calculated and if the estimated total dose (s) of the drug (s) missed was > 20%, the case was labeled as 'nonadherent'. The information was recorded as either **'adherent'** or **'nonadherent'** using the estimated total drug dose (s) missed.

Study Eligibility Criteria.

Inclusion criteria.

- All patients aged 13 years and above who presented with a diagnosis of asthma confirmed by a chest physician during the study period and had been on the clinic follow-up for at least 6 months or more were recruited.

Exclusion criteria

Known cases of;

- COPD
- Bronchitis
- Cor-pulmonale
- Pulmonary edema
- Upper respiratory tract obstruction
- Pulmonary embolus
- Heart failure
- Severe pneumonia
- Any other concurrent active or chronic medical illness for which the patient is on medications that may interfere with asthma management.

PATIENT RECRUITMENT PROCEDURE.

Patients were recruited by screening the patient files at the KNH chest clinic on each clinic day. The triage nurse/staff informed the principal investigator of patients with asthma reporting for clinic follow up and the patients files kept aside. The PI then reviewed the files to identify those patients aged more than 13 years and who had been on clinic follow up for more than six months. After selecting the cases, the other eligibility criteria were checked and if they met the inclusion criteria, they were given consent form as appropriate and included in the study using systematic sampling procedure. The information to be filled in the questionnaires included:

1. The sociodemographic data,
2. Duration of illness (i.e. years since the diagnosis was made),
3. Drug treatments given for the previous six months plus drug adherence status,
4. Level of disease (asthma) control according to ACQ criteria.

DATA COLLECTION PROCESS.

After recruiting the study subjects, data collection was done using two study instruments:

1. Data Abstraction form
2. Structured asthma control questionnaire

All patients who consented were interviewed using a validated asthma control interviewer administered questionnaire. Patients were assigned to three research assistants (2 medical students and a clinical officer employed in the chest clinic at KNH) by the principal investigator. The research assistants helped in data collection by selecting patients to fill the questionnaires plus the proforma.

The ACQ contains a set of questions that allow patients with asthma to rate the control of their disease *(Appendix 2)*. The ACQ has been validated and has been used to measure the effects of asthma treatment in clinical studies. Patients are asked to recall their symptoms during the previous one to four weeks and respond to each question on a 7-point scale ranging from 0 (well controlled) to 6 (extremely poorly controlled). Initially, the questionnaire included a question on pulmonary function, but omission of that question has not been shown to influence the validity of the ACQ *(70, 71)*.

Spirometry: - Spirometry measurements (FEV_1) were performed at the end of the interviews using the standard procedure, and the result recorded to the asthma control questionnaire. The patient's best FEV_1 was adopted as the current measure of the level of airway obstruction. The severity of airflow obstruction was defined by the degree of reduction of the FEV_1 below normal. By convention, the severity of airflow obstruction based on spirometry is graded as mild, moderate, severe, and very severe according to the following categories:

- FEV_1 80 to 99 percent: mild obstruction,
- FEV_1 51 to 79 percent: moderate obstruction,
- FEV_1 36 to 50 percent: severe obstruction,
- FEV_1 less than 35 percent: very severe obstruction

Proper technique with performance of spirometry was checked to ensure quality control. (It involves taking a deep inspiration, putting the mouthpiece quickly to the mouth and sealing the lips around the mouthpiece before exhaling as fast as possible, then reading is taken).

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Patients were then given a return date when the results of the study would be communicated to them, especially regarding their level of asthma control and the factors found to affect their disease control. At this stage, any changes to their treatments were effected in consultation with their primary care physicians.

DATA MANAGEMENT.

Data was entered onto the SPSS version 16.0 computer software, cleaned and coded.

Variables

1. **Continuous:** Age, dosages of drugs, duration of clinic follow-up.
2. **Nominal:** sex, level of education, place of residence.
3. **Ordinal:** class of drugs the patient is taking, presence or absence of any of the risk factors for asthma.
4. **Categorical:** level of asthma control, adherence status to drugs, reason(s) why patient is not adherent to drugs, inhaler technique.

Analysis of data was done within a period of one month after completion of data collection using the SPSS version 16.0 software programme. Ratios and percentages were calculated, and measures of central tendency used where applicable. The level of significance was set at 0.05. The data was presented in tabular form where appropriate.

Operational definitions were as indicated above. Cases of well-controlled asthma and poorly controlled asthma were defined by the criteria in **Table 1** above and the results summarized in tables 4 below.

Statistical Methods.

Qualitative variables were summarized with numbers and frequency distributions.

Quantitative variables summarized with size, mean, standard error, median, minimum and maximum. Unpaired t tests were used to compare drug adherence between different groups.

To identify the profile of subjects with good or poor asthma control, a multivariate analysis was performed (logistic regression including the following factors in the model: age, sex, education level, drug adherence status, type and dosage of drug (s) used, FEV1 at inclusion as percentage

of theoretical value, asthma control level, dose of inhaled corticosteroid at inclusion (low dose/high dose), and drug adherence status).

Figure 1: Study flow chart.

```
┌─────────────────────────────────────┐
│ Asthmatic aged more than 13 years +  │
│ clinic follow-up > 6 months (n=432)  │
└─────────────────────────────────────┘
                  │
                  ▼
┌─────────────────────────────────────┐
│ Screening to rule out other medical  │
│ conditions                           │──────────► ┌──────────────────┐
└─────────────────────────────────────┘            │ Excluded (n=72)  │
                  │                                  └──────────────────┘
                  ▼
┌─────────────────────────────────────┐
│ Consent given (n=360                 │
└─────────────────────────────────────┘
                  │
                  ▼
┌─────────────────────────────────────┐
│ Administer ACQ + Proforma            │
│ (Sociodemographic / Drug adherence   │
│ factors)                             │
│ n=360                                │
└─────────────────────────────────────┘
           │                    │
           ▼                    ▼
┌──────────────────┐   ┌──────────────────┐
│ Well controlled  │   │ Poorly controlled│
│ n=127            │   │ n=233            │
└──────────────────┘   └──────────────────┘
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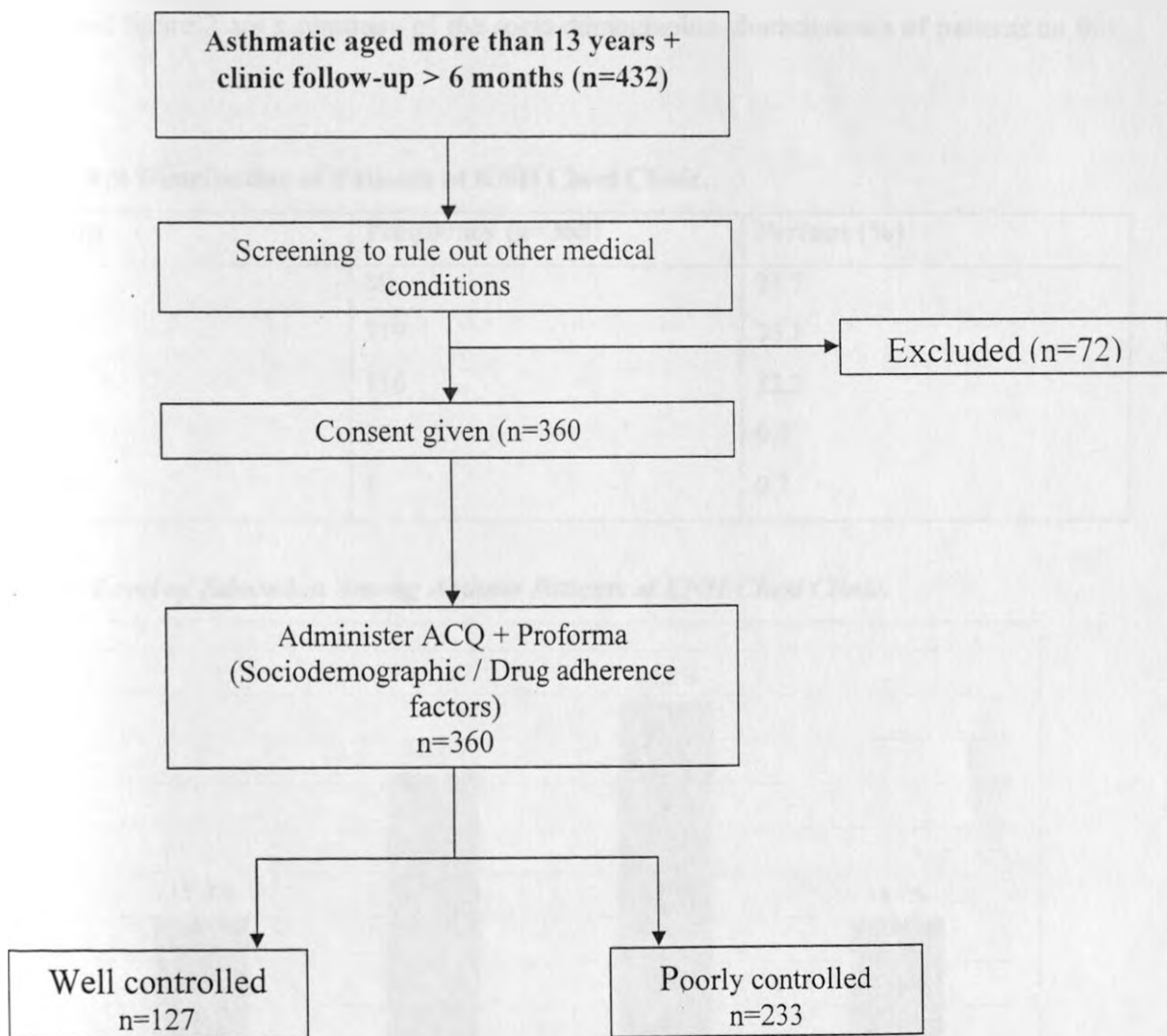
CHAPTER FOUR

4.0 RESULTS.

4.1 Socio-demographic Characteristics of Patients at KNH Chest Clinic.

Three hundred and sixty asthma patients with a mean age of 44.9 years (SD 17.7 years) and range of 13 to 100 years were recruited. Majority (75.3%) of patients attending this clinic were female and with secondary level of education (39.2%). Median age at diagnosis was 30 years (range 13-79 years) and median duration of follow up at KNH chest clinic was 24 months (range of 6 – 564 months).

Table 2 and figure 2 are a summary of the socio-demographic characteristics of patients on this clinic.

Table 2: Age Distribution of Patients at KNH Chest Clinic.

Age group	Frequency (n=360)	Percent (%)
10-29	89	24.7
30-49	119	33.1
50-69	116	32.2
70-89	35	9.7
Above 90	1	0.3

Figure 2: Level of Education Among Asthma Patients at KNH Chest Clinic.
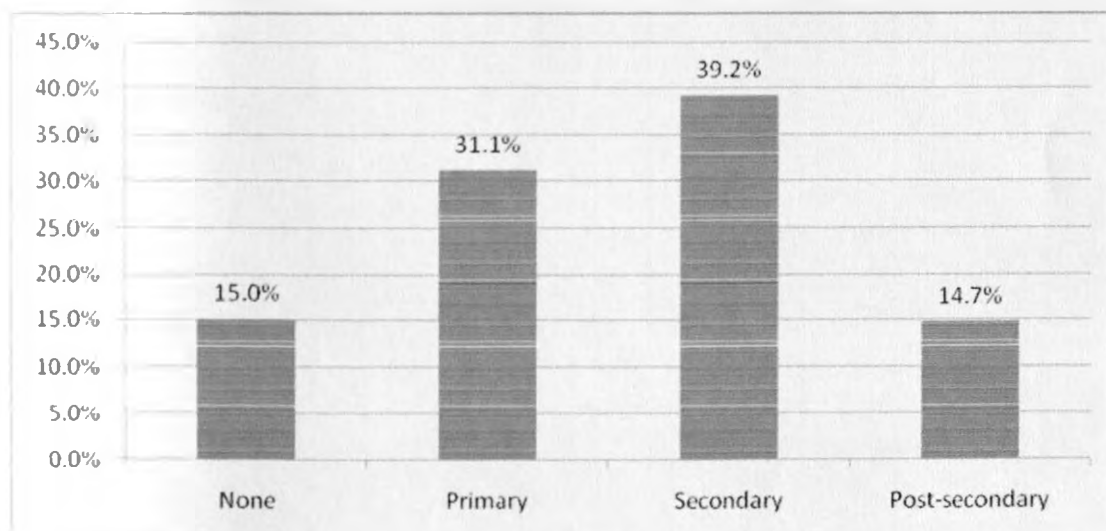
4.2 Overall Asthma Control.

1. Overall asthma control was assessed by the Asthma Control Questionnaire (ACQ) (*Appendix 2*). All the 360 patients filled the ACQ and the analysis of ACQ gave the overall control level irrespective of whether the patient had FEV_1 or not. According to tables 3a and 3b below, 46.4 % of patients did not have FEV_1 performed on them because they voluntarily were not willing to have the test. Most of these patients could not have spirometry done for them on the same day of the interview and most of those who were told to return did not do so despite all costs including transport costs for the return visits having been catered for by the study. This problem was not anticipated at protocol stage of the study and therefore could not be vetoed. These patients who did not have FEV1 thus completed the 6-question shortened version of ACQ. Despite this, analysis of the ACQ was done on all patients and there was no significant statistical difference between those who were well or poorly controlled and had or did not have FEV_1 (p-value =0.78) According to *Juniper EF et al*, analysis of ACQ for asthma control can be done with or without FEV_1 report and this would not influence the overall asthma control results *(68, 70 and 71)*. Therefore, in this study, the overall ACQ analysis revealed that most patients (64.7%) were poorly controlled for their disease *(Table 4)*.

Table 3a: FEV₁ Distribution versus Asthma Control.

	Overall asthma control	
FEV1	**Well controlled**	**Poorly controlled**
>95% predicted	32 (25.2%)	12 (5.2%)
95-90% predicted	10 (7.9%)	4 (1.7%)
89-80% predicted	9 (7.1%)	28 (12.0%)
79-70% predicted	11 (8.7%)	27 (11.6%)
69-60% predicted	3 (2.4%)	25 (10.7%)
59-50% predicted	3 (2.4%)	20 (8.6%)
<50% predicted	2 (1.6%)	7 (3.0%)
Not done	57 (44.9%)	110 (47.2%)
Total	127 (100.0%)	233 (100.0%)

Table 3b: FEV₁ Distribution versus Asthma Control (X^2).

	Well controlled	Poorly controlled	P-value
FEV_1			
Not done	57 (44.9%)	108 (46.4%)	0.789
Done	70 (55.1%)	125 (53.6%)	0.789

Table 4: Overall Asthma Control of Patients at KNH Chest Clinic (Using ACQ).

Overall asthma control	Frequency	Percent (%)
Well controlled	127	35.3
Poorly controlled	233	64.7

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Table 5: Association between Socio-demographic Characteristics and Asthma Control.

Variable	Overall asthma control		P-value
	Well controlled (n=127)	Poorly controlled (n=233)	
Age group			
10-29	31 (24.4%)	58 (24.9%)	0.919
30-49	43 (33.9%)	76 (32.6%)	0.811
50-69	43 (33.9%)	73 (31.3%)	0.624
70-89	9 (7.1%)	26 (11.2%)	0.213
Above 90	1 (0.8%)	0 (0%)	0.175
Sex			
Male	31 (24.4%)	58 (24.9%)	0.919
Female	96 (75.6%)	175 (75.1%)	0.919
Education level			
None	20 (15.7%)	34 (14.6%)	0.769
Primary	37 (29.1%)	75 (32.2%)	0.550
Secondary	52 (40.9%)	89 (38.2%)	0.610
Post-secondary	18 (14.2%)	35 (15.0%)	0.828

Majority of the poorly controlled asthmatics were females aged between 30-60 years with primary and secondary levels of schooling. However, there were no statistically significant differences between the socio-demographic characteristics and asthma control (p-value >0.05).

4.3 Drug Adherence.

Majority (85.8%) of the patients were adherent to the drugs prescribed. The patients that did not adhere to the prescribed medications cited lack of money (83.7%) and forgetfulness (67.4%) as the commonest reasons for their non-adherence *(Figure 4)*. Gender, age and educational level were not significantly associated with level of adherence *(Table 7)*.

Table 6: Drug Adherence Status among Patients at KNH Chest Clinic.

Adherence status (n=360)	Frequency	%
Yes	309	85.8
No	43	11.9
Unknown	8	2.2

Figure 4: Reasons for Non-adherence to Drugs.
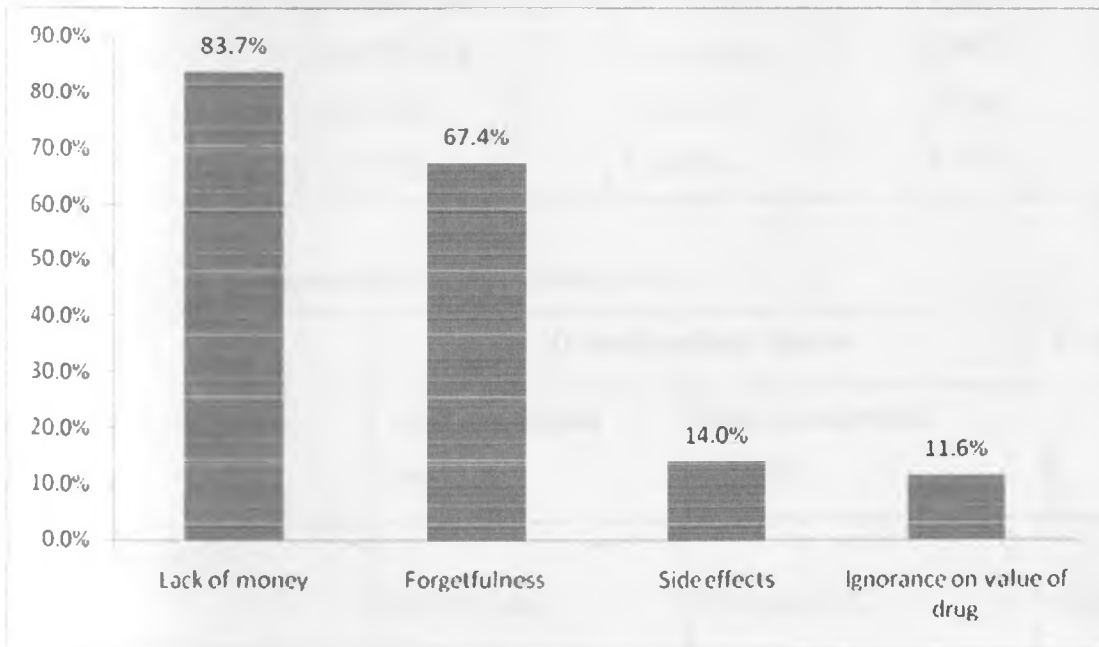
Table 7: Association between Drug Adherence and Socio-demographic Characteristics.

	Adherence status		p-value
	Yes	No	
Sex			
Male	75 (88.2%)	10 (11.8%)	0.884
Female	234 (87.6%)	33 (12.4%)	
Education level			
None	49 (94.2%)	3 (5.8%)	0.147
Primary	91 (84.3%)	17 (15.7%)	
Secondary	127 (90.1%)	14 (9.9%)	
Post-secondary	42 (82.4%)	9 (17.6%)	
Age. mean (SD)	44.1 (17.4)	48.0 (17.8)	0.181
Age group			
10-29	81 (26.2%)	7 (16.3%)	0.159
30-49	101 (32.7%)	16 (37.2%)	0.555
50-69	101 (32.7%)	14 (32.6%)	0.987
70-89	26 (8.4%)	5 (11.6%)	0.486
Above 90	0 (0.0%)	1 (2.3%)	0.007

Table 8: Adherence Status and Asthma Control (x^2).

Variable	Overall asthma control		P-value
	Well controlled (n=121)	Poorly controlled (n=231)	
Adherence status			
Yes	115 (95.0%)	194 (84.0%)	0.003
No	6 (5.0%)	37 (16.0%)	

4.4 Drug Regimens Used for Asthma Control at the KNH Chest Clinic.

Common asthma drugs used on the clinic included Short-Acting B_2-Agonists (SABA), Long-Acting B_2-Agonist (LABA), Inhalation Corticosteroids (ICS), Anticholinergics, Methylxanthines (e.g. Theophyllines), Leukotriene Modifiers, Oral Steroids (Prednisolone) and others such as Franols *(Table 9)*.

The commonest drug used was inhalational corticosteroid (budesonide) (94.7%) followed by short-acting B_2-agonist inhaler (92.5%). Majority of the patients were on a combination therapy consisting of either 2 (58.5%) and 3 (25.8%) drugs with the commonest drug combinations being inhalational corticosteroid with short-acting B_2 –agonist *(Tables 9 and10)*.

Among the three drug combination therapies. inhalation corticosteroid +short-acting B_2-agonist inhaler+theophyllines was the most widely used three-drug combination regimen.

None of the patients were on no drug at all and there were also no patients on more than five drugs. The two patients who were on five drug regimens consisted of [ICS+LABA+SABA+Oral Pred+Theophyllines] and [ICS+LABA+SABA+Oral Pred+Leukotriene Modifiers].

Both patients who were on five –drug combination regimens were uncontrolled for their disease *(Table 11)*.

Table 9: Common Asthma Drugs Used at KNH Chest Clinic.

Class of drug	Number of patients using it out of the total
Inhalation Corticosteroids (ICS)	341 (94.7%)
Short Acting B_2 Agonist (SABA)	333 (92.5%)
Long Acting B_2 Agonist (LABA)	73 (20.3%)
Theophyllines	72 (20.0%)
Oral Steroids (Prednisolone)	35 (9.7%)
Leukotrine Modifiers	9 (2.5%)
Anticholinergics	4 (1.1%)
Other (Franols, etc)	4 (1.1%)

Table 10: Common Asthma Drug Regimens Used at KNH Chest Clinic.

Drugs	N (%)
One drug regimens	17 (5.2)
Two drug regimens	193 (58.5)
Three drug regimens	85 (25.8)
Four drug regimens	31 (9.4)
Five drug regimens	4 (1.2)

The distribution of asthma therapies shows that single therapies were used in 6.1 % of cases and commonest single agent used was short-acting B_2. agonist inhaler followed by steroid inhaler.

Table 11: Association between Number of Drugs and Asthma Control.

Variable	Overall asthma control		P-value
	Well controlled (n=127)	Poorly controlled (n=233)	
Number of drugs			
One	10 (7.9%)	7 (3.0%)	0.037
Two	79 (62.2%)	120 (51.5%)	0.051
Three	31 (24.4%)	68 (29.2%)	0.332
Four	7 (5.5%)	31 (13.3%)	0.021
Five	0 (0.0%)	7 (3.0%)	0.049

Table 12: Association between Common Asthma Drug Regimens Used at KNH Chest Clinic and Asthma Control.

Variable	Overall asthma control		p-value
	Well controlled	Poorly controlled	
One drug regimens (n=17)	**(n=10)**	**(n=7)**	
Short acting B$_2$-Agonist (SABA)	7 (70.0%)	4 (57.4%)	0.501
Inhalation Corticosteroids (ICS)	2 (20.0%)	2 (28.6%)	
Anticholinergics	1 (10.0%)	0 (0.0%)	
Theophyllines	0 (0.0%)	1 (14.3%)	
Two drugs regimens (n=193)	**(n=77)**	**(n=116)**	
ICS + SABA	73 (94.8%)	113 (97.4%)	0.423
ICS + LABA	2 (2.6%)	2 (1.7%)	
SABA+ Leukotrine Modifier	1 (1.3%)	0 (0.0%)	
SABA+ Anticholinergics	0 (0.0%)	1 (0.9%)	
Leukotrine Modifiers+Others	1 (1.3%)	0 (0.0%)	
Three drugs regimens (85)	**(n=25)**	**(n=60)**	
ICS+SABA+Theophy	9 (36.0%)	31 (51.7%)	0.224
ICS+Oral Pred+Anticholinergics	1 (4.0%)	0 (0.0%)	
ICS+LABA+SABA	11 (44.0%)	19 (31.7%)	
ICS+SABA+Oral Pred	2 (8.0%)	6 (10.0%)	
ICS+Oral Pred+Theophy	0 (0.0%)	1 (1.7%)	
ICS+SABA+Leukotri	1 (4.0%)	0 (0.0%)	
ICS+LABA+Leukotri	1 (4.0%)	0 (0.0%)	
ICS+LABA+Theophy	0 (0.0%)	2 (3.3%)	
ICS+LABA+AntIcholin	0 (0.0%)	1 (1.7%)	
Four drugs regimens (n=31)	**(n=4)**	**(n=27)**	
ICS+SABA+Oral Pred+Theophy	2 (50.0%)	7 (25.9%)	0.082
ICS+LABA+SABA+Theophy	0 (0.0%)	12 (44.4%)	
ICS+LABA+SABA+Leukotri	0 (0.0%)	4 (14.8%)	
ICS+LABA+Oral Pred+Theophy	0 (0.0%)	2 (7.4%)	
ICS+LABA+SABA+Oral Pred	2 (50.0%)	2 (7.4%)	
Five drugs regimens (n=4)	**(n=0)**	**(n=4)**	
ICS+LABA+SABA+Oral Perd+Theophy	None	3 (75.0%)	-
ICS+LABA+SABA+Oral Pred+Leukotri	None	1 (25.0%)	

KEY: ICS=Inhalational Corticosteroids; Theophy=Theophyllines; SABA=Short-Acting B$_2$ agonist; LABA=Long-Acting B$_2$ agonist; Oral Pred=Oral Prednisolone; Leukotri=Leukotriene Modifiers.

Table 13`: Overall Association between Number of Drugs and Asthma Control (X^2).

	Overall Asthma Control		p-value
	Well Controlled (n=127)	Poorly Controlled (n=233)	
Number of drugs			
1.00	12 (9.4%)	9 (3.9%)	0.005
2.00	90 (70.9%)	141 (60.5%)	
3.00	21 (16.5%)	67 (28.8%)	
4.00	4 (3.1%)	16 (6.9%)	

Table 14: Corticosteroids Distribution Among Study Subjects (X^2).

	Well controlled	Poorly controlled	P value
Inhalation steroids	115 (90.6%)	225 (96.6%)	0.017
Oral Pred	10 (7.9%)	25 (10.7%)	0.382

Use of inhaled corticosteroids was significantly higher in the uncontrolled than in the controlled group (controlled group 90.6% vs. uncontrolled group 96.6%; p-value=0.017).

The use of oral corticosteroids was however nonsignificantly higher in uncontrolled than in controlled asthma (10.7 vs. 7.9%, respectively; P = 0.382) and the dosages of the oral steroids varied from 10 milligrams per day up to a maximum of 60 milligrams per day.

The dosages of the anti-asthma drugs varied from 200 micrograms per day of corticosteroid up to a maximum of 1000 micrograms per day in all the combination drug categories *(Table 15).*

Table 15: Distribution of Inhalational Steroid Dosages among the Study Subjects.

	Overall	Well controlled	Poorly controlled
1 drug regimens (inhalation steroids doses)			
400 mcg	3 (75.0)	2 (100%)	1 (50.0%)
800 mcg	1 (25.0)	0 (0.0%)	1 (50.0%)
2 drug regimens (inhalation steroids doses)			
400 mcg	108 (54.3)	53 (67.1)	55 (45.8)
800 mcg	84 (42.2)	22 (27.8)	62 (51.7)
Not on inhalation steroids	7 (3.5)	4 (5.1)	3 (2.5)
3 drug regimens (inhalation steroids doses)			
320	7 (7.1)	4 (12.9)	3 (4.4)
400 mcg	34 (34.3)	8 (25.8)	26 (38.2)
480	1 (1.0)	1 (3.2)	0 (0.0)
800 mcg	52 (52.5)	13 (41.9)	39 (57.4)
Not on inhalation steroids	5 (5.1)	5 (16.1)	0 (0.0)
4 drug regimens (inhalation steroids doses)			
400 mcg	22 (57.9)	4 (57.1)	18 (58.1)
800 mcg	16 (42.1)	3 (42.9)	13 (41.9)
5 drug regimens (inhalation steroids doses)			
400 mcg	5 (71.4)	None	5 (71.4)
800 mcg	2 (28.6)	None	2 (28.6)

According to table 16 below, the overall predictors of asthma control at KNH Chest Clinic in a logistic regression analysis were the number of drugs the patient was taking and the adherence status to the drugs.

Table 16: Overall Predictors of Poor Asthma Control at KNH Chest Clinic (Logistic Regression).

Factor	OR (CI 95%)	P-value
Number of drugs		
1.00*		
2.00	2.2 (0.7 – 6.7)	0.164
3.00	3.2 (1.0 – 10.4)	0.051
4.00	6.5 (1.7 – 25.5)	0.007
Adherence status		
Yes*		
No	3.7 (1.5 – 9.4)	0.004

*reference categories.

CHAPTER FIVE

5.0 DISCUSSION.

Sociodemographic Characteristics of the Patients

Most of the patients who attended the chest clinic during the study period were females (75.3%) with a mean age of 44.9 years. This finding is consistent with a study done in Brazil at a specialist outpatient asthma clinic which found that majority of the clients were female (74.9%) with a mean age of 51.0 years **(68, 71)**. Other studies have also shown that women ashmatics have better health seeking behaviour than men **(71, 74)**. The other sociodemographic characteristics (occupation and education level) did not have significant variance among the clinic attendants in the study at KNH, unlike the study in Brazil and the one in Europe **(68, 74)**. Among the diagnosed asthma sufferers in the European National Health and Wellness Survey (ENHWS), those who were not well-controlled (n = 1,159) were significantly (p<0.001) older and less likely to be college educated than the at least well-controlled (n = 1,178). As opposed to the at least well-controlled asthma sufferers, the not well-controlled asthma sufferers were also more likely to reside in Germany and less likely to reside in Spain or the UK. Sex, marital status and residing in France or Italy did not significantly vary by asthma control **(76)**.

Overall Level of Asthma Control at KNH Chest Clinic

The overall prevalence of uncontrolled asthma at KNH chest clinic was 64.7% during the study period, and the majority of the clinic patients were female aged between 30-69 years with schooling of up to secondary education level. Despite the fact that a big proportion (46.4%) of patients did not have FEV_1, the results are a true reflection of the level of control at this clinic because there were no statistically significant differences in asthma control among those who had FEV_1 and those who did not, which agrees with the findings by *Juniper EF et al* in their analysis of ACQ for asthma control. *Juniper EF et al* found that analysis of ACQ can be done with or without FEV_1 report and this would not influence the overall asthma control results (*66, 70*). . By and large, the findings of this study show that a significant proportion of patients (64.7 %) attending KNH chest clinic have poorly controlled asthma. These results are comparable with other studies which have shown that a considerable proportion of patients with asthma experience suboptimal guideline targets of asthma control despite availability of effective drugs.

The AIRE (Asthma Insights and Reality in Europe) study done in Europe found that more than half (56%) of the respondents (identified by telephone interviews of randomly selected households) suffered daytime symptoms in the previous 4 weeks, a clear indicator of poorly controlled disease (25). Similar findings to the AIRE study have been reported from the INSPIRE (INternational aSthma Patient Insight REsearch) study (26). The INSPIRE study, conducted in eleven countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, Sweden, UK, USA), included 3,415 adults with asthma who were treated with regular maintenance therapies for asthma, and recruited via their physicians. The respondents were interviewed by telephone using the ACQ and revealed that nearly three-quarters of the patients (74%) used a short-acting bronchodilator every day and half of all patients (51%) had at least one exacerbation requiring medical intervention in the past one year (26).

Compared to the AIRE and INSPIRE studies, the high figure for uncontrolled asthma at KNH could not be explained from the study findings but a number of postulations can be advanced to elucidate this finding. First of all, a majority of patients at KNH chest clinic were on insufficient medication dosages of the corticosteroids. As seen from the results, most patients did not attain the maximum corticosteroid recommended dosages. Secondly, a number of other factors, though not ruled out in my study, may have contributed to the high prevalence of uncontrolled asthma at KNH. These include unavailability of drugs hence use of inaccurate combination medications, wrong inhalation techniques for those using inhalational medicines, existence of co-morbid conditions and therapy –resistant disease. Steroid-resistant asthma is a category that would not be controlled despite use of corticosteroids (72, 73). All these factors were not ruled out in my study thus limiting the ability to attribute the findings of the study to the factors studied alone. Furthermore, the patients who attend this clinic at KNH could be those with more severe disease since this is a referral centre, hence a community survey designed to rule out all the factors that could influence asthma control would be ideal. It is still also possible that some patients at this clinic might have had chronic obstructive airways disease (COPD) rather than asthma, therefore giving the impression of more uncontrolled disease since asthma medications will not control COPD (75). Studies have shown a tendency for increased bronchoconstriction in response to a variety of exogenous stimuli, including methacholine and histamine as one of the defining features of asthma (75). However, many patients with COPD also share this feature of airway

hyperresponsiveness. Therefore, there is considerable overlap between persons with asthma and those with COPD in airway responsiveness, airflow obstruction, and pulmonary symptoms and this has led to the formulation of the 'Dutch hypothesis', which suggests that asthma, chronic bronchitis, and emphysema are variations of the same basic disease, which is modulated by environmental and genetic factors to produce these pathologically distinct entities **(75)**.

A review of asthma control from the European National Health and Wellness Survey (ENHWS), an internet-based survey, reported the prevalence of uncontrolled asthma at 50.4% compared with well-controlled at 49.6% in 2007 **(74)**. However, in this survey, unlike in my study findings at KNH, uncontrolled patients were older ($p<0.001$), less likely to be college educated (28.7 *versus* 36.3%; $p<0.001$) and more likely to be obese (30.0 *versus* 22.7%; $p<0.001$). The subjects who had poorly controlled disease in the ENHWS were also more likely to have experienced depression (28.0 *versus* 18.7%; $p<0.001$) and smoked (34.7 *versus* 25.0%; $p<0.001$). My study therefore did not look at all the variables that were covered in the ENHWS, which influence asthma control. The only similarity between this study and that of ENHWS is that the poorly controlled patients in both the two studies were using regular controller and rescue medications for asthma control, and with less adherence to their medications. Additional new findings on asthma control have been shown in The Reality of Asthma Control (TRAC) study **(76)**, conducted in Canada in 2004 at an outpatient asthma clinic. The study established that **53%** of adults aged 18–54 years who reported having asthma were uncontrolled as assessed by Asthma Control Questionnaire (ACQ). **(76)**.

Peters et al assessed 1812 adult patients (aged 11 years and above) in the REACT study to determine the prevalence of uncontrolled asthma in the United States (in 2007) using the Asthma Control Test. Similar to findings at KNH, they demonstrated that **55%** of patients had uncontrolled disease. Most of the patients in both studies were on standard asthma medications. Most patients in REACT study had health care coverage and received care from general practitioners. Inhaled corticosteroid plus long-acting β-agonist was the most common medication regimen in patients with controlled asthma (60%) and patients with uncontrolled asthma (48%) in the REACT study **(77)**.

The lowest prevalence of uncontrolled asthma has been the one reported by Cazzoletti et al. in Europe who assessed 1042 adults with asthma in 2007 using the asthma control questionnaire and demonstrated the prevalence of uncontrolled disease in **32%** of them (**78**).

Patient Adherence to Asthma Medications.

The results on adherence show that 84% of the patients who were uncontrolled were adherent to their drugs, and that drug non-adherence was a major predictor for asthma control (p=0.004). Sex, age and educational level were not significantly associated to adherence status even though other studies have shown that male gender and younger age and advanced age are predictors of poor drug adherence among asthmatics (**74, 79**). The major causes of medication non-adherence were lack of money (83.7%) and forgetfulness (67.4%) while 11.6% of respondents were ignorant on the value of their drugs and 14% stopped taking medication when they felt worse from the side effects. For that reason, one may conclude that better adherence was associated with poor asthma control at this clinic because most of the uncontrolled asthmatics were adherent to their medications. However, scrutiny of the results additionally shows that even of the well-controlled sufferers, up to 95% were adherent to the asthma medications and when compared to the uncontrolled group (84 % adherent), drug non-adherence was major predictor for poor asthma control (p=0.004). This shows that nonadherence to medications was not the only reason for poor asthma control in this study. Other factors such as control of triggering factors, existence of co-morbidities, technique of inhalation, occupation of the patient, place of residence and smoking history are factors that need to be explored since they too have been shown to influence asthma control and they were not excluded in this study (**60**). The method used to test adherence in this study (patient self- reports) has been reported as a less reliable method and further studies need to be done on this clinic to test adherence using more reliable methods of testing drug non-adherence, even though there is no gold standard for quantifying patient adherence (**79, 80, 81, 82,84**). In general, nonetheless, direct measures of assessing patient drug adherence status, such as direct observation therapy or electronic inhaler monitoring devices as well as repeated measurement of serum concentrations of the drug (or a metabolite) in question, give a more accurate and valid indication of adherence than indirect methods such as patient

diaries, self-reporting (as used in our study at KNH), and weighting of inhaler devices or doctors' judgment (80, 81, 84).

From our study, it is clear that patient adherence to the treatments given was a key determinant of overall asthma control (p-value=0.004). As shown in other studies, asthma patients may not take the medications they have been prescribed due to a number of reasons contributing to poor disease control and this can happen regardless of age, gender and socioeconomic status of patients (63, 82, and 83). Non-adherence rates of over 30% have consistently been noted across chronic asthma and with even higher rates of nonadherence to inhaled corticosteroids (63, 82, and 83). Inhaled corticosteroids are the cornerstone of modern asthma treatment because they control the underlying airway inflammation in asthma by inhibiting many aspects of the inflammatory process (81, 84). However, the delayed clinical impact of inhaled corticosteroids compared with the immediate relief obtained with bronchodilator drugs makes them susceptible to noncompliance (81, 84, 85), such that typically, adherence with reliever medications has been shown to be better than with controller medications (57, 81, 85). This was similarly the case in our study.

Non-adherence may also be higher for more complex drug regimens (57, 87), but it has been documented that significant non-adherence to asthma drugs linger even when the frequency of dosing is reduced (83, 84). Furthermore, it has been noted that providing clear information – although essential – is not enough to guarantee adherence (84) and other measures such as motivational interventions to enhance adherence with asthma medications are therefore needed (87). The Behavioral Model of Health Services Utilization, organized as predisposing, enabling, and need variables, as outlined by De Smet BD et al. in the Annals of Pharmacotherapy in 2006 may be useful in identifying variables related to adherent medication-taking behavior among asthmatic patients attending outpatient clinics (87).

Drug Treatment Modalities.

Asthma medications play a key role in gaining good control of asthma. As shown from the study findings at KNH, majority of the patients were on two drugs (inhalational steroid and short-

acting B$_2$ agonist inhalers), followed by three drugs (inhalational steroid+short-acting B$_2$ agonist+theophylline). None of the patients was on no drug at all. There was also no patient on more than five drugs. The dosages of the inhalational steroids varied from 200 micrograms per day of steroid up to a maximum of 1000 micrograms per day among the study subjects. This falls far below the guideline recommendations for maximum steroid dosages (57, 81). Unlike in other studies that have shown that the use of inhaled corticosteroids was significantly lower in the uncontrolled than in the controlled group (respectively, 83.7 vs. 97.5%; P < 0.001) (78, 81). In our study this was the reverse (controlled group 90.6% vs. uncontrolled group 96.6%; p-value=0.017), which might be explained by either the nonavailablity of drugs or lack of knowledge of the primary physician who prescribe the drugs on the guideline recommendations. The use of oral corticosteroids was nonsignificantly higher in uncontrolled than in controlled asthma (10.7 vs. 7.9%, respectively; P = 0.382) and the dosages of the oral steroids varied from 10 milligrams per day of steroid up to a maximum of 60 milligrams per day per. The indications, and hence the duration of therapy with oral corticosteroids could not be established in this study.

For those patients who were on combination therapies, two- and three-drug combinations had better asthma control unlike 4 or 5 drugs combinations, while all the patients who were on five-drug regimens were poorly controlled. This agrees with asthma treatment guideline recommendations although the choice of the combination therapies will be influenced by the availability and cost of the medications as well as patient preferences.

The distribution of asthma therapies additionally shows that single therapies were used in 5.8 % of cases and commonest single agent used was short-acting B$_2$. agonist inhaler followed by steroid inhaler. This use of single therapy for asthma control has not been shown to be effective (52, 57, 85), unless for the intermittent and mild persistent asthma cases. However, this categorization of asthma patients by severity was not done at KNH chest clinic at initiation of the therapies which makes it difficult to tell the criterion used to select which patients were to receive single agents in this study. Furthermore, some patients were uncontrolled for their disease yet still on single therapies which makes it difficult to rationalize why.

Inferring from existing literature, the most effective way to control asthma using drugs has been shown to be the use of combination therapies. In the Gaining Optimal Asthma Control (GOAL) Study for example, it was shown that total control of asthma is possible and that the outcomes are better with combination therapies than with steroids alone (52, 57, 88). The most effective combination therapy for asthma control in the GOAL study was shown to be a combination of two drugs (LABA+ICS). A small number (20.3%) of the patients on the study were on this regimen at the KNH chest clinic. The reason (s) for the low uptake of the ICS+LABA regimen could not be established in our study but a combination of factors including the cost of these combination therapies as well as lack of knowledge on the efficacy of these drugs could have contributed. In one study, [89] one third of physicians (35%) reported that the cost of medication was a considerable barrier to prescribing effective medications for asthma. Inhaled corticosteroids now cost at least Ksh. 2,500 per month in Kenya and many families cannot afford these drugs. This high cost of medicines is associated with decreased use of maintenance medicines. Eliminating cost barriers could therefore improve outcomes in asthma control (89, 90).

Current asthma treatment guidelines are not clear for use of four or five-drug combination therapies, yet a substantial number of the patients in the study were on four drugs (52, 57, 88). This means that guideline-based practice should be clarified on when to use four or five-drug combination therapies for asthma control. The rationale for the selection (choice) of the combination therapies could not be established in this study because of the study design and further studies to interview the primary care physicians on the criteria they use to decide who should use which combination of drugs should be conducted in future.

Study Limitations.

1. **Recall bias**: most patients were expected to recall events in their disease which occurred 4 to 24 weeks previously.
2. Poor knowledge and evaluation of drug factors. Not all drug factors contributing to the control of asthma were covered in this study.
3. It was a cross-sectional study, and therefore it is not possible to establish the temporal sequence between the factors studied and asthma control.

4. KNH is a referral institution providing specialist care for patients in public health system. As a consequence, our study population was made up of people with low incomes and education. Our patient sample was therefore biased toward the socially disadvantaged in our society.

5. The study population was also, selected from patients referred to a referral center and was probably biased toward the more severe disease, hence the high value of uncontrolled asthma reported in this study.

CONCLUSION.

- In conclusion, this study has illustrated the association of asthma control with disease treatment, and selected socio-demographic factors.

- The study shows that most patients with asthma at Kenyatta National Hospital (KNH) chest clinic are uncontrolled.

- Majority of the sufferers who were not well controlled were aged between 30-60 years and staying within an urban setting. They also were more likely to use multiple drugs (combination therapy of two or three drugs) and more than 84% of them were not adherent to their drugs.

- The two chief predictors of poor asthma control among the asthma clients at the KNH chest clinic were the number of drugs the individual patient was taking and the drug adherence status. In addition, this study performed in a setting reflecting normal clinical practice shows that asthma combination therapies at KNH chest clinic do not conform to the international guidelines for optimum asthma control and there is underutilization of corticosteroids in the management of asthma at this clinic.

- Finally, patient education programmes need to be initiated at this clinic in order to address the importance of treatment adherence for asthma control and prospective studies at this specialist clinic should in future be conducted to establish actual causal relation between asthma control and drug adherence factors with utilization of more accurate methods of assessing drug adherence.

RECOMMENDATIONS.

1. Large prospective and randomized controlled studies designed to assess the proportion of patients able to achieve overall control of asthma when treatment is titrated appropriately based on current asthma management guidelines.

2. Primary care physicians managing patients at the Kenyatta National Hospital chest clinic should try as much as possible to adhere to the guideline-based recommendations for drug prescriptions to control asthma, although the study did not approach doctors to directly examine the level of dissemination of guideline-based prescriptions.

3. Patient education programs should be initiated at this clinic to educate patients on the value of adherence to drugs for optimum asthma control.

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APPENDIX 1.

CONSENT TO PARTICIPATE IN THE STUDY.

Respondents' consent form.

Dear respondent,

My name is Dr. Andale. I am a student at the University of Nairobi pursuing a master's degree in internal medicine. One of the requirements for award of the degree is to carry out a research. In regard to this, am carrying out a research on **"Factors associated with control of asthma at KNH"**. The research has been approved by the Ethics and Research Committee of KNH and permission to carry it out granted by the hospital. It involves interviewing patients attending KNH chest clinic.

In order to obtain the information, I have developed a questionnaire. I am kindly requesting you to participate in the study by filling in the questionnaire. Participation is voluntary and there is no penalty for declining to participate. There are no risks involved for participating in this study and the information you provide will be treated with total confidentiality as permitted by biomedical research law. You are not required to write your name or any other identification number on the questionnaire. You are free to withdraw from the study at any stage without fear of victimization.

The results of the study will help improve clinical decision making at this hospital which in turn will help improve patient care outcomes and inform policy on training and development of expert clinical guidelines on asthma management. If you wish to know the results, they will be given to you once the study is completed. You may ask any questions about your rights as a participant or anything else about the research that is not clear. You can also contact me on **0733-347700** incase you have any questions later.

Thank you for your time.

APPENDIX 2.

QUESTIONNAIRE FOR ASTHMA PATIENTS.

Questionnaire for the research on 'Factors associated with clinical control of asthma at KNH'

Instructions:

1. The purpose of this questionnaire is to obtain information for study purposes only. The information obtained will go along way in improving the clinical functioning of Nurses and also may re-direct the socialization for Nurses as clinical experts. Your responses will be held in total confidence.
2. Do not write your name or any other identification anywhere on the questionnaire.
3. The questionnaire has four sections. Complete all the sections.
4. Put the filled in questionnaire in the given envelope and seal it. Hand it over to the researcher or the research assistant.

PATIENT'S HOSPITAL NUMBER----------
SERIAL NUMBER----------------

A. SOCIODEMOGRAPHIC CHARACTERRISTICS.

1. Age (in years):------------
2. Sex: Male [] female []
3. Occupation:--------------
4. Residence: Urban [] Rural []
5. Level of education: none [] Primary [] secondary [] post-secondary [].
6. Age at onset or diagnosis of asthma (in years)----------------------
7. Duration of clinic follow-up at KNH (in months)-------------------

B. DRUG ADHERENCE FACTORS .

1) Asthma drugs used and dosages (for the previous > 6 months)--------------------------------
2) Is the Patient Adherent to the drugs? Yes [] no []
   a. If non-adherent, why?
   - wrong inhalation technique yes [] no []
   - Lack of money yes [] no []
   - Ignorance on value of the drugs yes [] no []
   - Side-effects of the drugs yes [] no []
   - Forgetfulness yes [] no []
   - Cultural/Social beliefs and hindrances yes [] no []
   - Psychiatric/ psychological factors yes [] no []
   b. If on inhalational drugs, proper inhalation technique being applied? Yes [] no []
   c. Is the Patient on Regular Clinic Follow-up? yes[] no[]
3) Any other drugs the patient is taking? --------------------

C. ASTHMA CONTROL QUESTIONNAIRE

Please answer Questions 1-6.

Circle the number of the response that best describes how you have been during the past 4 weeks.

1. On average. during the past 4 weeks, how often were you **woken by your asthma** during the night?

    0 Never

    1 Hardly ever

    2 A few times

    3 Several times

    4 Many times

    5 A great many times

    6 Unable to sleep because of asthma

2. On average. during the past 4 weeks, how **bad were your asthma symptoms when you woke up in the morning?**

    0 No symptoms

    1 Very mild symptoms

    2 Mild symptoms

    3 Moderate symptoms

    4 Quite severe symptoms

    5 Severe symptoms

    6 Very severe symptoms

3. In general, during the past 4 weeks, how **limited were you in your activities** because of your asthma?

    0 Not limited at all

    1 Very slightly limited

    2 Slightly limited

    3 Moderately limited

    4 Very limited

    5 Extremely limited

    6 Totally limited

4. In general, during the past 4 weeks, how much **shortness of breath** did you experience because of your asthma?

0 None

1 A very little

2 A little

3 A moderate amount

4 Quite a lot

5 A great deal

6 A very great deal

5. In general, during the past 4 weeks, how much of the time did you **wheeze**?

0 Not at all

1 Hardly any of the time

2 A little of the time

3 A moderate amount of the time

4 A lot of the time

5 Most of the time

6 All the time

6. On average, during the past 4 weeks, how many **puffs of short-acting bronchodilator** (e.g., Ventolin) have you used each day?

0 None

1 1-2 puffs most days

2 3-4 puffs most days

3 5-8 puffs most days

4 9-12 puffs most days

5 13-16 puffs most days

6 More than 16 puffs most days

7. *To be completed by a member of the clinic staff*

FEV$_1$ prebronchodilator:

0 > 95% predicted

1 95-90%

FEV$_1$% predicted: 2 89-80%

3 79-70%

FEV$_1$% predicted: 4 69-60%

(Record actual values on the 5 59-50% dotted lines and score the FEV$_1$% 6 < 50% predicted in the next column)

The Asthma Control Questionnaire is copyrighted. It may not be changed, translated, or sold (paper or software) without the permission of Elizabeth Juniper.

D. OVERALL ASTHMA CONTROL SCORE ON ACQ.

1. Well controlled (Controlled) yes [] no [].
2. Poorly controlled (uncontrolled) yes [] no [].

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Dr. Andaie Thomas
Dept. of Clinical Medicine & Therapeutics
School of Medicine
University of Nairobi

Dear Dr. Andaie

Research proposal: "Socio-Demographic and Drug Adherence Factors Associated with Poor Asthma Control at Kenyatta N. Hospital" (P22/1/2009)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above revised research proposal for the period 15th April 2009 –14th April 2010.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF. A N GUANTAI
SECRETARY. KNH/UON-ERC
c.c.   The Chairperson, KNH/UON-ERC
         The Deputy Director CS, KNH
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