HEALTH RELATED QUALITY OF LIFE AND ITS DETERMINANTS IN ASTHMATIC PATIENTS AT KENYATTA NATIONAL HOSPITAL

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DEDICATION STATEMENT

I dedicate this work to: my Lord Jesus Christ who has given me insight into understanding, my parents for giving me support and encouragement, and to my three children Harvey, Jason and Lisa for believing in me.

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ABBREVIATIONS AND ACRONYMS

ACT – Asthma Control Test

AHR - Airway Hyper responsiveness

AIA - Aspirin Induced Asthma

AQLQ – Asthma Quality of Life Questionnaire

COPD – Chronic Obstructive Pulmonary Disease

CVD – Cardiovascular Disease

DALYS – Disability Adjusted Life Years

DM – Diabetes Mellitus

EIB – Exercise Induced Bronchoconstriction

ERC – Ethics and Research Committee

FEV_1 – Forced Expiratory Volume in one second

FVC – Forced Vital Capacity

GERD – Gastro-esophageal Reflux Disease

GINA – Global Initiative for Asthma

HCP – Health Care Provider

HIV – Human Immunodeficiency Virus

HRQoL - Health Related Quality of Life

ICS – Inhaled Corticosteroids

ISAAC – International Study of Asthma and Allergies

KAPTLD – Kenya Association for the Prevention of Tuberculosis and Lung Diseases

KEML – Kenya Essential Medicines List 2016

KNH- Kenyatta National Hospital

LABA – Long acting beta-2 agonists

LAMA – Long acting muscarinic antagonists

LTRA – Leukotriene Receptor Agonists

NAEPP - National Asthma Education and Prevention Program

PEF – Peak Expiratory Flow

PI – Principal Investigator

PMDI – Pressurized metered-dose Inhaler

Prn – to be administered on need basis

QoL – Quality of life

OCS – Oral Corticosteroids

RVD – Retroviral Disease

SABA – Short acting beta-2 agonists

SES – Socioeconomic Status

SLIT – Sublingual Immunotherapy

UoN – University of Nairobi

WHO – World Health Organization

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OPERATIONAL DEFINITION OF TERMS

Adherence/compliance –are synonymously used. Adherence is the degree to which a patient's behavior corresponds with the collaborative agreed recommendations from a health care provider. Compliance refers to the extent to which a patient's behavior matches the prescriber's advice.

Airway hyper responsiveness – a state characterized by easily triggered bronchospasms. It consists of an increased sensitivity of airways to inhaled stimuli.

Asthma control – implies the extent to which the various manifestations of asthma are reduced or removed by treatment.

Asthma exacerbation – is an acute or sub-acute episode of progressive worsening of symptoms of asthma including shortness of breath, wheezing, cough, sputum production and chest tightness.

Atopy – refers to the genetic tendency to develop allergic diseases such as asthma, eczema and is associated with heightened immune responses to common allergens especially inhaled or food allergens.

Comorbidity – the presence of one or more additional diseases or disorders occurring together with the primary disease or disorder.

Efficacy - the capacity for therapeutic effect of a given intervention.

Optimal – the most favorable interventions and their amounts for achieving asthma control

Outcomes – the end result of asthma interventions**.**

Sensitivity – the ability of a test to correctly identify cases.

Variables – a measurable characteristic that can change from group to group, person to person or even within one person over time.

Employment- formal = employee or self-employed with a regular source of income, **non-informal** = not having a regular source of income.

ABSTRACT

Background

Health Related Quality of Life (HRQoL) is an important measure of health outcomes since it reflects the impact of an illness and its treatment, from the patient's perspective. The disease though common and whose control is achievable, it is often misdiagnosed and undertreated in most parts of the world Kenya included, causing its burden to rise. A significant proportion of patients with asthma, especially from poor settings, suffer daily activity limitations, reduced productivity and the associated socioeconomic burden.

Objective

To determine the Health Related Quality of Life (HRQoL) and factors influencing it in asthmatic patients who attend Kenyatta National Hospital (KNH) chest clinic for their routine management.

Methodology

A cross-sectional study was conducted at Kenyatta National Hospital (KNH) chest clinic in the year 2018. The study targeted teenage and adult asthmatic patients on treatment at this facility. Consecutive sampling technique was used to obtain a representative sample of 140 consented participants. Data on HRQoL was obtained using Asthma Quality of Life Questionnaire with Standardized activities (AQLQ(S)), Asthma Control Test and Determinants of HRQoL Questionnaires in a patient-guided interview. Data analysis was done using STATA version 13 software. Inferential statistics was used to compare the distribution of variables across patients with good asthma control versus those with poor asthma control and also those with high versus those with low HRQoL. Logistic regression was conducted to determine the variables that are the independent predictors of asthma control and HRQoL in this population. A p-value of <0.05 was considered statistically significant.

Results

Asthma was controlled in 80% of the asthmatics with more than half (53%), reporting high asthma related quality of life. Poorly controlled asthma in the 20% was significantly

associated with low HRQoL, P<0.05. Variables in the study found to be significantly associated with uncontrolled asthma were occupational exposure, incorrectness of inhaler technique, presence of gastroesophageal reflex disease (GERD), type 2 diabetes mellitus coexistence, suboptimal inhaled corticosteroids dosage, lack of prescriber guideline usage and inappropriate treatment choice at the asthma severity step. Independent predictors of asthma control and thus HRQoL were; occupational exposure to asthmagens, GERD, diabetes mellitus and cigarette smoking.

Conclusions

Asthma-HRQoL outcome among patients was largely dependent upon the degree to which asthma was controlled. Asthma was controlled in 80% of the participants who slightly over half reported high HRQoL scores (53%). All the 20% participants in whom asthma was uncontrolled had low HRQoL scores. The independent predictors of asthma control and HRQoL included occupational risk exposure, GERD, type 2 diabetes mellitus and cigarette smoking. The symptoms and activity limitation domains of the HRQoL were the most negatively impacted by poorly controlled asthma**.**

Recommendations

1. Incorporation of HRQoL into routine practice as an important measurement for assessing the outcomes of asthma therapy.
2. Dissemination and support of adherence to current treatment guideline recommendations to all healthcare facilities for uniformity in asthma care.
3. Screening, early diagnosis and prompt treatment of GERD in asthmatic patients.
4. Recheck and re-demonstration of inhaler technique at every consultation.
5. Reduction in occupational exposure to asthmagens by shifting affected workers to departments with minimal or no exposure. Work-related stress reduction for those working in professions not associated with asthmagens.

Expected outcomes

Uptake and assimilation of HRQoL measure as an important tool in determining therapeutic outcomes leading to better managed patients and well controlled asthma.

CHAPTER ONE: INTRODUCTION

1.1 Background

Health was in 1948 defined by the World Health Organization (WHO) as a state that encompasses complete normal functioning in the mental, physical and social faculties in addition to absence of disease (1). The concept of Health related quality of life (HRQoL) has many dimensions which relate to the mental, physical, social and emotional domain functioning of an individual (1). Its importance as a measure of health outcomes lies in its ability to reflect the impact a disease and its treatment have on a patient from his or her perspective.

Asthma has been rated as the most common and heterogeneous chronic non-communicable lung disorder in the world. The disease is quite common in Kenya, affecting 7-10% of the population (2). It often begins in childhood and affects all ages (3–5). It has been identified as a major cause of morbidity, poor quality of life and increased health expenditure. Despite this, its diagnosis and treatment still remain suboptimal in most parts of the world especially the low income regions, resulting in low quality of life and deterioration in lung function of its sufferers (3,6). In most Kenyan government hospitals, lack of drugs, diagnostic centers, asthma specialists is not uncommon (7). Asthma has been stigmatized and sidelined in Kenya with treatment and prevention focusing on other respiratory diseases such as Tuberculosis. In addition, the disease has commonly been misdiagnosed as cold or flu leading to patients being given wrong medications for flu or even malaria (7). An estimated 1.3 million asthmatic children in Kenya are forced to stay out of school due to poor diagnosis (7). The poor and those living in slums in Kenya were the most affected by asthma due to inability to access proper health care (7).

The disease sets in at an early age with a quarter of the general population developing it before age 40 (4). It is characterized by chronic inflammation of the airways resulting into bronchospasms that lead to airflow limitation and airway hyper-responsiveness (8). These effects produce symptoms such as wheezing, tightness in the chest, shortness of breath and coughing which occurs mostly at night or early in the morning when air is

cold (5,9). These episodes lead to obstruction within lungs, a situation which is usually reversible either by medication or spontaneous (3).

Asthma affects both the developing and the developed countries, posing a major public health problem. According to the latest analysis by Global Burden of Disease (GBD), an approximate 334 million people worldwide are estimated to be suffering from the disease (10). The rates are reported to be rising by about 50% every decade. It is projected that by the year 2025, 400 million people will be asthmatic (5,11). At least 4 million people in Kenya are affected by the disease with the highest prevalence reported among children aged 12-14 years and especially those residing in Nairobi, Eldoret and their environs (7). An approximate 600,000 asthmatics are reported to be residing in Nairobi (2). The disease spans across all ages, ethnic groups, geographic regions, races and either sex (3,5). Incidences have been increasing for both sexes over time with higher estimates for females from the adolescence stage (9). It is more prevalent in urban compared to rural settings (3,6). This could be attributed to the growing urbanization in most countries and adoption of modern lifestyles (4,11). The high prevalence observed in Kenya's capital city has been attributed to air pollution, a situation which if left unchecked may predispose many to developing the disease (2).

Although morbidity and mortality due to asthma had been shown to be more common in poorer regions of the world, it has recently been established that high income regions mostly have the adult asthma sufferers. Mortality from asthma rises with age, being more common among adults than children in whom it is expected to be uncommon (12). A significant socioeconomic burden is associated with the disease as a result of direct and indirect expenditures. Worldwide, it accounts for approximately 1% of Disability Adjusted Life Years (DALYs), a reflection of its high prevalence and severity. Globally, it accounts for at least 250,000 deaths annually, a figure lower to that due to Chronic Obstructive Pulmonary disease (COPD) (11,12). In Kenya, the age adjusted Death Rate was 7.62 per 100,000 population in the year 2017 (13). In high income regions, mortality is mainly an adult problem. Although asthma is not curable, it can be controlled (3,5,9).

Since it is a chronic condition, continuous monitoring and optimal medical care is essential. This entails good prescribing practices as stipulated in the current guidelines,

appropriate pharmaceutical care, follow-up, patient education on the disease and its control as well as their compliance (14,15). In recent decades, morbidity and mortality has drastically decreased due to the dissemination and utilization of evidence based guidelines that emphasize on the use of corticosteroids for controlling the disease (12,16). Unfortunately, recent studies show that despite receiving appropriate treatments, it remains uncontrolled in majority of asthmatics (17).

The degree to which asthma is controlled influences HRQoL outcomes. Inadequacy in asthma control produces increased frequency and severity of attacks (18). Although mortality due to asthma is lower than that due to COPD, failure to correctly diagnose, prescribe and acquire appropriate medication or comply with treatment while avoiding triggers often leads to progression of the disease, poor HRQoL and eventually to unnecessary deaths (5).

1.2 Problem statement

Asthma has been rated as an important disease of public health interest, with its prevalence and burden steadily increasing worldwide. Its prevalence in the world is 8.6% and in Kenya it has been shown to affect about 10% of the total population (3,4) which was estimated as 47 million in 2017 (19). It however remains underdiagnosed and undertreated especially in low income countries, with rural settings being the most affected (3,6).

Being a heterogeneous disease that is chronic in nature, it causes major limitations to daily activity such as work, night sleep, school attendance and social interactions (6). The number of hospital admissions has been on the rise especially in children reflecting an increase in severe attacks, poor disease management and poverty (6). Lack of strategies put in place to ensure optimal control of the disease often leads to progression of the disease, with concomitant reduction in patient quality of life, increased health care cost burden and unnecessary deaths which usually occur outside hospitals (5,6). Studies have shown that the financial burden due to asthma is high and is especially skewed towards those with severe disease. It includes in-patient admission costs, transport costs to health facilities, purchase of medications, loss of productivity due to work and school absenteeism which negatively impact a patient's HRQoL (6,20–22). Childhood asthma

accounts for many lost school days and the affected children may be denied academic achievement and social interaction (21,23).

Several studies have examined the optimality of asthma therapies and their impact on asthma control and thus HRQoL. They have shown that use of inhaled corticosteroids makes positive impacts on outcomes especially in lowering mortality rates (21,23). Medical measures such as spirometry provide an assessment of outcomes of asthma therapy. However, they are not sufficient to fully evaluate the effects the infirmity and its therapy have on the quality of life of the sufferer (21,23). A number of studies worldwide have assessed the impact this disease and its treatment have on the HRQoL of its sufferers. However, in Kenya, the HRQoL and factors that impact it in asthmatic patients remain unknown since no study has documented it.

1.3 Purpose of the study

The purpose of this study was to determine the asthma-related quality of life as an outcome for measuring asthma control. Health related quality of life assessment will enable comprehensive assessment of the patients' response to medical treatment in their own perspective and evaluation of illness control that cannot be adequately assessed by medical outcomes alone. This study at Kenyatta National Hospital, being the largest public referral health institution in Kenya is aimed to provide information on HRQoL, an outcome measure of asthma control and also provide insight into factors that impact quality of life in the teenage and adult asthmatic population in Kenya.

1.4 Objectives

1.4.1 Main Objective

To assess the Health Related Quality of Life and its predictors in asthmatic patients who attend KNH chest clinic for routine management.

1.4.2 Specific objectives

1. To investigate the level of asthma control in patients at KNH.
2. To assess the HRQoL of asthmatic patients at KNH

3. To determine the patient and clinical factors that impact asthma control and the HRQoL of asthmatic patients at KNH.

1.5 Research Questions

1. What is the prevalence of poorly controlled (uncontrolled) asthma among patients treated at KNH?

2. What is the HRQoL of asthmatic patients managed at KNH?

3. What patient and clinical factors have major impact on asthma control and quality of life of the asthmatic patients at KNH?

1.6 Significance and anticipated output

Given that the prevalence of asthma along with its disability is rising worldwide, it is important to understand this burden from the patient's perspective (24). Knowledge gaps on asthma control at both the health care provider and patient levels often result in sub-optimal therapy that impacts negatively on a patient's well-being and health care resource utilization (9).

Findings of this study will provide insight into the outcomes of asthma management at KNH. This will influence provision of individualized patient care by addressing the factors that are impacting negatively on the individual's quality of life. It will in effect benefit the patients in that it will inform the need to institute effective therapies as per individual patient parameters leading to a reduction in the associated morbidity and mortality with a positive impact on their well-being. Health care providers will benefit by knowing the outcomes of their treatment strategies hence lead to their improvement or maintenance.

An additional expected output is the uptake and assimilation of HRQoL measure as an important tool in determining asthma control in the same capacity as the clinical measures. This will enhance patient participation in their therapy thus increasing the effectiveness of treatment. Better managed patients and well controlled asthma are thus expected from future subsequent evaluations in this population.

1.7 Delimitations

The study was conducted among asthma patients already diagnosed and receiving treatment at KNH. The study did not enroll asthmatic patients on follow up from other facilities outside KNH or other clinics in KNH other than the chest clinic. Patients enrolled were those in whom asthma treatment had been initiated at the clinic for at least the past three months.

1.8 Limitations

Spirometry being an objective investigation for measuring the level of asthma control was not employed in this study (23). The HRQoL measure being subjective, information collected from participants might have been under-reported or exaggerated.

1.9 Conceptual Framework

Patient reported HRQoL outcome is a dependent indicator variable for asthma control. There are various independent variables that impact asthma control and consequently determine the HRQoL outcome of asthmatic patients. These variables include: Patient specific non-modifiable factors such as genetics, gender and atopy/allergy are known to predispose individuals to develop asthma (3,6,9). Modifiable factors including comorbidities and environmental factors influence development of asthma either independently or in the setting of non-modifiable factors. The comorbidities and medical states include obesity, allergic rhinitis, eczema, Human immunodeficiency virus (HIV) infection and frequent respiratory tract infections, among others. Some of the environmental factors include air pollution, allergen exposure, occupation, smoke, fog, cold air, dust, pet dander and cigarette smoking. Patient compliance or adherence, the pharmacotherapy of asthma and health care provider factors also play a significant role in asthma control. All these variables interact in a complex way to bring about the level of asthma control which consequently determines the quality of life of the asthmatics (3,6,9) (Figure 1.1).

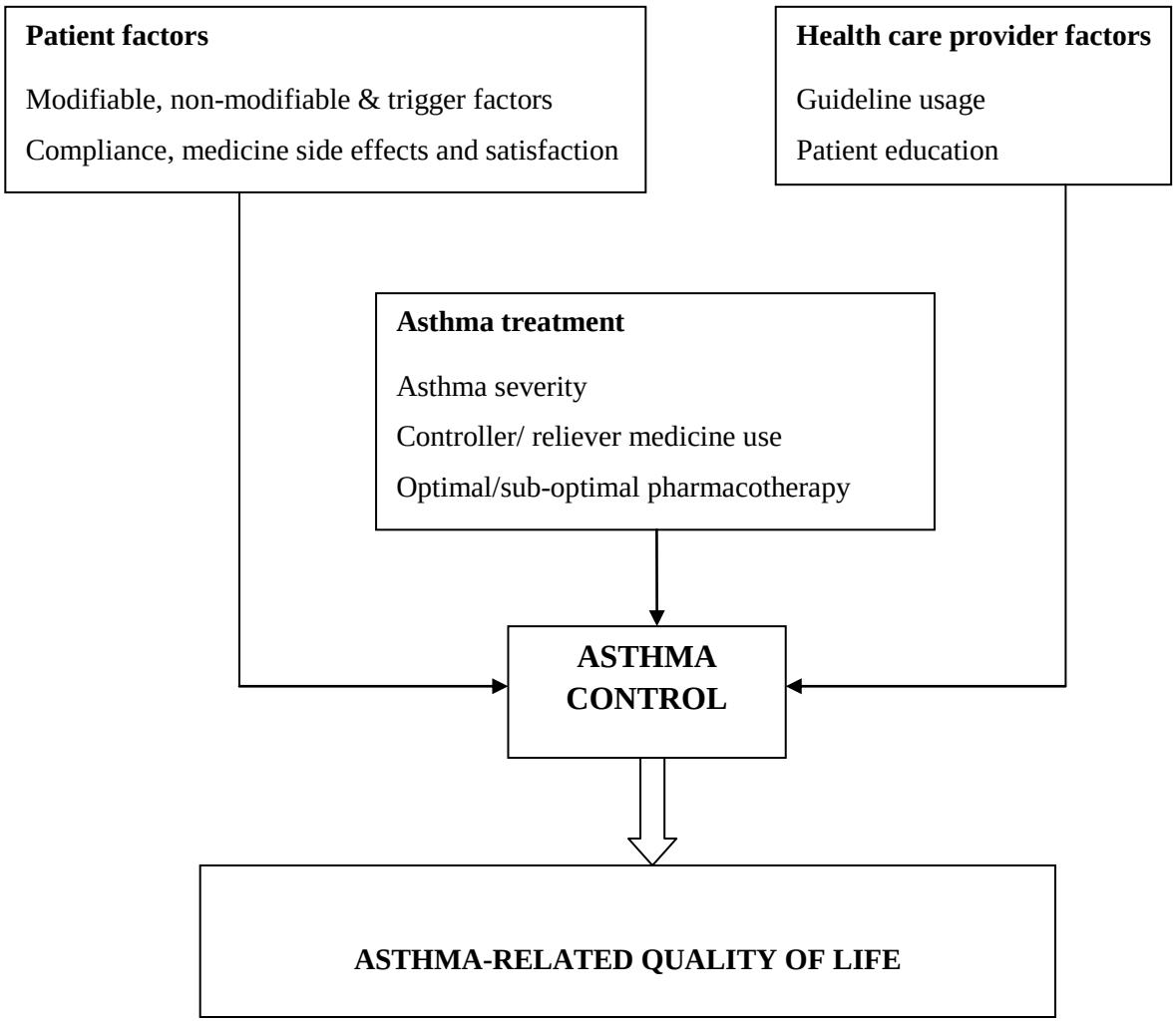


Figure 1.1: Conceptual Framework.

CHAPTER TWO: LITERATURE REVIEW

2.1 Asthma

Asthma has been recognized as the most prevalent, chronic, non-communicable lung disease worldwide. It often begins in childhood and affects all ages (3–5). It is associated with major disability, low quality of life and increased health resource expenditure. Despite this, its diagnosis and treatment have been suboptimal in most parts of the world and especially the low income regions (3,6). It sets in at an early age with approximately quarter of the general population developing the disease before age 40 (4). It is characterized by a chronic inflammatory process of the airways resulting in bronchospasms that cause airflow limitation and airway hyper-responsiveness (8). These effects produce the symptoms of the disease such as wheezing, tightness in the chest, shortness of breath and coughing which occurs mostly at night or early in the morning when air is cold (5,9). These episodes lead to obstruction within lungs, a situation that is usually reversible either by medication or spontaneous (3).

2.2 Diagnosis of asthma

Asthma is frequently misdiagnosed, often leading to under treatment (3,24). According to the National Asthma Education and Prevention Programs (NAEPP) Expert Panel Report 3, the proposed guidelines for diagnosing and managing asthma are applicable to all ages (25). These guidelines put emphasis on two key elements in diagnosing asthma. First, the clinician should determine the presence of episodic symptoms of airflow obstruction or airway hyper-responsiveness. Airflow obstruction should at least be partially reversible and differential diagnoses (Table 2.1) excluded (25).

Table 2.1: Common Differential diagnoses for asthma

12-39 years old	>40 years old
Foreign body aspiration	Bronchiectasis
Congenital heart defects	Vocal cord/laryngeal dysfunction
Cystic fibrosis	Hyperventilation
Chronic cough	Alpha1-antitrypsin deficiency (AAT_1)
Bronchiectasis	COPD
Vocal cord dysfunction	Left Ventricular Heart Failure
Hyperventilation	Drug induced cough (ACEIs)
Alpha1-antitrypsin deficiency (AAT_1)	Parenchymatous lung disease
Tumors	Pulmonary embolism
	Central airway obstruction
	Tumors

Source: Guidelines for management of asthma in Kenya 2011; Horak, 2016; Reed, 2010 (3,25,26).

To be able to do this, the clinician is required to take the patient's medical history in detail, carry out a physical examination that is focused on the upper respiratory tract, chest and skin. This is then followed by spirometry to demonstrate obstruction and assess reversibility (3,25). Reversibility is established when after inhalation of a short acting bronchodilator there is an increase of ≥ 12% in Forced Expiratory Volume in one second (FEV_1) from the initial value or by an increase of ≥ 10% of the population predicted FEV_1 values (3,25).

Peak Expiratory Flow (PEF) measurement tests demonstrate variability of airway limitation. A peak flow meter is used to measure diurnal PEF and patient values are compared to the population predicted values. The FEV_1 and PEF tests are used to support clinical diagnosis and also estimate the severity of asthma (Table 2.2) while guiding treatment decision (3). A reduction in FEV_1 and PEF is indicative of presence of airway limitation in the patient with the degree of reduction being proportional to the severity of

the disease (6). Airway challenge using broncho-constrictor stimuli to ascertain AHR is useful for patients with normal spirometry yet with symptoms of asthma.

Global Initiative for Asthma (GINA) proposed that an increase of ≥ 12% in FEV_1 equivalent to 200ml within 15-20 minutes following inhalation of 200-400 µg of salbutamol or a 20% increase in PEF from baseline can be used as the standard for diagnosing asthma (6). However, many asthmatic patients especially those on controller medications, on assessment, may fail to show an increase in FEV1 and PEF as these two lack sensitivity (6).

Significant reversibility of airway obstruction being a characteristic of asthma, its absence however, does not rule out the disorder (6). It could be in coexistence with COPD especially in the elderly due to severe airway remodeling. Investigations in patients suspected thus should be extended to diagnose other lung diseases if FEV_1 remains low after treatment (25,27).

Table 2.2: Asthma severity categories of untreated patients

Intermittent asthma (STEP 1)	Patients have symptoms less than thrice weekly. Night awakenings less than thrice monthly. Patient uses a SABA less thrice weekly. Lack of interference in normal activities. FEV_1 of > 80% predicted.
Mild persistent asthma (STEP 2)	Patients have symptoms > twice weekly but not daily. Night time awakenings 3-4 times monthly. Patient uses a SABA > twice weekly but not daily. Minor limitations in normal activities. FEV_1 of > 80% predicted.
Moderate persistent asthma (STEP 3)	Patients have symptoms daily Night time awakenings > than 1 night per week but not every night. Patient uses SABA daily FEV_1 of 60-80% predicted.
Severe persistent asthma (STEP 4)	Patients have symptoms throughout the day. Night time awakenings every night. Patient uses a SABA multiple times per day. Patients have extreme interference with normal activity. FEV_1 of < 60% predicted.
Severe persistent asthma (STEP 5)	Patients continue to have persistent symptoms or exacerbations despite correct inhaler use and good adherence on Step 4 treatment. Patient needs referral to a specialist who has expertise in managing severe asthma.

Source : Asthma-Pulmonary- Medbullets Step2/3, NEW GINA 2017 Report (27,28).
SABA = Short acting $beta_2$ agonists, FEV_1 = Forced expiratory volume in one second.

2.3 Asthma treatment

The treatment goal of asthma is to keep the disease controlled. This entails reduction of risk and impairment (29). Risk reduction involves: prevention of frequent attacks of asthma with reduction in emergency hospital visits or admissions, preventing lung function loss, preventing lung growth reduction in children and the provision of optimal pharmacotherapy with minimal or no adverse effects. Impairment reduction involves: preventing persistent and bothersome symptoms, reducing reliever medication need (to less than 2 days a week), maintaining normal or near normal pulmonary function, maintaining usual levels of activity such as exercise, school attendance, physical activity, work and satisfying patients' and families' expectations of asthma care (28–30).

How patients respond to treatment is paramount thus GINA has come up with recommendation of the concept of asthma control and therapy steps. Based on this, asthma severity is established retrospectively after a treatment period of several months and could change over time. Asthma severity classification therefore emanates from the therapy step that is required to achieve asthma control (28–30).

2.3.1 Control based asthma management

It encompasses both the non- pharmacological and pharmacological therapy. Asthma management aimed at control entails assessment, adjustment and review. Assessment involves diagnosis, control of symptoms, lung function tests, risk factor evaluation, inhalation technique, therapy adherence and patient preference evaluation (31,32). Adjustment takes into consideration asthma medications, non-pharmacological interventions and modifiable risk factor treatment. Review targets symptoms, exacerbations, side effects of medications, patient satisfaction and lung function determination (31,32). For a minority of patients with severe and worsening asthma, though not recommended in the current guidelines, Fractional Exhaled Nitric Oxide (FENO) measurement and induced sputum analysis for the specific inflammatory phenotype could be done (31,32).

2.3.2 Choice of therapy

The inhalation route is the preferred route for asthma medication administration. It delivers drugs directly to the site of action producing higher local concentrations, less systemic side effects and better medication toleration in comparison to systemic routes of administration (31,33). For long term asthma treatment, three pharmaceutical categories are preferred. Symptom reliever medication is taken on as-need basis (prn) to reduce symptoms in case of an attack or exacerbation. Symptom control produces reduced asthma exacerbations (28,34–36). Keeping the need for reliever medication to a minimum is the key objective in asthma therapy. Controller medication needs to be taken on a regular basis to reduce inflammation, risk of exacerbation and control symptoms. Add-on medications are indicated for patients whose asthma is severe who experience persistence in their symptoms or get frequent attacks despite high dose combination therapy with controller medication and optimal management of modifiable risk factors (28,34–36).

Table 2.3: Classes of medications for asthma treatment

Relievers	Controllers	Add-on therapy
Short acting $beta_2$ agonists (SABA). Short acting anticholinergics (SAMA).	Inhaled corticosteroids (ICS). ICS/long acting $beta_2$ agonist (LABA) combination. Leukotriene receptor agonist (LTRA). Long acting anticholinergics (LAMA). Methylxanthines: theophylline. Sublingual allergen immunotherapy (SLIT).	Anti IgE therapy: omalizumab Oral corticosteroids (OCS). Anti InterLeukin5 therapy: mepolizumab, reslizumab Specialist interventions such as phenotype specific treatments.

Source: NEW 2017 GINA Report, British Guidelines on Asthma management 2014 (28,36). IgE = Immunoglobulin E.

2.3.3 Post initial diagnosis treatment

Maintenance therapy using a controller such as low dose ICS is to be initiated promptly after an exacerbation so as to improve or reduce deterioration of lung function to enable achievement of best possible results. Further management will be dictated by the level of asthma control and individual patient presentation after the initial diagnosis (28,32,34,37,38).

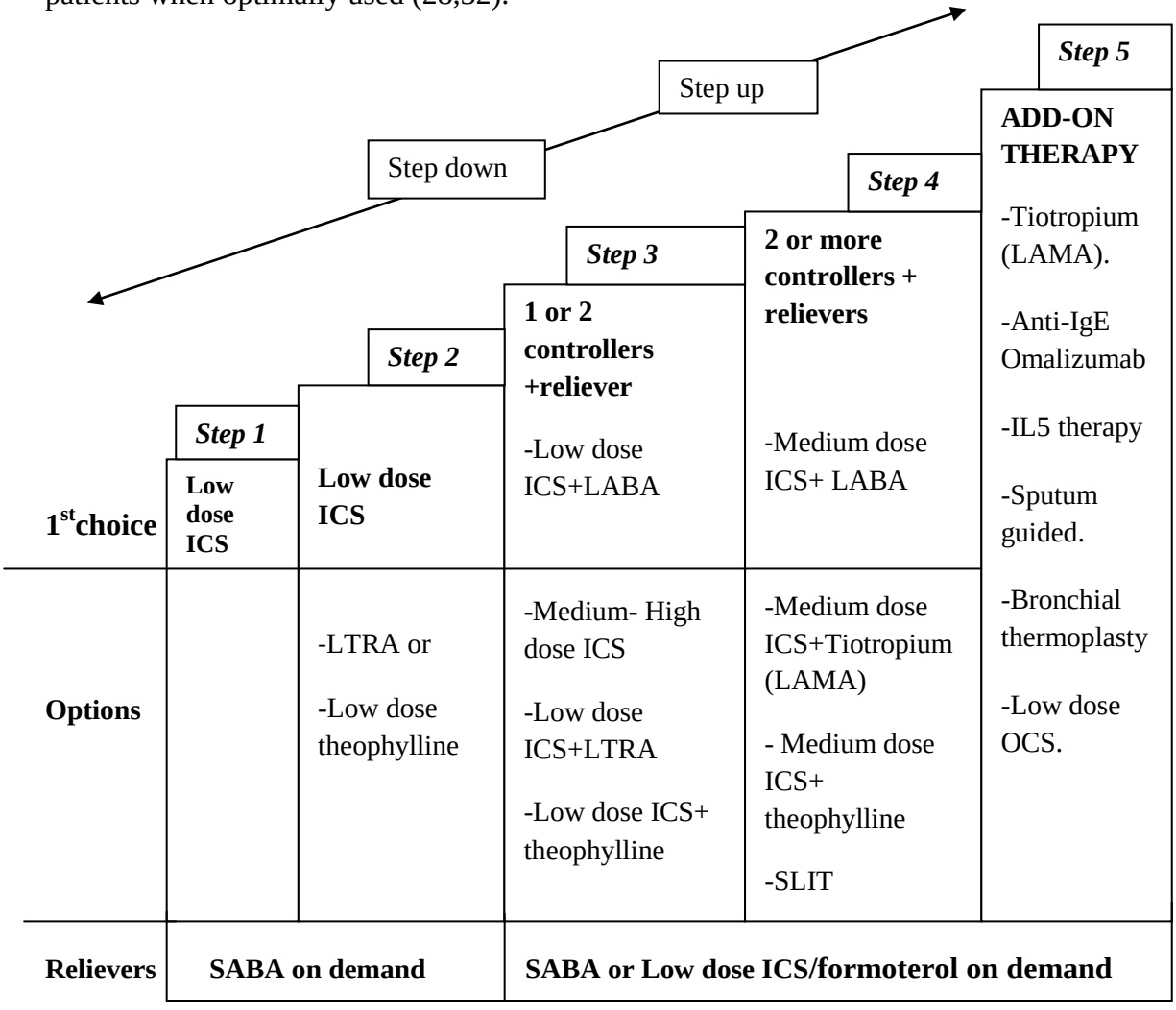
Table 2.4: Indications for reliever and/or controller medication use

Reliever	SABA alone	Presence of occasional daytime symptoms / Symptoms of short duration (a few hours) / Needs SABA less than twice per month / No nocturnal awakening and normal lung function / Lack of risk factors for exacerbation or absence of exacerbation over the last 12 months.
Controller + prn reliever	Low dose ICS	Normal lung function or FEV_1 <80% predicted / Presence of more frequent symptoms / Need for SABA < twice monthly / No night waking / One exacerbation over the past 12 months or presence of at least one factor for exacerbation.
		Presence of more frequent symptoms / Need SABA> twice monthly / Night awakening > once monthly.
		Frequent symptoms / Need for SABA > twice monthly.
	Medium dose ICS / High dose ICS / Low dose ICS+ LABA	Symptom occurrence on most days / Night waking > once monthly / Presence of at least one exacerbation risk factor.

Source: NEW 2017 GINA Report. SABA= Short acting $beta_2$ agonists, ICS= Inhaled corticosteroids, FEV_1= Forced expiratory volume in one second, LABA= Long acting beta agonists.

2.3.4 Stepwise approach in asthma management

Guidelines for asthma therapy recommend a stepwise approach whereby treatment is increased until asthma control is obtained. Before stepping up therapy, incorrect inhaler technique, non-compliance, environmental asthmagen exposures and differential diagnoses need first to be assessed and ruled out. Treatment may be stepped down once control has been achieved and maintained for 3 or more months. The available controller and reliever medications have proved to be effective in achieving asthma control in most patients when optimally used (28,32).



Source: Horak 2016, NEW 2017 GINA Report.

ICS = Inhaled corticosteroids, LABA = Long acting beta$_2$ agonists, LTRA = Leukotriene receptor agonists, LAMA = Long acting muscarinic antagonists, SLIT = Sublingual immunotherapy, IgE = Immunoglobulin E, IL = Interleukin, OCS = Oral corticosteroids.

Figure 2.1: Stepwise algorithm of asthma therapy for patients >12 years old.

Step1 treatment involves the use of prn reliever inhaler. The preferred reliever is a SABA since it is highly effective for quick relief of symptoms (28,32). Other options not recommended for routine use include short acting muscarinic antagonists (SAMA) such as Ipratropium, oral SABA and short acting theophylline. Their onset of action is slow when compared to inhaled SABA. Oral SABA is associated with high risks from side effects and is thus, contraindicated (28,32). Formoterol, a LABA is as effective as a SABA for symptom relief although frequent use without ICS is contraindicated due to an increased risk of exacerbations (34,37,38).

Step 2 treatment involves the use of Low dose controller in addition to prn reliever. The preferred choice at this step is regular low dose ICS and SABA prn (28,38,39). The low doses of inhaled corticosteroids decrease symptoms of asthma, improve pulmonary function and quality of life. In addition, they also lower the risk of exacerbations, hospitalizations or death. Other options include LTRA though lower in efficacy when compared to ICS. Leukotriene receptor agonists could be appropriate as controller medication for a subset of patients unable or unwilling to use ICS or experience intolerable adverse effect of ICS. Leukotriene receptor agonists in combination with ICS are indicated for asthmatic patients with concomitant allergic rhinitis (34,37,38).

For patients who were previously not on any controller medications, use of low dose ICS/LABA as the initial controller produces reduction in symptoms and improvement in lung function when compared to low dose ICS alone though more costly and associated with greater risk of exacerbations than ICS alone (28,34,39). For patients with purely seasonal allergic asthma (such as to pollen) and who are devoid of asthma symptoms during intervals, an ICS needs be initiated immediately symptoms begin and maintained for a month after the asthmagen season is over. Cromones and sustained release theophylline have weak and low efficacy and are thus options not recommended for routine use. The side effects of theophylline abound and are life-threatening at higher doses (28,32,34,37,38).

Step 3 treatment involves the use of one or two controllers in addition to prn reliever (28,34,39). Maintenance with low dose ICS/LABA in addition to prn SABA or alternative low dose ICS/formoterol as both reliever and maintenance are the

recommended therapy at this step. Low dose ICS either budesonide or beclomethasone could be used as both reliever and maintenance therapy. Low dose ICS/formoterol used both as reliever and maintenance significantly reduces the risk of exacerbations. It produces equal asthma control levels at low doses of ICS just as fixed dose ICS/LABA with prn SABA or high dose ICS plus prn SABA. Examples of low dose ICS/LABA fixed dose combinations include; beclomethasone/formoterol, budesonide/formoterol, mometasone/formoterol, fluticasone propionate/formoterol, fluticasone furoate/vilanterol and fluticasone propionate/salmeterol (28,32,38,39).

For adults who have allergic rhinitis that has been sensitized to house dust mites and who experience frequent exacerbations despite low to high dose ICS, sublingual allergen immunotherapy (SLIT) could be added as long as FEV_1 is >70% predicted. Other options less efficacious include increasing low dose ICS to medium dose or low dose ICS plus LTRA or low dose sustained release theophylline. All these three alternatives are less effective than the preferred low dose ICS/LABA (28,32,38,39) .

Step 4 treatment involves the use of two or more controllers in addition to prn reliever medication (28,32). The preferred choice at this step is low dose ICS/formoterol both as controller and reliever. This regimen has been found more effective in reducing exacerbations than medium dose ICS/LABA and prn SABA. Low dose ICS/formoterol maintenance dose may be increased if necessary while using budesonide/formoterol or beclomethasone/formoterol as relievers. Patients on low dose ICS/LABA maintenance with prn SABA whose asthma remains uncontrolled need stepping up of their regimen to medium dose ICS/LABA. Other options include tiotropium (a long acting muscarinic antagonist (LAMA)), theophylline, SLIT and high dose ICS which provide little additional benefits with increased side effects such as adrenal suppression for high dose ICS (34,38,39).

Step 5 treatment involves specialist asthma care alongside add-on treatment (28,32,34). Patients who experience persistent symptoms or exacerbations despite good adherence at step four with controller options having been considered and correct inhaler use technique need referral to a severe asthma management specialist. Considerations at this step include; Tiotropium which improves lung function and decreases the frequency of

severe exacerbation. Anti-Immunoglobulin E (Anti-IgE) medications such as Omalizumab have been proven useful in patients with moderate or severe allergic asthma not stabilized at step four. Interleukin 5 treatment such as subcutaneous Mepolizumab and intravenous Reslizumab has been recommended for severe eosinophilic asthma patients uncontrolled at step four (28,32,34). Sputum guided therapy is indicated for asthmatics with persistent symptoms or attacks despite treatment with high dose ICS or ICS/LABA. Adjustment of therapy based on eosinophilia of more than 3% in induced sputum is recommended. This strategy leads to decreased exacerbations and or stabilization on lower doses of ICS. Some adults with severe asthma may benefit from Bronchial thermoplasty although long term function or effect is unknown (38–40).

Low dose oral corticosteroids (OCS) such as prednisolone are effective in a subset of adults with severe asthma although their chronic use produces substantial adverse effects (28,32,34). Adults who experience frequent exacerbations or who have poor symptom control in whom all other contributory factors have been ruled out could be beneficiaries (28,32,34). Short term side effects include sleep disturbance and increased appetite. Patients on long term use of OCS need to be followed up and monitored for the risk of developing corticosteroid induced diabetes and osteoporosis. The step-wise asthma management along with medications used in the population under study has not been fully investigated (34,38,39).

2.4 Health Related Quality of Life

Health related quality of life (HRQoL) is defined as the value given to an individual's length of life that is influenced by disease or treatment (41). It is a concept that has many dimensions that not only covers effects of an ailment and its therapy on one's life but also domains related to the psychological, social, and physical function of a patient (42).

The Physical domain deals with the degree to which one's perception of their life's quality is impacted by physical symptoms emanating from the disease itself or its treatment. It defines the degree to which respondent's ability to engage in strenuous activities such as hurrying, raising heavy objects, sports or exercise, running up the stairs and walking for long distances. It also consists how individuals perform in moderate activities such as walking, climbing stairs, shopping, housework, and self-care (41). The

Psychological domain entails functions that may range from psychological distress to a sense of positive well-being. It refers to the extent to which one is happy, calm, tired or nervous (41). The Social domain involves the qualitative and quantitative aspects of social relationships and interactions with others such as family members, neighbors, friends, among others (41).

Quality of life (QoL) as used synonymously with HRQoL is an abstract term that is personal and unique to each individual and society and encompasses everything from physical health, family, education, employment, wealth, spirituality, finance and environment (41). Health related quality of life exceeds direct measures of population health, life expectancy and mortality causes to focus on the impact health status has on an individual's QoL (1). It puts the patient in the center and reflects one's own subjective view of their functioning and wellbeing status. Variables such as age, socioeconomic status, gender and social support play a role in an individual's perceived HRQoL (43).

2.5 HRQoL Measurement Instruments

Measurement of HRQoL has been rated as an important end point in reflecting the effects of an illness and its treatment from a patient's perspective (42). Some tools/instruments used in its measurement are generic while others are disease specific. An instrument which is disease-specific collects data on a patient's perception on specific aspects of their health that is affected by that disease. On the other hand, a generic instrument measures general health which includes physical symptoms, the social and emotional functioning domains that are relevant to all health states including those of healthy persons (44).

Various tools have been developed to measure Patient Reported Outcomes (PROs). They include PROMIS Global 10, EQ-5D, SF-36, VR-12 and AQL(45). Others are the Health Utility Indexes, Mark-28, Mark-3, Mark-AQLQ, SF-6D, MiniAQLQ, AQLQ(S) and PACQLQ among others (21,23,45,46). The SF-36 (Short Form 36) tool measures overall health unlike other tools that target a specific disease or area of the body. It is often paired with a more disease specific PROs such as AQLQ in case of asthma.

Asthma Quality of Life Questionnaire with Standardized activities (AQLQ(S)) is disease-specific and measures both the physical and emotional impact asthma has on individuals aged 12 years and above (23,45). The Pediatric Asthma Quality of Life Questionnaire (PAQLQ) is also disease-specific measuring both the physical and emotional impact asthma has on children. The Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) is an instrument for grading a parent's impairment in activities due to their child's disease (23). The Patient Reported Outcomes Measurement Information System Global 10 (PROMIS), a global assessment tool, measures symptoms, functioning and HRQoL for many chronic diseases and conditions (45).

The European Quality of Life group (EQ-5D) is a tool applied to a wide range of health conditions used to quantify HRQoL. It is a self-reported tool which measures a patient's health across 5 different domains; mobility, self-care, usual activity, pain/discomfort and anxiety/depression (45). The Veterans RAND 12 (VR-12) is a self-reported global health measure tool used to assess a patient's overall rating of their health (45). The Mark-AQLQ, a 20 item self-administered questionnaire, measures QoL in adults with asthma (47). Tools for measuring the level of asthma control include the Asthma Control Questionnaire (ACQ) and the Asthma Control Test (ACT). The ACT is a short, simple, patient-based tool that identifies patients with poorly controlled asthma (48,49).

In this study, the AQLQ(S) and the ACT research instruments were employed to quantify patient reported outcomes of therapy. The AQLQ(S) was preferred for this study since it is specific for measuring HRQoL in asthma and is also suitable for age above 12 year. The ACT was preferred over the ACQ for this study since evidence from a systematic review and meta-analysis suggested it to be suitable in clinical practice and that the ACQ required further cross-validation (49).

2.6 Importance and benefits of HRQoL evaluation

Majority of patients seek help from health care providers because they perceive their health and well-being to be impaired. This could be as a result of troublesome symptoms, limitation of their day to day activities or anxiety about their disease. It is therefore imperative that the health care providers to not only manage the underlying clinical

disorder but also address the patient's impaired life quality, the primary reason he/she sought help (23).

HRQoL evaluation assists in identifying health associated problems affecting different dimensions of an individual's life. Measurement of HRQoL can also be used to influence individuals to make improvements to their own quality of life and also assess the success or failure of interventions (1).

2.7 HRQoL and Asthma

The disease asthma, is known to negatively impact the quality of life of those who suffer from it (42). Studies have revealed that spirometry measures such as FEV_1 though being objective in measuring asthma control, correlate weakly with symptoms and with disease targeted HRQoL. Since the impact asthma has on a patient's QoL cannot be directly inferred from clinical indices, it must therefore be directly measured (23). This view is supported by the National Asthma Education and Prevention Program (NAEPP) which recommends asthma control assessment using patient reported outcomes such as HRQoL measures (21).

2.8 Patient factors influencing HRQoL in Asthma Patients

The onset of asthma in individuals is influenced by various risk factors of which some are modifiable while others are not. The non-modifiable factors encompass genetics, gender and atopy whereas modifiable ones include environmental and comorbid factors. Triggers are factors that cause attacks and exacerbations and include exercise, air pollution among others. These factors need to be established and controlled in order to meet the goal of therapy which is optimal asthma control that will eventually determine patient HRQoL (17,18,50–52). Health related quality of life is influenced by various individual patient factors listed in Table 2.5.

Table 2.5: Asthma Risk factors and Triggers

Risk factors for asthma development		**Triggers**
Non-modifiable factors	**Modifiable factors**	
Age/onset Gender Atopy/allergy Airway hyper responsiveness	Allergen exposure- pollen, chemicals Infestations (helminths) & infections:- RTIs ,HIV Occupational exposures Tobacco/cigarette smoking Comorbidities;- GERD, allergic rhinitis, obesity Drugs;- NSAIDs use Female sex hormones Socioeconomic status	Environmental/ air pollution:- Dust, fog or cold air, smoke, pet dander Viral /bacterial RTIs Strong smells Stress/emotional reactions NSAIDs Menses Exercise

Source: Guidelines for Asthma management in Kenya 2011, Adeloye 2013, Horak 2016 (3,6,26) KEY: GERD - gastroesophageal reflux disease, NSAIDs - non steroidal anti-inflammatory drugs, RTI = Respiratory tract infection, HIV= Human immunodeficiency virus. .

2.8.1 Age

Studies have revealed that majority of asthma cases begin in childhood (5,53). The main risk factors for this age group include; genetic predisposition, positive history of allergy and asthma in the family line, respiratory tract bacterial colonization and viral infections, tobacco smoke exposure and allergic sensitization (53). Older adults have more severe, less reversible asthma compared to younger patients whose asthma may be reversible (8,25). The impact asthma has on the QoL on various age groups has not been adequately studied and compared.

2.8.2 Age of onset

Early onset asthma begins at or below age 12 and is mainly associated with atopy. It usually runs a less severe course with good response to corticosteroids compared to late

onset asthma which begins after age 12 (5,53,54). Early onset asthma may resolve as the child grows older. Late onset asthma is not known to be atopy associated and often follows a severer course which responds poorly to inhaled corticosteroids. It also presents with faster decline in lung function and impacts a patient's HRQoL more negatively (5,53,54). Comparison of HRQoL in early and late onset asthma has not been adequately studied.

2.8.3 Gender

In children under 6 years of age, more males than females are reported to suffer from asthma. By age 11, the ratio of male to female asthmatics gets to 1:1. Beyond age 16 the number of females with asthma supersedes that of males. In addition, females beyond this age also suffer a severer course of the illness than their male counterparts. This has been attributed to female sex hormones and obesity (3,8,55). In the population under study, it is not known whether females have a worse HRQoL than their male counterparts or vice versa since it has not been reported in the literature.

2.8.4 Atopy/ Allergy

Atopy implies the genetic susceptibility of an individual to develop eczema, atopic dermatitis, allergic rhinitis (hay fever), allergic conjunctivitis and asthma, diseases that are of classic allergy nature. Atopy can also be termed as an exaggerated immune reaction in which there is production of Immunoglobulin E (IgE) in response to common environmental proteins (foreign antigens) such as house dust mites, grass pollen and food allergens. It's a type 1 hypersensitivity disorder (56) and has a hereditary component associated with maternal psychological trauma in utero (55,57). The HRQoL in asthmatic patients with allergy in this population remains unknown since no studies have been documented in literature.

2.8.5 Occupational exposure

This refers to asthma that originates from exposures in a particular occupation's environment without involvement of external stimuli. Some of the occupations associated with development of asthma include, laboratory work, bakery, chemical processing, rubber and plastic work, electronic assembly, printing, nursing profession, cleaning,

spray painting, saw mill work, wood work, metal treatment work, food processing, hairdressing and tobacco processing (18,58). Agents at workplace are said to induce asthma through specific immunologic responses or via unknown mechanisms. Sensitizers mostly implicated are usually high molecular weight agents that induce specific IgE antibody production that mediates typical allergic responses. Low molecular weight chemical sensitizers induce asthma via unclear mechanisms (18,58). The proportion of asthmatic patients in this population who have developed asthma as a result of work exposure has not been documented.

2.8.6 Tobacco /Cigarette smoking

Smoking adversely affects the pulmonary function. Environmental smoke exposure for instance maternal smoking is a significant risk factor for asthma development in children. Environmental exposure to tobacco smoke in asthmatics produces more severe symptoms, decline in quality of life, decreased lung function and increased health care utilization (51,59,60). Active smoking is a major risk factor for adult onset asthma that is associated with worse pulmonary function and asthma morbidity and mortality hence a low HRQoL (51,59,60). Patients with asthma are thus encouraged to stop smoking. The HRQoL of current smokers and former smokers in comparison to non-smokers remains undocumented in this population.

2.8.7 Stress

Stress is an increasing risk factor for asthma. Emotional events like illness or death of a loved one, marital issues, separation, divorce and conflict have been linked to asthma onset (53,61). Previous studies that have investigated the association between work related stress and asthma onset in adults have suggested a strong association for both sexes that lacked alternative explanations (53,61). Stress modulates and activates biological pathways involved in the asthma pathophysiology. It modulates inflammation through release of hormones and neuropeptides which interact with immune cells. In addition, stress causes release of cortisol and adrenaline which shift immune responses from T-helper 1 (antibacterial) towards T-Helper 2 (humoral) response. Thus, stress alters the psychological, immunological and endocrine systems which contribute to the onset of asthma (53,61). A population based cohort by Lietzen et al indicated that life's stressful

events are a risk to developing asthma. The proportion of asthmatics whose onset of the disease is attributable to stress or whose asthma is worsened by stress remains unknown as no studies have documented it in literature (61).

2.8.8 Obesity

Prevalence of symptomatic asthma in individuals may be more due to overweight and obesity than aeroallergen sensitization (62). Abdominal obesity is implicated especially in women (63). Obesity has been known either to cause or worsen asthma. Adipokine-leptins and adiponectin are involved in the inflammatory pathogenesis of asthma. Obesity is not associated with eosinophilic airway inflammation hence patients respond less well to corticosteroids (50). Obesity and asthma are said to share common etiology such as genetics, similar in-utero conditions and dietary factors. Comorbidities associated with obesity such as dyslipidemia, GERD, Obstructive sleep apnoea, type 2 Diabetes Mellitus or hypertension may provoke or worsen asthma (64). Overweight and obese asthmatics exhibit poorer asthma control that is known to respond less to inhaled corticosteroids when compared to their normal weight counterparts. Weight reduction could thus result in improvement of clinical symptoms and outcomes of asthma management in this subset of asthmatics (26,65). It remains unknown whether poor asthma control and subsequent low HRQoL is a feature in all obese asthmatic patients in the population under study.

2.8.9 Exercise

Exercise Induced Bronchoconstriction (EIB) is a common feature in asthmatic children and adolescents due to increased physical activity in this population. It causes daily life activity limitations in up to 30% of asthmatics (66). It results in bronchoconstriction that occurs immediately or soon after physical exercise. This has been attributed to increased production of respiratory water and heat loss due to increased ventilation during exercise (66). This subsequently causes the release of inflammatory mediators with consequent airway receptor stimulation. The diagnosis of Exercise Induced Asthma (EIA) is made by standardized exercise tests whose sensitivity is raised by cold air conditions (66).

Exercise Induced Asthma is effectively managed with controller inhaled corticosteroids in combination with pre-exercise inhaled $Beta_2$ agonists (SABA or LABA) and or LTRAs. Although physical training improves physical fitness, it does not improve

baseline pulmonary function and airway responsiveness (66). Other studies have shown some evidence of benefit of fruit intake (antioxidants) in adults and children with asthma suggesting that Vitamin C supplementation may decrease exacerbation in EIA (67). The HRQoL in asthmatics with EIB has not been studied in this population.

2.8.10 Socio-Economic Status

A study by a group of investigators assessed the association between socioeconomic status (SES) and asthma. Their findings indicated that cumulative incidences of asthma generally were lowest among professionals who included intermediate and high level workers in the civil service and also executives. Manual workers in industry and those in service demonstrated identical patterns of recurrent wheeze, chronic productive cough, shortness of breath attacks and were at a significantly greater risk of developing asthma. The population attributable risk was approximately 10% implying low SES was a risk for developing asthma and having poor HRQoL (68,69).

Other researchers reported that persons with low SES face double burden in that they have a higher number of health impairments alongside reduced HRQoL once health is compromised (43). The impact that SES has on the HRQoL of patients in the population under study is unknown as no studies have documented it in literature.

2.8.11 Respiratory infections

New evidence shows that frequent respiratory infections were a strong determining factor for adult-onset asthma. Efforts to reduce such infections may prevent adult asthma onset especially in those who are atopic (70). Recently, a longitudinal study incorporating 138 asthmatic adults conducted to establish the role of respiratory viruses in asthma noted that symptomatic asthma and decreased peak flow were attributable to colds and respiratory viruses. It was concluded that respiratory virus infections commonly cause or lead to exacerbations in adults and children and negatively impact HRQoL (71). The proportion of asthma patients who experience exacerbations that is attributed to respiratory infections and thus a poorer HRQoL has not been documented in this population.

2.8.12 Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is the regurgitation of stomach acid into the esophagus (52). It affects more than 75% of patients with asthma and if untreated could cause lung damage. A clear association between GERD and asthma has not been established. In co-existence, it is known to cause worsening of asthma symptoms. On the other hand, asthma along with some of the medications for managing it may in turn worsen GERD symptoms (52). Possibilities to explain this relationship suggest that acid flow causes irritation to the lining of the throat, airways and lungs which produces persistent coughing. In addition, acid stimulates the vagus nerve causing airway narrowing that result in shortness of breath. Non-pharmacologic measures such as bed propping, diet modifications, smoking cessation, adorning loose belt and clothing as well as treating GERD helps relieve asthma symptoms thus suggesting a relationship (52,72). The HRQoL of patients with GERD and asthma remains unstudied in this population.

2.8.13 Allergic Rhinitis

Allergic rhinitis is a disease characterized by chronic inflammation in the upper respiratory tract whose prevalence is approximately 5-50% worldwide (73). It occurs in association with asthma, sinusitis and conjunctivitis. Major symptoms of allergic rhinitis include nasal congestion, rhinorrhea, sneezing, itching and post nasal drip that are induced after allergen exposure mediated via IgE (73). Asthma onset is preceded by allergic rhinitis and when in coexistence, it is associated with worsening of asthma symptoms and poor quality of life (73). Current treatment options available for this type of asthma include antihistamines, anticholinergic agents, decongestants, intranasal cromolyn, LTRAs and ICSs (73,74). The HRQoL of patients with coexisting asthma and allergic rhinitis remains unknown in this population as it has not been documented in literature.

2.8.14 Female sex hormones

Female sex hormones are known to play a role in adult onset asthma (75) . Evidence from recent studies suggest a relationship between puberty and increased incidence of asthma in young females with higher remission rates in young males (75). Asthma incidence

decreases after menopause while hormone replacement therapy in post-menopausal women raises the risk of asthma onset (75). Asthma prevalence decreases with the number of years of combined oral contraceptives pill (COCs) used (75). Parity has been associated with an increase in asthma prevalence from 8% (one birth) to 29% (≥ 4 births) (53). Studies show that asthma exacerbation occurs in the premenstrual period and affects up to 40% of asthmatic females (75). Evidence suggests that increased AHR, a sign of underlying airway inflammation occurring during the luteal phase of the menstrual cycle could be attributed to these exacerbations (75). Other implicated impairments include altered $beta_2$ adrenoceptor function and regulation in asthmatic female. Asthma attacks in most women are known to respond to the standard treatment of bronchial asthma (75). For a subset of women experiencing significant morbidity or adverse events of treatment, COCs or gonadotrophin-releasing hormone analogues have shown efficacy in them (75). The proportion of women whose HRQoL worsens during premenstrual period has not been documented for this population.

2.8.15 Non-steroidal anti-inflammatory drugs

Aspirin as well as other Non-steroidal anti-inflammatory drugs (NSAIDs) can precipitate bronchospasms in some asthmatic patients with aspirin intolerant asthma (76). The prevalence of aspirin induced bronchospasms is 5-6% with 20% of the asthmatic population being sensitive (76). The pathogenesis of aspirin-induced asthma implicates both the Lipooxygenase (LO) and cyclooxygenase (COX_1) pathways. Aspirin inhibits the COX_1 pathway thus diverting arachidonic acid metabolites to the LO pathway which also leads to a reduction in prostaglandin E_2 (PGE_2) along with increased synthesis of cysteinyl leukotrienes (76).

Studies suggest that asthmatics have raised Leukotriene C_4 (LTC_4) synthase activity – the rate limiting enzyme in LTs synthesis favoring inflammation (76). Leukotriene modifiers are effective in antagonizing bronchoconstriction provoked by aspirin and are used in the management of NSAID-induced asthma. For aspirin induced/intolerant asthmatics with comorbidities such as thromboembolic disorders, myocardial infarction and stroke who need aspirin prophylaxis, desensitization is recommended in such [Medscape Aspirin and Asthma] (76). Use of paracetamol poses a risk to asthma development as it promotes

glutathione depletion in airways causing increased oxidative stress (53). The proportion of asthmatics intolerant to NSAIDs in this population has not been studied.

2.9 Medication-related factors influencing HRQoL in asthma patients

2.9.1 Medication side effects and their impact on HRQoL

Side effects from the medications used to treat asthma may affect a patient's compliance thereby resulting into poor asthma control which negatively impacts the HRQoL of the patients (33,77). Relievers which include inhaled $beta_2$ agonists such as salbutamol or terbutaline are first line in treating symptomatic asthma. However, some patients use oral salbutamol which is relatively ineffective, has a narrow therapeutic window and more adverse effects (33,77). Some of the reasons for its continued use include the high cost of inhaled dosage forms, ease of administration and stigma in using devices. Oral salbutamol causes palpitations, tachycardia, behavioral and sleep disturbance, hypokalemia and hypoglycemia (33,77). It can lead to hypertension, angina, cardiac arrhythmias, seizures, cardiac arrest and death. Inhaled salbutamol is relatively safe but can cause some of these side effects at high dosages. Oral salbutamol interacts with drugs such as monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs) as well as loop and thiazide diuretics (33,77).

Studies conducted on controllers such as inhaled corticosteroids show that they cause side effects that include oral candidiasis which is usually attributed to incorrect inhaler use technique (78). Although systemic side effects of OCS are well established, studies have not focused on the systemic effects of ICS. Recent evidence suggests that patients using ICS especially high doses are at risk of adrenal suppression, hyperglycemia, decreased bone density, cataracts, thinning of skin and immune suppression thereby increased risk of pneumonia (78). Healthcare providers are therefore advised to use the lowest possible doses of ICS to control a patient's asthma. Budesonide poses a much lower risk of systemic side effects compared to fluticasone. Newer ICSs such as Ciclesonide are of more benefit in the reduction of systemic side effects on chronic use (78).

Oral corticosteroids are known to cause hypernatremia that leads to edema, weight gain, hypertension and headache. They also cause hypokalemia that requires cautious use with

other hypokalemic drugs. They also promote facial hair growth, easy bruising from skin thinning, slow wound healing, glaucoma, cataracts, stomach and duodenal ulcers due to inhibition of prostaglandin E_2 synthesis. Prolonged use may lead to growth retardation in children, obesity, type 2 diabetes, convulsions, osteoporosis, and psychiatric disturbances such as depression, insomnia and euphoria. Oral corticosteroids interact with drugs such as erythromycin, clarithromycin, ketoconazole, ephedrine, warfarin, estrogens, phenytoin, rifampicin, diuretics and amphotericin B (79). The impact of asthma medication side effects on patient HRQoL has not been described in literature hence remains unknown in this population.

2.9.2 Compliance to asthma medication

Optimal asthma control with positive impact on a patient's HRQoL entails adherence to controller medication at rates above 75% of the time (9). The availability of diagnostic equipment and controller medications alone is not sufficient to control asthma. A patient's compliance to medical advice such as lifestyle modification, avoidance or elimination of aggravating factors and proper use of therapeutic agents is important (9,29).

A retrospective cohort study conducted on 69,652 asthmatics of all ages, who had persistent asthma and with prescriptions of inhaled ICS, LTRA, ICS/LABA found that adherence to asthma controller medication was poor (29). Other studies have revealed that approximately 60% of asthma related hospitalizations are associated with poor adherence to controller medication (29). Under-usage of controller medications is attributed to healthcare provider under-diagnosis, under-treatment and patient non-adherence (29).

Adherence to medication is influenced by several factors including those connected to the patient such as presence of physical disorders, cognitive difficulties (forgetfulness), age, psychiatric comorbidities, inappropriate treatment expectations, denial, stigma, social or family support, culture, religious issues, education level and knowledge on the disease (9,28). Variables linked to the disease such as its chronicity nature, absence of symptoms or their stability also play a role (9,28). Adherence is also linked to variables related to

treatment such as presence of side effects, misunderstanding instructions, number of daily doses, complexity of regimens, cost and difficulty in inhaler device use. Healthcare provider-patient relationship such as dissatisfaction with services offered by healthcare provider also plays a role in adherence (9,28). The adherence rates to controller medications and how they impact asthma control and HRQoL in the population under study have not been described in literature hence remain unknown.

2.10 Healthcare provider factors influencing HRQoL in asthma patients

Asthma control impacts a patient's HRQoL and is influenced among other variables, by healthcare provider factors (9). These include misdiagnosis that may be due to limited awareness of asthma prevalence and inadequate patient assessment. Lack of consciousness and familiarity with current evidence-based practice guidelines and deep seated routines may hinder uptake and usage of the information therein (9). Adoption of a cooperative approach with patient involvement in his or her management process is therefore important. Provision of sufficient health education to patients in regard to the disease and its control along with demonstration of inhaler device use is important (9). The health care provider factors that impact the HRQoL of asthmatic patient population under study have not been investigated.

2.11 Previous studies on asthma and HRQoL

The Pediatric Asthma Caregivers Quality of life Questionnaire (PACQLQ) was in February 1996, developed to assess the quality of life in asthmatic children's parents. The investigators applied the tool to measure its properties in a nine week single cohort. They recruited primary caregivers of 52, 7-17 year old asthmatics children. Asthma quality questionnaire results, spirometry and beta agonist use was recorded. The study showed that the PACQLQ instrument is functional for both evaluation and discrimination (46).

Another study examined the psychometric characteristics of the AQLQ tool in a sample of asthmatics from United States of America (USA). Some 161 adults undergoing standard care of asthma in USA clinics were studied. The investigators found no relationship between the AQLQ scores and FEV_1 % predicted values. Males were found to have better overall QoL, fewer limitations in activity and less environmental stimulation compared to their female counterparts. Participants who were in the low

education category up to high school level reported severer asthma with poorer QoL. They concluded that AQLQ was a useful outcome measure tool for clinical trials (80).

A retrospective medical record data study on a sample size of 1546 patients having a diagnosis of either asthma, COPD or both was conducted. The investigators evaluated patient characteristics associated with HRQoL in this population. The study showed that patients with coexisting asthma and COPD (overlap syndrome) had poorer HRQoL compared to those who had either asthma or COPD alone. They also found that being female, obese, disabled, having long disease duration and coexistent cardiovascular disease impacted participant HRQoL (81).

A prospective study on 316 patients evaluated the QoL and the impact allergic rhinitis had on asthma. Participants studied had a diagnosis of either asthma or rhinitis, or both. The investigators used the SF-36 tool and also collected data on sociodemographic characteristics, atopic status, BMI and education. Of the 316 enrollees, 65% were female, 232 had allergic rhinitis alone, 40 had asthma and the remaining 44 had both diseases. The average age of participants was 32 years. They established that HRQoL was lower in subjects who had both asthma and rhinitis compared to those who had either disease alone. They also concluded that female gender, advanced age, obesity and lower education level were the main determinants of HRQoL among patients with allergic rhinitis or asthma in their population (82).

Another team of researchers investigated the relationship between asthma control hinged on guideline recommendations and HRQoL. The AQLQ tool was employed to assess patients with uncontrolled asthma whose therapy was adjusted to achieve the highest possible asthma control level. They conducted a randomized double-blind trial with one arm on Fluticasone propionate (FP) and the other on Salmeterol/fluticasone propionate (SFP) to compare the efficacy of FP and SFP in achieving control. Doses of the ICS and ICS/LABA were increased till participants achieved total control or reached maximum doses which were maintained throughout the study. Quality of life was measured at baseline and at follow up visits. The researchers noted that AQLQ scores improved throughout the study to reach near-maximum levels in patients who achieved total control (TC) and well controlled (WC) asthma. Clinically meaningful improvement from

baseline was also noted. These results led to the conclusion that treatments aimed at controlling asthma improve HRQoL to levels that approach normal. Differences in AQLQ score between TC and WC confirm a distinction even between these high levels of control (83).

A cross-sectional study of 967 asthmatic participants was carried out to elucidate the differences between gender in regard to HRQoL. The assessors found that asthmatic females had low HRQoL scores when compared to their male counterparts. In these women, age groups 16-34 and 56-75 year olds had lower HRQoL than age group 35-55 year olds. They concluded that subjective disease state was not related to disease severity since all the women studied had high levels of pulmonary function (84).

Another group of investigators conducted a cross-section on 160 adolescent athletes to examine the effect mild asthma, allergic rhinitis and EIB have on HRQoL. The assessors used the teen version of the Pediatric Quality of Life inventory (PaedQL) to assess the QoL. They discovered that adolescent athletes with asthma had lower HRQoL than their non-asthmatic counterparts. They also reported low scores in the physical, emotional and school functioning domains in addition to experiencing more frequent dyspnea symptoms during exercise. The researchers concluded that difficulty in breathing during exercise was common and associated with a low HRQoL (85).

In a study on 122 subjects to assess the association between asthma control and rhinitis on HRQoL, investigators found that 44.27% of the subjects had uncontrolled asthma and consequently low HRQoL. They also noted that regardless of their degree of asthma control, patients who had symptomatic rhinitis had poorer HRQoL. The conclusion made was that, the control of rhinitis in asthmatics could lead to optimization of HRQoL, strengthening the recommendation emphasizing the need to evaluate rhinitis in asthmatics and vice versa (86).

In a prospective study of 987 asthmatic adults followed up for 12 months, the degree of quality of life impairment associated with different levels of asthma control was quantified using the MiniAQLQ and EQ-5D tools. The assessors indicated that baseline poor asthma control was a predictor of worse AQLQ and ED-5D scores even on follow

up. They concluded that asthma control was the most important independent predictor of asthma related quality of life (87).

Another group of investigators set out to evaluate the impact uncontrolled asthma has on absenteeism and the HRQoL of adults, school children with asthma and caregivers of pediatrics with asthma. They collected data on absenteeism which was defined as the number of days in the previous six months participants missed work or school that was attributed to their asthma. They studied 15149 subjects using the Marks-AQLQ and PACQLQ tools for adults and caregivers respectively. They found out that asthmatic adults and caregivers of asthmatic children with uncontrolled asthma reported higher absenteeism than their counterparts in whom the disease was controlled. The ratios 43%:24% (6:3 days) represented uncontrolled versus controlled asthmatic adults' work absenteeism while 31%:16% (4:2 days) represented uncontrolled versus controlled caregivers' work absenteeism and 70%:45% (6:4 days) represented uncontrolled versus controlled pediatrics' school days missed. The investigators noted that lower HRQoL was reported in adults, caregivers and pediatrics with uncontrolled asthma. They concluded that the impact of uncontrolled asthma had far reaching implications on productivity and QoL of asthmatics and their caregivers. Therefore, targeted therapy to improve asthma control may reduce the impact of uncontrolled disease on patients and their caregivers (22).

According to a recent Kenya Association for the Prevention of Tuberculosis and Lung Disease (KAPTLD) report, studies in Kenya have shown that Nairobi, Eldoret and their environs have the highest asthma rates especially among school going children aged 13-14 years. This was attributed to exposure to cold air especially early mornings and late evenings when children reported to and left school respectively. Exposure to environmental pollutants due to industrialization, urbanization and chemicals used in agriculture as well as pollen trigger was reported to cause asthma exacerbations. The prevalence of asthma in Nairobi County was reported as 18% (3,24).

Literature gap

The HRQoL of asthmatic patients who receive treatment at KNH is unknown since no studies are documented in literature. The levels of asthma control and HRQoL with their determinant factors (patient and clinical) in this population are also not documented to the best of our knowledge. This study seeks to fill this gap and inform treatment of asthma while incorporating the quality of life measures.

CHAPTER THREE: METHODOLOGY

3.1 Study Design

This study employed a descriptive cross-sectional design. The design is the most appropriate for evaluating persistent conditions such as asthma at a given point in time, and in this study, it was suitable for collecting data from respondents on factors that impacted their life's quality. The level of asthma control in individual patients was directly established from the patient's self-reporting. No investigator intervention was required and no further patient follow-up was necessary (88).

3.2 Study site

The study was located at Kenyatta National Hospital (KNH) chest clinic. Kenyatta National Hospital is the largest public referral health facility in Kenya that also serves as a teaching hospital for the University of Nairobi College of Health Sciences and Kenya Medical Training College. It has a bed capacity of 1800 which can be stretched to 3000. The hospital is strategically located near the central business district of Nairobi, the most densely populated county and capital city of Kenya. It provides specialized health care services not only to patients from the county itself, its environs and referrals from all over the country, but also to non-Kenyans hailing from neighboring countries (89,90). The asthma clinic runs from Monday to Friday and reviews at least 300 asthmatic patients monthly as per the KNH records. Its human resource includes chest physicians, clinical officers, nurses, support staff, the recommended medicines and equipment and therefore has capacity to manage asthma patients.

3.3 Study period

Data collection for the study was conducted in the period between June and July 2018.

3.4 Study population

The study targeted teenage and adult patients diagnosed with asthma who attended the chest clinic in KNH for their routine management. The study participants were sourced from the asthma section of the chest clinic.

3.4.1 Inclusion criteria

Patients were recruited into the study if they:

- Were aged 13years and above.
- Had a case definition for asthma (as defined in Section 3.5) and on treatment.
- Attended KNH asthma clinic for their routine management and follow-up.
- Gave their informed consent confirming their willingness to participate in the study.

The rationale for choosing age 13 and above years: Literature has revealed that most studies on asthma have been conducted in children up to 12 years old, with the most recent one conducted at this same study site on factors affecting levels of asthma control. In terms of pharmacotherapy, there are no variations in asthmatic patients aged 13 years and above.

3.4.2 Exclusion criteria

The following categories of asthmatic patients were excluded;-

- Patients who had overlap syndrome (COPD plus asthma) or Tuberculosis.
- Pregnant patients.
- Patients from vulnerable groups (prisoners, orphans, mentally disabled).
- Patients requiring admission.

Reasons for exclusion: COPD and Tuberculosis are confounders. In the setting of these two comorbidities, asthma treatment outcomes are unreliable. Pregnant females are required by ethics to participate in research only if it is relevant for them. Persons from vulnerable groups are required by ethics not to participate in research. Patients requiring admission usually have suffered an exacerbation and would over-exaggerate their HRQoL in favor of lower scores.

Eligibility was assessed using the Eligibility Assessment form (Appendix 4).

3.5 Case definition

A patient with asthma was defined as one who at diagnosis, had demonstrated the presence of episodic symptoms of airway obstruction such as breathlessness, cough, chest

tightness/pain, wheeze and or airway hyper-responsiveness. The airway obstruction should have been at least partially reversible having excluded other differential diagnoses (25).

3.6 Sampling and Sample size determination

3.6.1 Sampling Technique

The consecutive sampling technique was employed where every subject that met the inclusion criteria was enrolled into the study until achievement of the desired sample size of 140 was met. An approximate number of 10-15 patients visited the clinic daily between Monday to Friday.

3.6.2 Sample size

More than 300 asthmatic patients attend the asthma clinic on a monthly basis. A representative sample was drawn from this population. The sample size was determined using the Cochran formula for calculating sample size in descriptive studies (91,92).

$$n = \frac{Z^2\, p\, (1-p)}{e^2}$$

Where*: n* = sample size

Z = is the statistic for 95% level of confidence. Its value = 1.96.

p = is the estimated proportion or prevalence of asthma in the Kenyan population which is 10% (3).

e = is the level of precision which in this study was set at 5% (0.05).

$$n = \frac{1.96^2 * 0.1\,(1-0.1)}{0.05^2}$$

n= 138.3 …. (139 subjects)

The calculated minimum representative sample size of 139 asthmatic patients was sufficient. This number was rounded off to 140 patients. Eligible participants were

consecutively sampled till the sample size of 140 was achieved to ensure the study was adequately powered.

3.7 Patient Recruitment

Study participants were recruited by the Principal Investigator (PI) with the help of the research assistants. Participants were briefly informed about the study while waiting to be attended to by their care givers during their scheduled clinic visit. Patients were called one at a time into one of the clinic rooms for their routine vital signs check before the physician's appointment. It is in this room where each had a chance to be given more information about the study and thereafter, briefly assessed whether eligible using the eligibility screening criteria (Appendix 4). This arrangement ensured confidentiality of the participant's information. Those found eligible had their files labelled with a small colored sticker. Potential enrollees were requested to remain behind briefly after their physician appointment. Patients were thereafter allowed to obtain their physician's attention.

After the physician's appointment, those found eligible and willing to take part in the study were introduced to the consenting process. After having understood the process, they were offered the consent form outlined in Appendix 5A/5B or assent form in Appendix 6A/6B to sign. Participants were thereafter engaged for the interview.

3.8 Data Collection

3.8.1 Research Instruments

The ACT and AQLQ(S) tools were employed in this study to measure the levels of asthma control and the HRQoL, respectively (Appendices 7 and 8). These tools are standardized and are applicable across populations worldwide (23,45). Since the AQLQ tool is copyrighted, it had to be sourced from its developers together with permission to use it only for the purposes of this study (Appendix 3). For this population, investigators administered the questionnaires to participants in a questionnaire-guided interview, mitigating against such obstacles as language barrier and low literacy levels. A separate questionnaire that collected information on the determinants of the asthma control and HRQoL was administered (Appendix 9).

The ACT tool (Appendix 7) is a simple test for asthmatic patients aged 12 years and above and measures the level of asthma control. It contains 5 questions on a 5 point scale depicting the frequency of asthma symptoms and usage of rescue medication by participants in the previous four weeks. The overall score is in the ranges of 5 (worse control) to 25 (total control) (49).

The AQLQ(S) (Appendix 8) is a disease specific tool for measuring the HRQoL due to asthma**.** It contains 32 sections in four domains: Symptoms, Activity Limitation, Emotional Function and Environmental Stimuli. Participants were asked about how their conditions had been in the previous two weeks prior to enrollment into the study. Investigators recorded participant responses to each of the 32 questions on the 7 point scale onto the questionnaire. The overall AQLQ score was the mean of all the 32 responses while each domain score was the mean of responses to items in that particular domain (23).

The Determinants of asthma control and HRQoL Questionnaire (Appendix 9) was used to collect data on predictors of asthma-related quality of life in the population under study. These variables included sociodemographic traits, modifiable and non-modifiable traits, triggers, patient compliance and clinical factors that influence asthma control and consequently, HRQoL.

3.8.2 Data Collection Techniques

Questionnaires were used to collect all the necessary data for this research. These were a set of closed-ended questions that were administered to participants by the researchers after recruitment. The investigators indicated participant responses to the questions onto the questionnaires. The height and weight of participants was measured directly by the assessors to enable determination of BMI. For participants aged 13 to 20 years old, BMI was determined using the CDC Body mass index-for-age percentiles' chart for boys and girls (Appendix 10A/B). Patient information relating to their asthma treatment and comorbidities including atopy (positive skin test for allergens) was abstracted from their treatment files and filled into the questionnaire (Appendix 9).

3.8.3 Study variables

The study variables for which data was collected are outlined below. The main outcome variables of the study were the levels of asthma control and HRQoL scores. These were the dependent variables and data for these variables was sourced from patient interview using the ACT and AQLQ(S) tools (Appendix 7 and 8). The main predictor variables were asthma treatment, health care provider factors and patient factors such as sociodemographic (age, gender, level of education, marital status, income level, occupation and residence), smoking habit, comorbidities, exercise, adherence/compliance to treatment plans and satisfaction. Health care provider factors included; relationship with patients, health education provision and compliance with guideline recommendations based on a patient's disease severity. Data on these predictor variables was sourced from patient interview and patient files using the Determinants of asthma control and HRQoL questionnaire (Appendix 9).

3.9 Quality Assurance of Data

3.9.1 Training of research assistants

The principal investigator (PI) identified one research assistant and trained her before commencement of the research. The assistant was a nurse working in the chest clinic who possessed a Kenya Enrolled Community Nurse (KECHN) qualification certificate. The training entailed an explanation of the nature of the study, its objectives and importance. Demonstration and practical training of use of the data collection tools was done. Ethical considerations and overall conduct expected of a scientific research was explained. The competence of the research assistant was assured by the PI during piloting before the study begun. This was done by assessing how correctly the assistant extracted data and filled up the questionnaires. Where further training was required, it was provided and reinforced until competence was ascertained.

3.9.2 Pilot Study/ Pre-Testing

Pre-testing: Five copies of the questionnaires were administered to 5 members of the target population at the chest clinic. Based on the results obtained, modification of the questionnaires was done.

Pilot study: The modified questionnaires were administered to another group of 5 patients by the principal investigator to ensure they were flawless and capable of collecting the kind of data required. Thereafter, the questionnaires were revised in accordance to the weaknesses seen during piloting.

3.9.3 Validity

The validity of the study was maintained by ensuring that the questionnaires were well structured and able to collect all the relevant data with regard to objectives of the study. The questions were arranged sequentially using simple, clear, concise and acceptable language. A research assistant was selected from among the nursing staff of the asthma clinic. She was adequately trained by the PI before the actual study begun. The study site chosen gave a good representation of the general population since KNH, being a referral institution, attends to patients from all parts of the country. In addition, the sample size used in the study was adequate and in accordance to scientific requirements.

3.9.4 Reliability

Data collection tools were pre-tested as described in the pilot study for reproducibility before the actual study to prevent ambiguities in responses. Amendments were made on the instruments where it was necessary in order to improve on their efficiency and effectiveness before rolling them out.

3.10 Data Management

Each of the participants' questionnaires bore a unique serial number for identification purposes. Each individual participant's coded data was entered onto the participant's form created in Epi Info Version 7 database. Data entries were made on a daily basis and checked routinely for accuracy and completeness. Any inconsistencies and ambiguities were rectified promptly. Data was backed up daily onto a hard drive. On completion of the data entry process, data was cleaned and exported onto Stata version 13 software for analysis.

3.11 Data Analysis

The analysis was done using Stata version 13 software (StataCorp,USA). Results obtained were presented in form of tables, charts and graphs. At commencement of data

analysis, the Shapiro Wilk test was conducted on all continuous variables to check for normal distribution. Variables that were normally distributed were summarized as means and standard deviation of the means. Those that were not normally distributed were summarized as median and Inter-Quartile Range (IQR). Categorical variables were summarized as frequencies and percentages. Inferential statistics was conducted to compare the distribution of variables across patients with good asthma control versus those with poor asthma control and also those with high versus those with low HRQoL. Logistic regression was done to determine the independent predictor variables of asthma control as well as HRQoL in the study population.

3.12 Ethical Considerations

3.12.1 Ethical Approval to carry out the Study

Ethical approval was sought from the Kenyatta National Hospital/University of Nairobi-Ethics and Research Committee (KNH/UON-ERC) prior to conducting the study (Appendix 1). Institutional approval was obtained from Kenyatta National Hospital (Appendix 2).

3.12.2 Informed Consent

All eligible patients were guided through information on what the study involved and an explanation on what concerned them as stipulated in the forms. Once they had fully understood and chosen to participate in the study, they were presented with a consent or assent declaration form (Appendix 5A/5B and Appendix 6A/6B, respectively) to sign. Patients were informed upfront that participation in the study was voluntary and that they were at liberty to withdraw from the study at any point during engagement without any consequences. Adequate information on the nature of the study was also provided. No coercion or incentives whatsoever were provided in order to take part in the study. Patients were free to ask any questions about the study in the course of the interview and were informed that if they had any concerns about their rights as study participants they were to contact the KNH/UoN-ERC.

3.12.3 Confidentiality

Study serial numbers were generated and used in place of patient names during the data collection and analysis process in order to conceal and safeguard participant's identity. All the data collection materials were safely kept in a cabinet under lock and key. The database was password protected by the Principal Investigator for limited access during the entire study period. The data collected was used only for the purpose of the study.

3.12.4 Risks involved

Being a descriptive study, it did not involve any invasive procedures therefore participants were not exposed to any risks. Participant privacy and confidentiality was maintained at all times. Informed consent declaration forms were signed voluntarily without any coercion.

3.12.5 Benefits from the Study

During patient interviews, the Principal Investigator was able to address the concerns the participants had, regarding their disease condition and its management. The preliminary findings of the study were discussed with individual participants. Enrollees in the study had an opportunity to be informed of their levels of illness control and factors that needed to be addressed to ensure they lived a normal or near normal life. The final report would be shared with the various concerned parties so as to improve asthma patient care. There were no direct benefits to participants other than the ones mentioned.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter describes the results obtained from analysis of data collected from a sample of 140 participants with asthma at the KNH chest clinic. Descriptive, inferential and logistic regression analyses were conducted on the sample to determine the level of asthma control, HRQoL and evaluate the sociodemographic, patient and clinical factors that impact asthma control and HRQoL in that population.

4.2 Sociodemographic characteristics of the cohort

Summary data analyses from the sample are presented in Table 4.1. The population under study was largely female (n=108, 77.1%). The median age of the participants was 45 years (IQR 37, 50.5) with a range of 13 to 68 years. More than half the population comprised participants in the middle-age bracket (40-64, 63.6%). Adolescents (13-19 years) made up 10% of the population whereas young adults (20-39 years) and the elderly (>65 years) made up 22.9% and 3.6% of the population respectively. Most participants were married (n=91, 65%) and majority resided in urban areas (n=112, 80%). Slightly over half the population (n=90, 64.3%) had low level education with the highest in this category having acquired secondary school education. Low socioeconomic and non-formal employment statuses were highly represented in equal proportions (n=100, 71.4%).

Normally distributed continuous variables

Variable	Mean	SD	Minimum	Maximum
BMI	26.74	6.02	14.9	46.2

Skewed continuous variables

Variable	Median [IQR]	Smallest	Largest
Age	45 [IQR 37,50.5]	13	68

Table 4.1: Sociodemographic traits of asthma patients at the KNH asthma clinic

Variable	Category	Participants (N=140)	Percentage (%)
Age category	Adolescents	14	10
	Young adults	32	22.9
	Middle age	89	63.6
	Elderly	5	3.6
Gender	Male	32	22.9
	Female	108	77.1
Marital status	Minor	13	9.3
	Single	36	25.7
	Married	91	65.0
Residence	Rural	28	20
	Urban	112	80
Level of education	Low	90	64.3
	High	50	35.7
Employment status	Non-formal	100	71.4
	Formal	40	28.6
Socioeconomic status	Low	100	71.4
	High	40	28.6

4.3 Patient-specific characteristics of the population

In most patients, asthma diagnosis was made after 12 years of age (n=112, 80%) (Table 4.2). Occupational risk was present in a third of the population (n=47, 33.6%). Majority of the population was primarily made up of persons who did not smoke cigarettes (n= 121, 93.6%) while only 9 (6.4%) were former smokers. None of the participants reported current use of cigarettes. Slightly over half the population (n= 86, 61.4%) had exacerbation of their asthma symptoms during exercise and only a small proportion demonstrated poor inhaler technique (n=6, 4.3%).

Table 4.2: Patient-specific characteristics of the population

Variable	Category	Participants (N=140)	Percentage (%)
Age of asthma onset	Early (≤12 yrs)	28	20.0
	Late (>12 yrs)	112	80.0
Occupational risk	Absent	93	66.4
	Present	47	33.6
Cigarette smoking status	Non-smoker	121	93.6
	Current smoker	0	0
	Former smoker	9	6.4
Exercise associated asthma		86	61.4
Inhaler technique	Incorrect	6	4.3
	Correct	134	95.7
Stress associated		7	5.0
Adherence to treatment	Poor	15	10.7
	Good	125	89.3
Menses associated (N=108)		12	11.1
BMI	Underweight	8	5.7
	Normal weight	47	33.6
	Overweight	43	30.7
	Obese	42	30.0

BMI = Body mass index.

Generally, a large proportion of the population (n=125, 89.3%) indicated that they were adherent to their asthma medications with 46% having used them for more than ten years (Figure 4.1).

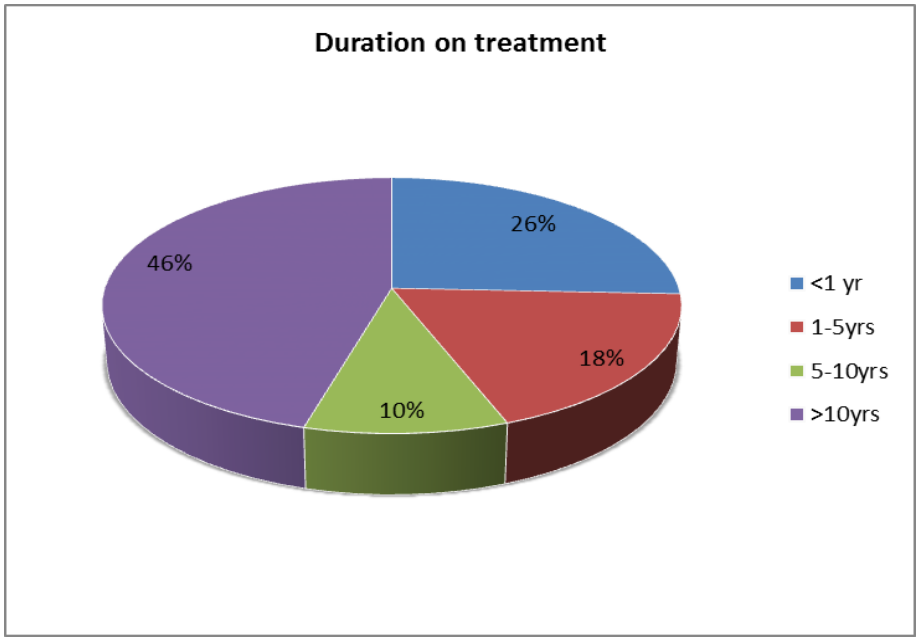
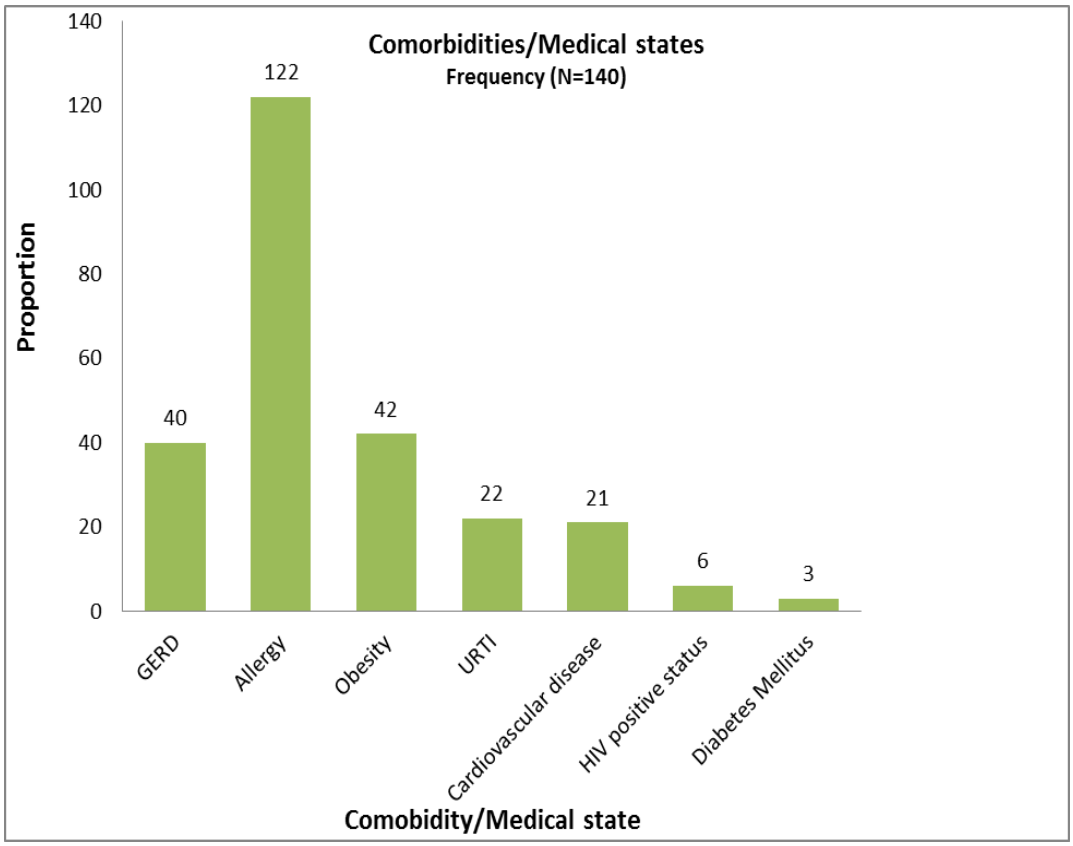


Figure 4.1: Duration patients had been on asthma treatment.

More than 50% of the participants were either obese or overweight (Table 4.2) with a few members of the population reporting worsening of asthma symptoms during stressful periods in their lives (n=7, 5%). Among the women, twelve (11.1%) experienced worsening of their symptoms during menstruation.

Comorbidities and other medical states that could have an impact on a patient's level of asthma control or HRQoL are presented in Figure 4.2. A large proportion of the population had allergies (n=122, 87.1%) to either of the allergens that had been tested and recorded in their medical record files. These allergens included animal dander, cockroaches, dust mites and animal proteins such as milk, among others.



GERD= Gastroesophageal reflux disease, URTI= Upper respiratory tract infection, HIV= Human immunodeficiency virus.

Figure 4.2: Comorbidities identified in asthma patients enrolled in the study.

4.4 Clinical characteristics of the population

Most patients were prescribed SABA (n=135, 96.4%) as reliever medication over ICS/LABA (n=5, 3.6%) (Table 4.3). Except for one participant, the rest of the 139 (99.3%) participants were on controller medication and thus considered treated as per the current asthma guideline recommendations. Of the controller medications, budesonide/formoterol was the most frequently prescribed (n=87, 62.1%). Majority of the patients had moderate persistent asthma at treatment step 3 (n=86, 61.4%). A large proportion (n=125, 89.3%) were on optimal dosages of their asthma medication at their various treatment steps. Those in whom asthma medication combinations were appropriately selected were 128 (91.4%). In their prescribing patterns, about 10% of prescribers had not adhered to the current guideline recommendations. Nearly all

participants were adequately educated on their asthmatic state and its management (n=139, 99.3%) and were thus, satisfied**.**

Table 4.3: Clinical / Treatment traits of the population

Variable	Category	Participants (N=140)	Percentage (%)
Relievers	SABA	135	96.4
	Low dose – ICS/ Formoterol	5	3.6
Controllers	Low dose ICS	21	14.5
	Low dose ICS/LABA	99	71
	Medium dose ICS	15	10.9
	Add on Medications	5	3.6
Corticosteroid type	Beclomethasone	6	4.3
	Budesonide	87	62.1
	Fluticasone	47	33.6
LABA type	Formoterol	87	62.6
	Salmeterol	26	18.7
	None	26	18.7
Asthma severity	Step 1/intermittent asthma	1	0.7
	Step 2/mild persistent	25	17.9
	Step 3/moderate persistent	86	61.4
	Step 4/severe persistent	28	20
	Step 5/severe persistent	0	0
Dosage	Optimal	125	89.3
	Suboptimal	15	10.7
LTRA	Usage	18	12.9
Proportion of Patients	Treated	139	99.3
Treatment	Appropriate	128	91.4
Guideline	Adherence	126	90
Patient information	Health educated	139	99.3
Patient service	Satisfactory	140	100

SABA= Short acting $beta_2$ agonists, ICS= Inhaled corticosteroids, LABA= Long acting beta agonists, LTRA= Leukotriene receptor agonists.

4.5 Asthma Control Test and HRQoL outcomes

Most patients reported that in the month prior to enrollment into the study, their asthma had been under control. The median ACT score was 22[IQR 20, 24], range (5, 25) while the median HRQoL score was 6.0[IQR 5.2, 6.35], range (2.1, 7). In individual domain

performance, activity limitation and environmental stimulation had the lowest median scores (Table 4.4).

Table 4.4: ACT and HRQoL outcomes

Variable	Median [IQR]	Lowest	Highest
ACT	22 [IQR 20, 24]	5	25
HRQoL	6.0 [IQR 5.2, 6.35]	2.1	7
Symptoms	6.3 [IQR 37, 50.5]	2.1	7
Activity Limitation	5.6 [IQR 4.8, 6.5]	1.6	7
Emotional Function	6.3 [IQR 5.6, 50.5]	1.6	7
Environmental Stimulation	5.8 [IQR 4.4, 6.5]	1	7

ACT = Asthma control test, HRQoL = Health related quality of life, IQR = Inter-quartile range.

A large proportion of the population (n=112, 80%) recorded a high ACT score (>19) (Figure 4.4) while 74 participants (52.9%) had high HRQoL (≥6) (Figure 4.5). The domain in which most patients experienced greatest limitation was the activity (n=86, 61.4%) while most reported good performance in the emotional function domain (n=90, 64.3%).

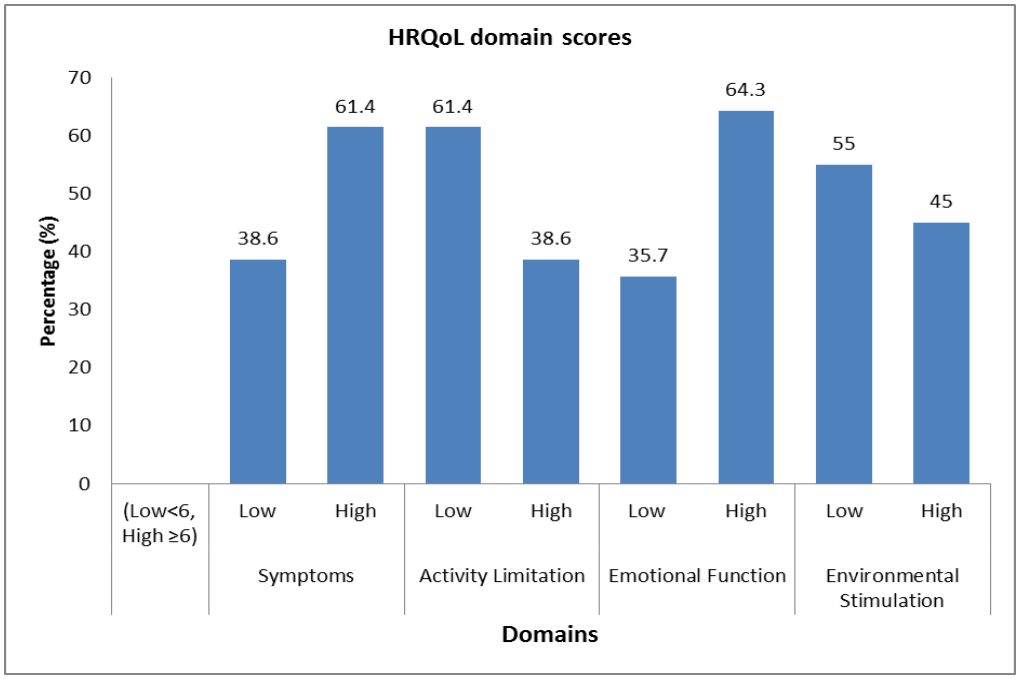


Figure 4.3: HRQoL domain scores for the study population.

4.6 Asthma control among asthma patients at KNH Asthma Clinic

Determination of asthma control level was made using the ACT questionnaire mean score. Out of the 140 participants, 112 (80%) had their asthma under control while 28 (20%) had uncontrolled asthma (Figure 4.4). Further data analysis was conducted to identify associations between asthma control and the variables under study that influence it.

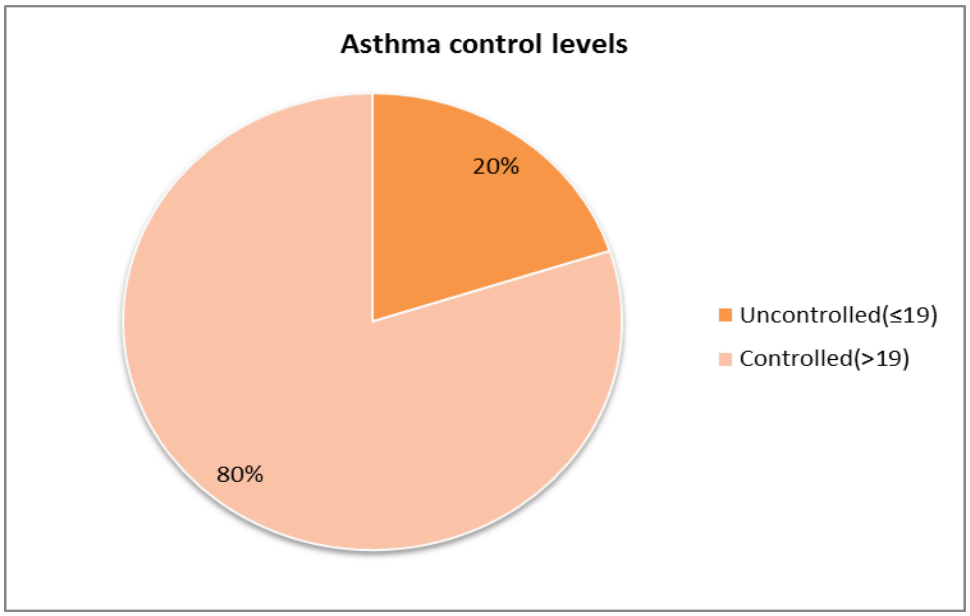


Figure 4.4: Asthma control among asthmatic patients at KNH.

4.6.1 Association between asthma control and sociodemographic characteristics of the cohort

Asthma control score was compared with sociodemographic traits of the study participants and the results presented in Table 4.5.

Table 4.5: Association between asthma control and sociodemographic characteristics

VARIABLE		ACT SCORE N=140		Fisher's (F) or Chi^2 (χ) test p-value
	Category	**Low (≤19) n(%)**	**High (>19) n(%)**	
Age	Adolescents	4(28.6)	10(71.4)	
	Young adults	5(15.6)	27(84.4)	0.421 (F)
	Middle age	17(19.1)	72(80.9)	
	Elderly	2(40)	3(60)	
Gender	Female	24(21.4)	84(78.6)	0.316 (F)
	Male	4(12.5)	28(87.5)	
Marital	Minor	4(30.8)	9(69.2)	
	Single	7(19.4)	29(80.6)	0.549 (F)
	Married	17(18.7)	74(81.3)	
Residence	Rural	7(25)	21(75)	0.460 (χ)
	Urban	21(18.8)	91(81.2)	
Level of education	Low	16(17.8)	74(82.2)	0.378 (χ)
	High	12(24)	38(76)	
Employment status	Non-formal	18(18)	82(82)	0.350 (χ)
	Formal	10(25)	30(75)	
Socioeconomic status	Low	19(19)	81(81)	0.640 (χ)
	High	9(22.5)	31(77.5)	

ACT = Asthma control test.

Young adults (n=27, 84.4%) and middle aged (n=72, 80.9%) categories had the highest number of participants in whom asthma was well controlled. The low performers were the adolescents (n=4, 28.6%) and the elderly (n=2, 40%). This difference among the age groups was however, not statistically significant (p= 0.421). As pertains gender, 28 (87.5%) of males as compared to 78.6 (84%) had their asthma under control although this difference was not statistically significant (p= 0.316). Other variables not significantly associated with asthma control include marital status, residence, level of education, employment and socioeconomic statuses.

4.6.2 Association between asthma control and patient-specific traits

The results of analysis for the association between asthma control and patient-specific traits are indicated in Tables 4.6 and 4.7.

History of occupational risk was positive in forty-seven participants, thereby increasing their risk of developing asthma. Of these 47 individuals, 33 (70.2%) had their asthma under control whereas 14(29.85%) did not, the difference being statistically significant ($p= 0.046$). Six participants did not demonstrate adequate knowledge of correct inhaler technique and scored low on ACT. In contrast, 112 out of 134 (83.6%) participants who demonstrated knowledge of correct technique had high ACT scores. Thus, there was an association between knowledge of correct inhaler technique and asthma control ($p<0.001$). In this population, age at onset, cigarette smoking status, exercise, stress, menses, BMI and adherence to asthma medications were found to have no significant statistical association with asthma control (Table 4.6).

Of the comorbidities, GERD was found to have a statistically significant association with asthma control ($p=0.033$). None of the other comorbidities namely allergy, diabetes mellitus, obesity, HIV positive status, cardiovascular disease and respiratory infections had statistical association with asthma control as illustrated in Table 4.7.

Table 4.6: Association between asthma control and Patient-specific traits of the cohort

VARIABLE		ACT SCORE N=140		Fisher's (F) or Chi^2 (χ) test p - value
	Category	**Low (≤ 19) n(%)**	**High (>19) n(%)**	
Asthma onset age	Early	4(14.3)	24(85.7)	0.597 (F)
	Late	24(21.4)	88(78.6)	
Occupational risk	Absent	14(15.1)	79(84.9)	**0.040** (χ)
	Present	14(29.8)	33(70.2)	
Cigarette smoking	Non-smoker	25(19.1)	106(80.9)	0.383 (F)
	Current smoker	0	0	
	Former smoker	3(33.3)	6(66.7)	
Exercise associated	No	7(13)	47(87)	0.099 (χ)
	Yes	21(24.4)	65(75.6)	
Inhaler technique	Incorrect	6(100)	0	**<0.001** (F)
	Correct	22(16.4)	112(83.6)	
Stress associated	No	26(19.5)	107(80.4)	0.627 (F)
	Yes	2(28.6)	5(71.4)	
Adherence	Poor	5(33.3)	10(66.7)	0.181 (F)
	Good	23(18.4)	102(81.6)	
Menses associated (N=108)	No	22(22.2)	74(77.8)	1.00 (F)
	Yes	2(16.7)	10(83.3)	
BMI	Underweight	1(12.5)	7(87.5)	0.747 (F)
	Normal weight	12(25.5)	35(74.5)	
	Overweight	8(18.6)	35(81.4)	
	Obese	7(16.7)	35(83.3)	

ACT = Asthma control test, BMI = Body mass index.

Table 4.7: Asthma control and comorbidities/medical states relationship

VARIABLE		ACT SCORE N=140		Fisher's (F) or Chi^2 (χ) test
	Category	**Low (≤ 19) n(%)**	**High (>19) n(%)**	**p-value**
GERD	Absent	15(15)	85(85)	**0.019** (χ)
	Present	13(32.5)	27(67.5)	
Allergy	No	3(16.7)	15(83.3)	1.000 (F)
	Yes	25(20.5)	97(79.5)	
Diabetes mellitus	No	27(19.7)	110(80.3)	0.490 (F)
	Yes	1(33.3)	2(66.7)	
Obesity	Absent	23(22.5)	79(77.5)	0.246 (F)
	Present	5(13.2)	33(86.8)	
HIV positive status	Negative	28(20.9)	106(79.1)	0.600 (F)
	Positive	0	6(100)	
Cardiovascular disease	Absent	22(18.5)	97(81.5)	0.287 (χ)
	Present	6(28.6)	15(71.4)	
Respiratory infection	No	21(18.8)	97(82.2)	0.131 (χ)
	Yes	7(31.8)	15(68.2)	

ACT = Asthma control test, GERD = Gastroesophageal reflux disease, HIV = Human immunodeficiency virus.

4.6.3 Relationship between asthma control and clinical characteristics

Asthma control was compared with clinical traits of the cohort. Statistically significant associations ($p< 0.001$) were found between asthma control and optimality of dosage, use of guidelines during prescribing and appropriateness of treatment choice at the asthma severity step (Table 4.8)**.** Participants who were managed based on current guideline recommendations (n= 109, 86.5%) and those who were optimally treated (n= 109, 87.2%) had their asthma under control. On the other hand, enrollees whose treatment was not based on guideline recommendations (n=11, 78.6%) and those who received sub-optimal treatment (n= 12, 80%) had uncontrolled asthma. Asthma relievers or controllers, disease severity, patient education and satisfaction variables were found not to have any significant association with asthma control.

Table 4.8: Relationship between asthma control and clinical characteristics

VARIABLE		ACT SCORE N=140		Fisher's (F) or Chi^2 (χ) test p-value
	Category	**Low (≤ 19) n(%)**	**High (>19) n(%)**	
Relievers	SABA	26(19.3)	109(80.7)	0.261 (F)
	ICS/Formoterol	2(40)	3(60)	
Controllers	Low dose ICS	2(10)	18(90)	0.370 (F)
	Low dose ICS/LABA	20(20.4)	78(79.4)	
	Medium dose ICS/LABA	5(33.3)	10(66.7)	
	Add-on medications	1(20)	4(80)	
ICS Type	Beclomethasone	0	6(100)	0.139 (F)
	Budesonide	22(25.3)	65(74.7)	
	Fluticasone	6(18.4)	41(81.6)	
LABA Type	Formoterol	22(24.7)	65(75.3)	0.128 (F)
	Salmeterol	2(7.7)	24(92.3)	
	None	4(15.4)	22(84.6)	
Treated	On Relievers only	0	1(100)	1.000 (F)
	On Controllers	28(20.1)	111(79.9)	
Dosage	Sub optimal	12(80)	3(20)	**<0.001** (F)
	Optimal	16(12.8)	109(87.2)	
Guideline use	Noncompliance	11(78.6)	3(21.4)	**<0.001** (F)
	Compliance	17(13.5)	109(86.5)	
LTRA	No	22(18)	100(82)	0.130 (χ)
	Yes	6(33.3)	12(66.7)	
Asthma severity	Step 1/intermittent asthma	0	1(100)	0.779 (F)
	Step 2/mild persistent	4(16)	21(84)	
	Step 3/moderate persistent	17(19.8)	69(80.2)	
	Step 4/severe persistent	7(25)	21(75)	
	Step 5/severe persistent	0	0	
Treatment choice at severity step	Inappropriate	9(75)	3(25)	**<0.001** (F)
	Appropriate	20(15.6()	108(84.4)	
Patient information	Not educated	1(100)	0	0.200 (F)
	Educated	27(19.4)	112(80.6)	
Patient service	Unsatisfied	0	0	
	Satisfied	28(20)	112(80)	-

ACT = Asthma control test, SABA= Short acting beta$_2$ agonists, ICS= Inhaled corticosteroids, LABA= Long acting beta$_2$ agonists, LTRA = Leukotriene receptor agonists.

4.7 HRQoL among asthma patients at KNH Asthma Clinic

Determination of HRQoL was made using the Asthma QoL questionnaire mean score. Out of the 140 participants, 74 (53%) had high HRQoL while 66 (47%) had low HRQoL (Figure 4.5). Further analysis was conducted to find out associations between HRQoL and other study variables.

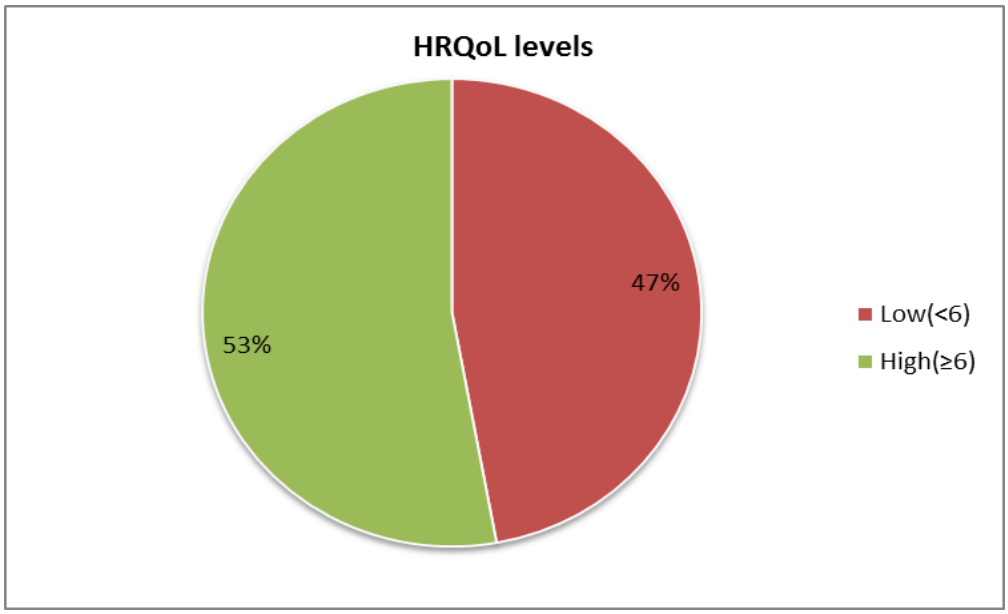


Figure 4.5: HRQoL among asthma patients at KNH.

4.7.1 Relationship between HRQoL and sociodemographic traits of participants

The sociodemographic traits: age, gender, marital status, residence, level of education, employment and socioeconomic statuses were not significantly associated with the HRQoL score of participants as depicted in Table 4.9.

Table 4.9: Relationship between HRQoL and sociodemographic traits

VARIABLE	CATEGORY	HRQoL SCORE, N=140		Fisher's (F) or Chi^2 (χ) test p-value
		Low (<6) n(%)	High (≥6) n(%)	
Age	Adolescents	10(71.4)	4(28.6)	0.136 (F)
	Young adults	11(34.4)	21(65.6)	
	Middle age	43(48.3)	46(51.7)	
	Elderly	2(40)	3(60)	
Gender	Female	51(47.2)	57(52.7)	0.880 (χ)
	Male	15(46.9)	17(53.1)	
Marital	Minor	8(61.5)	5(38.5)	0.491 (F)
	Single	15(41.7)	21(58.3)	
	Married	43(47.3)	48(52.7)	
Residence	Rural	15(53.6)	13(46.4)	0.446 (χ)
	Urban	51(45.5)	61(54.5)	
Level of Education	Low	42(46.7)	48(53.3)	0.880 (χ)
	High	24(48)	26(52)	
Employment status	Non-formal	48(48)	52(52)	0.748 (χ)
	Formal	18(45)	22(55)	
Socioeconomic status	Low	47(47)	53(53)	0.957 (χ)
	High	19(47.5)	21(52.5)	

HRQoL = Health related quality of life.

4.7.2 Association between HRQoL and patient-specific traits

There was a significant association (p= 0.010) between HRQoL and the inhaler technique. None of the other patient-specific characteristics such as age at onset, occupational risk, cigarette smoking, exercise, stress, adherence, menses and BMI category showed statistically significant association with HRQoL of the participants (Table 4.10).

Table 4.10: Association between HRQoL and patient-specific traits

VARIABLE		HRQoL SCORE N=140		Fisher's (F) or Chi^2 (χ) test p-value
	Category	**Low (<6) n(%)**	**High (≥6) n(%)**	
Asthma onset age	Early	14(50)	14(50)	0.735 (χ)
	Late	52(46.4)	60(53.6)	
Occupational risk	Absent	39(41.9)	54(58.1)	0.083 (χ)
	Present	27(57.4)	20(42.6)	
Cigarette smoking	Non-smoker	60(45.8)	71(54.2)	0.306 (F)
	Current smoker	0	0	
	Former smoker	6(66.7)	3(33.3)	
Exercise associated	No	21(38.9)	33(61.1)	0.121 (χ)
	Yes	45(52.3)	41(47.7)	
Inhaler technique	Incorrect	6(100)	0	**0.010** (F)
	Correct	60(44.8)	74(55.2)	
Stress associated	No	61(45.9)	72(54.1)	0.254 (F)
	Yes	5(71.4)	2(28.6)	
Adherence	Poor	8(53.3)	7(46.7)	0.611 (χ)
	Good	58(46.4)	67(53.6)	
Menses associated (N=108)	No	46(47.9)	50(52.1)	0.766 (F)
	Yes	5(41.7)	7(58.3)	
BMI	Underweight	2(25.0)	6(75.0)	0.547 (F)
	Normal weight	23(48.9)	24(51.1)	
	Overweight	19(44.2)	24(55.8)	
	Obese	22(52.4)	20(47.6)	

HRQoL = Health related quality of life, BMI = Body mass index.

Of the comorbidities associated with asthma, presence of a respiratory infection significantly related with the HRQoL of the participants (p= 0.031). The other comorbidities: GERD, allergy, Diabetes Mellitus, obesity, HIV and cardiovascular disease however, did not show any statistically significant association; (Table 4.11).

Table 4.11: Association between HRQoL and patient-specific traits (comorbidities / Medical states)

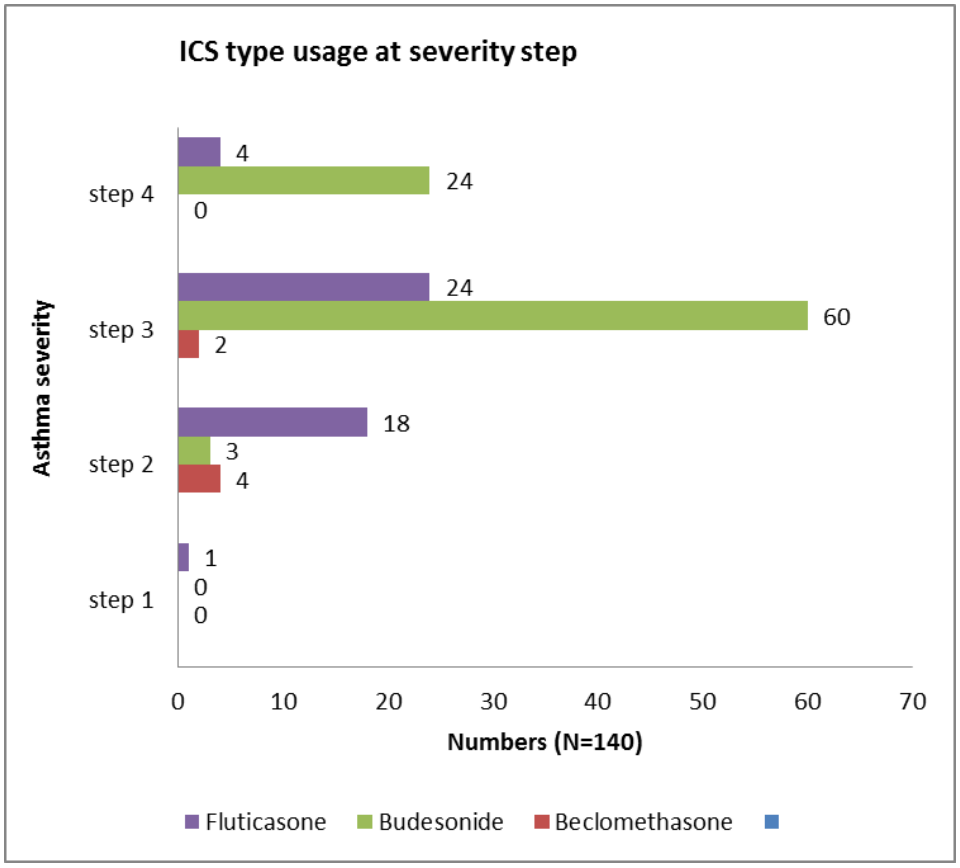
VARIABLE		HRQoL SCORE N=140		Fisher's (F) or Chi^2 (χ) test
	Category	**Low <6 n(%)**	**High ≥6 n(%)**	**p-value**
GERD	Absent	43(43)	57(57)	0.121 (χ)
	Present	23(57.5)	17(42.5)	
Allergy	No	7(38.9)	11(61.1)	0.452 (χ)
	Yes	59(48.4)	63(51.6)	
Diabetes mellitus	No	64(46.7)	73(53.3)	0.602 (F)
	Yes	2(66.7)	1(33.3)	
Obesity	Absent	46(45.1)	56(54.9)	0.427 (χ)
	Present	20(52.6)	18(47.4)	
HIV status	Negative	63(47)	71(53)	1.000 (F)
	Positive	3(50)	3(50)	
Cardiovascular disease	Absent	55(46.2)	64(53.8)	0.602 (χ)
	Present	11(52.4)	10(47.6)	
Respiratory infection	No	51(43.2)	67(56.8)	**0.031** (χ)
	Yes	15(68.2)	7(31.8)	

HRQoL = Health related quality of life, GERD = Gastroesophageal reflux disease, HIV = Human immunodeficiency virus.

4.7.3 Association between HRQoL and participant clinical characteristics

HRQoL score was compared with clinical characteristics of the group (Table 4.12). Associations were found between HRQoL score and the type of corticosteroid, LTRA usage, optimality of dosage, guideline adherence and appropriateness of treatment at the severity step. For instance, 5(83.3%) of those using beclomethasone, 39(44.8%) of budesonide users and 30(63.8%) of those on fluticasone reported higher HRQoL scores when compared to 1(16.7%) on beclomethasone, 48(55.2%) on budesonide and 17(36.2%) on fluticasone who had low scores. The association was statistically significant (p= 0.037) (Table 4.12). This implies that those on beclomethasone had higher HRQoL scores than those on budesonide or fluticasone. However, beclomethasone was

mainly used in those with mild asthma (Step 2) (Figure 4.6). For more severe asthma (Step 3 and 4), budesonide and fluticasone was preferred where those on fluticasone were found to have a higher proportion of individuals with high HRQoL scores (63.8% on fluticasone versus 44.8% on budesonide) (Table 4.12).



ICS = Inhaled corticosteroids.

Figure 4.6: Type of ICS used at severity step.

Participants whose controller medications were at optimal dosages 72(57.6%) reported higher HRQoL when compared to those on sub-optimal dosages 13(86.7%) who recorded low HRQoL scores. This finding was statistically significant (p= 0.002). The selection of treatment at the asthma severity step was also found to be associated with HRQoL outcome. Participants whose treatment was appropriate for the severity step (n=72, 56.3%) reported higher HRQoL scores compared to those whose treatment was inappropriately selected (n=10, 83.3%) who consequently reported low HRQoL scores.

Table 4.12: Association between HRQoL and Clinical characteristics

VARIABLE		HRQoL SCORE N=140		Fisher's (F) or Chi^2 (χ) test p-value
	Category	Low (<6) n(%)	High (≥6) n(%)	
Relievers	SABA	64(47.4)	71(52.6)	1.000 (F)
	ICS/Formoterol	2(40)	3(60)	
Controllers	Low dose ICS	7(33.3)	14(66.7)	0.300 (F)
	Low dose ICS/LABA	50(50.5)	49(49.5)	
	Medium dose-ICS/LABA	8(53.3)	7(46.7)	
	Add-on medications	1(20)	4(80)	
ICS Type	Beclomethasone	1(16.7)	5(83.3)	**0.037** (F)
	Budesonide	48(55.2)	39(44.8)	
	Fluticasone	17(36.2)	30(63.8)	
LABA	Formoterol	48(55.2)	39(44.8)	0.051 (χ)
	Salmeterol	9(33.3)	18(66.7)	
	None	9(34.6)	17(65.4)	
Treated	On Relievers only	0	1(100)	1.000 (F)
	On Controllers	66(47.5)	73(52.5)	
Dosage	Sub optimal	13(86.7)	2(13.3)	**0.002** (F)
	Optimal	53(42.4)	72(57.6)	
Guideline use	Noncompliance	12(85.7)	2(14.3)	**0.003** (F)
	Compliance	54(42.9)	72(57.1)	
LTRA	No	53(43.4)	69(56.6)	**0.041** (F)
	Yes	13(72.2)	5(27.7)	
Asthma severity	Step 1/intermittent asthma	0	1(100)	0.497 (F)
	Step 2/mild persistent	9(36)	16(72)	
	Step 3/moderate persistent	43(50)	43(50)	
	Step 4/severe persistent	14(50)	14(50)	
	Step 5/severe persistent	0	0	
Treatment choice at severity step	Inappropriate	10(83.3)	2(16.7)	**0.013** (F)
	Appropriate	56(43.8)	72(56.3)	
Patient information	Not educated	1(100)	0	0.471 (F)
	Educated	65(46.8)	74(53.2)	
Patient service	Unsatisfied	0	0	-
	Satisfied	66(47.1)	74(52.9)	

HRQoL = Health related quality of life, SABA= Short acting beta$_2$ agonists, ICS= Inhaled corticosteroids, LABA= Long acting beta$_2$ agonists, LTRA = Leukotriene receptor agonists.

Participants who were former smokers were found to have moderate to severe asthma that mostly required use of combination medications for control of their symptoms (Figures 4.7 and 4.8).

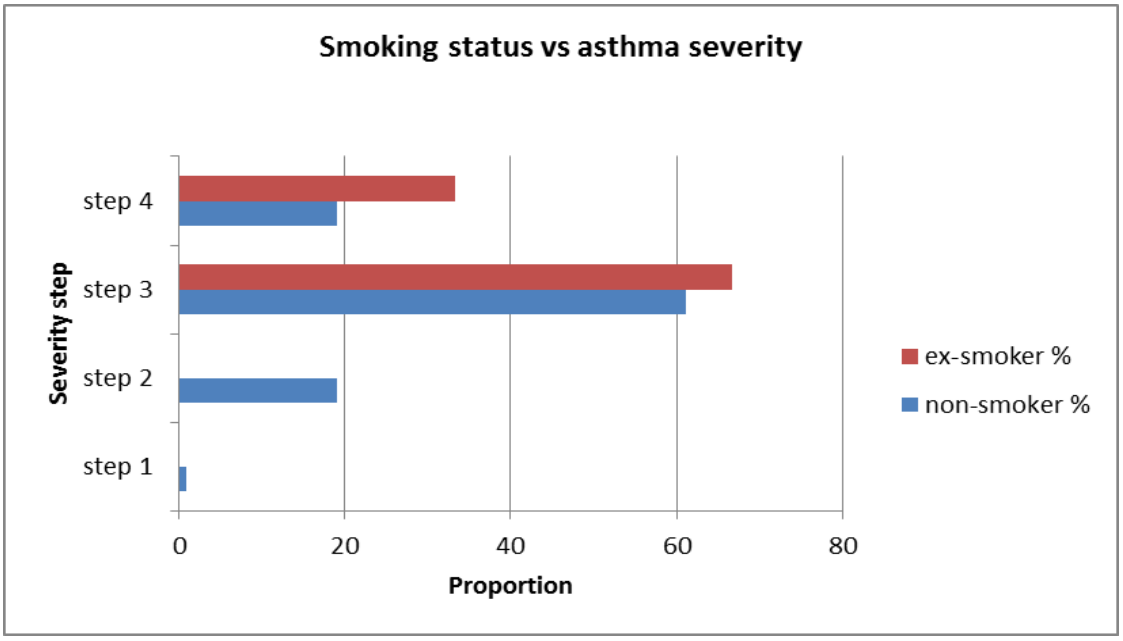


Figure 4.7: Cigarette smoking status and asthma severity.

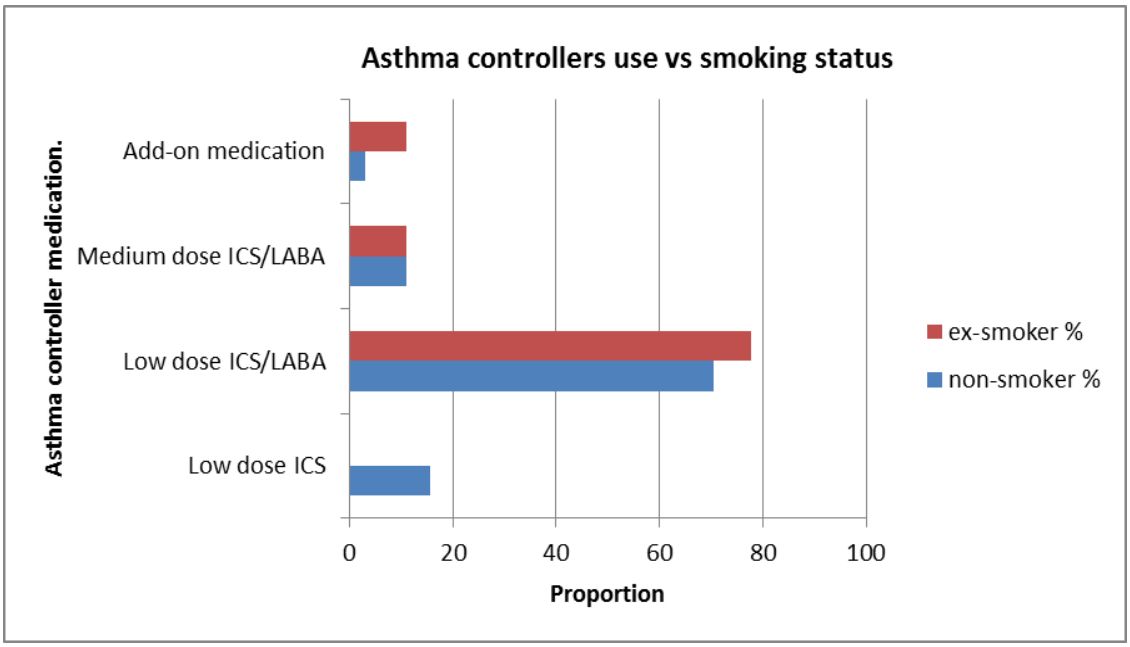


Figure 4.8: Cigarette smoking status and controller medication use.

4.8 Relationship between HRQoL score and performance in the individual HRQoL domains

HRQoL score was compared with the four main domains and results tabulated in Table 4.13 below. Each of the four domains had significant statistical association with HRQoL ($p< 0.001$).

Table 4.13: HRQoL score and performance in individual HRQoL domains

DOMAIN		**HRQoL SCORE N=140**		**Fisher's (F) or Chi^2 (χ) test.**
	Category	**Low (<6) n(%)**	**High (≥6) n(%)**	**p value**
Symptoms	Low	47(87)	7(13)	**<0.001** (χ)
	High	19(22)	67(78)	
Activity Limitation	Low	62(70.5)	24(29.5)	**<0.001** (F)
	High	4(8)	50(92)	
Emotional Function	Low	39(78)	11(22)	**<0.001** (χ)
	High	27(30)	63(70)	
Environmental stimulation	Low	57(74)	20(26)	**<0.001** (χ)
	High	9(16.7)	54(83.3)	

HRQoL = Health related quality of life.

4.9: Relationship between ACT and HRQoL

The HRQoL score of participants was compared with ACT score and the results tabulated in Table 4.14. Seventy-four (66.1%) participants whose asthma was adequately controlled had high HRQoL scores when compared to all the 28(100%) participants in whom asthma was uncontrolled. The association between ACT and HRQoL was significant ($p< 0.001$).

Table 4.14: Cross tabulation of ACT and HRQoL scores

VARIABLE	**Category**	**HRQoL SCORE N=140**		**Fisher's (F) or Chi^2 (χ) test. p- value**
		Low(<6) n(%)	**High(≥6) n(%)**	
ACT score	Uncontrolled≤19	28(100)	0	**<0.001 (F)**
	Controlled>19	38(33.9)	74(66.1)	

HRQoL = Health related quality of life, ACT = Asthma control test.

4.10 Logistic Regression analysis for independent predictors of asthma control and HRQoL

Logistic regression analysis was conducted to determine the independent predictors of asthma control and HRQoL after controlling for confounding.

4.10.1 Independent predictors of asthma control

Logistic regression analysis was done to identify variables that are the independent predictors of asthma control in the population under study (Table 4.15). Occupational risk was found to be an independent predictor of asthma control (cOR= 0.42; 95% CI 0.18-0.97; p= 0.043) on bivariate logistic regression analysis. Participants with a positive history of occupational exposure/risk had 0.42 times lower odds of having their asthma under control as opposed to those with a null history. On multivariate analysis, the measure of association for occupational risk became stronger as an independent predictor of asthma control (aOR= 0.05; 95% CI 0.00-0.44; p= 0.008).

The odds of asthma control in participants with GERD was 0.37 times that of those without GERD (95% CI 0.16-0.87, p=0.022). The effect of GERD on asthma control became more pronounced after multivariate analysis (aOR= 0.02; 95% CI 0.00-0.33; p= 0.006). Participants who were diabetic had 0.002 times the odds of having high HRQoL (95% CI 0.00-0.16; p= 0.006) when compared to their non-diabetic counterparts on multivariate regression. This association was absent on bivariate analysis. Optimality of controller medication dosage (cOR= 27; 95% CI 6.92-107.2; p<0.001), treatment choice at severity step (cOR= 17.2; 95% CI 4.26-69.41; p<0.001) and adherence to guideline recommendations (cOR= 23.5; 95% CI 5.94-92.99; p< 0.001) had very significant effect on asthma control during bivariate analysis. However, these significant effects were lost on multivariate regression analysis for all the three variables. In Table 4.15 reference categories for multi-level variables are each represented by the first level entry.

Table 4.15: Independent predictors of Asthma Control

Variable	Bivariate analysis		Multivariate analysis	
	cOR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**
Age category:				
Adolescents (13-19)	1		1	
Young adults (20-39)	2.16[0.48-9.69]	0.315	0.76[0.03-16.99]	0.865
Middle aged (40-64)	1.69[0.47-6.06]	0.417	0.53[0.02-12.47]	0.693
Elderly (>65)	0.60[0.07-5.06]	0.639	0.18[0.04-07.69]	0.370
Gender	2.00[0.64-6.26]	0.234	1005342[0]	0.992
Marital status:				
Minor	1		1	
Single	1.05[0.39-2.79]	0.921	1.22[0.42-3.56]	0.709
Married	0.54[0.13-2.29]	0.405	0.23[0.01-5.44]	0.359
Residence	1.44[0.54-3.84]	0.461	0.28[0.02-4.39]	0.359
Level of education	0.68[0.29-1.59]	0.379	0.08[0.00-1.97]	0.121
Employment status	0.66[0.27-1.59]	0.352	1.05[0.08-13.01]	0.968
Socioeconomic status	0.18[0.33-1.98]	0.640	3.23[0.15-70.15]	0.455
Age at onset	0.61[0.19-1.93]	0.402	0.31[0.02-4.82]	0.401
Occupational risk	**0.42[0.18-0.97]**	**0.043**	**0.05[0.00-0.44]**	**0.008**
Cigarette smoking	0.69[0.33-1.42]	0.311	0	0.987
Exercise	0.46[0.18-1.17]	0.104	0.69[0.15-3.25]	0.641
Stress	0.61[0.11-3.31]	0.564	0.17[0.01-2.92]	0.224
Adherence	2.22[0.69-7.10]	0.180	1.75[0.22-13.79]	0.594
Menses	1.48[0.30-7.29]	0.625	22.58[0.28-179]	0.163
BMI category:				
Underweight	1		1	
Normal weight	0.42[0.05-3.74]	0.43	1.15[0.19-6.99]	0.881
Overweight	0.63[0.07-5.82]	0.68	1.06[0.17-6.44]	0.954
Obese	0.71[0.08-6.76]	0.77	1.09[0.17-6.92]	0.927
GERD	**0.37[0.16-0.87]**	**0.022**	**0.02[0.00-0.33]**	**0.006**
Allergy	0.78[0.21-2.89]	0.705	1.21[0.04-34.84]	0.912
Diabetes Mellitus	**0.49[0.04-5.61]**	**0.567**	**0.00[0.00-0.16]**	**0.006**
Obesity	1.92[0.67-5.49]	0.222	8.41[0.39-183.8]	0.176
Cardiovascular disease	0.57[1.98-1.63]	0.291	0.08[0.00-1.03]	0.053
Respiratory infection	0.46[0.17-1.28]	0.138	0.21[0.02-1.99]	0.173
Relievers	0.36[0.06-2.25]	0.274	0.37[0.03-0.37]	0.431
Controllers:				
Low dose ICS	1		1	
Low dose ICS/LABA	0.42[0.09-1.93]	0.263	0	0.992
Medium dose ICS/LABA	0.21[0.03-1.29]	0.092	0	0.992
Add-on medications	0.42[0.03-5.86]	0.519	0	0.992

Corticosteroid type:				
Beclomethasone	1		1	
Budesonide	0.43[0.16-1.16]	0.095	1945265[0]	0.998
Fluticasone	1.00		1.00	
LABA type:				
Formoterol	1		1	
Salmeterol	4.23[0.93-19.33]	0.063	4166073 [0]	0.998
None	1.86[0.58-05.99]	0.298	31200000[0]	0.998
Asthma severity(Step):				
Step 1/intermittent asthma	1		1	
Step 2/mild persistent	1.75[0.44-6.88]	0.423	0.15[0.00-6.59]	0.328
Step 3/moderate persistent	1.35[0.49-3.70]	0.556	0.94[0.09-9.21]	0.958
Step 4/severe persistent	1.00		1.00	
Dosage optimality	**27.25[6.92-107.2]**	**0.001**	0	0.992
LTRA	0.44[0.15-1.30]	0.137	0.56[0.14-2.26]	0.413
Treatment choice at step	**17.2[4.26-69.41]**	**0.001**	0	0.991
Guideline usage	**23.51[5.94-92.99]**	**0.001**	0	0.996

cOR = Crude odds ratio, aOR = Adjusted odds ratio, CI = Confidence interval, BMI = Body mass index, GERD = Gastroesophageal reflux disease, ICS = Inhaled corticosteroids, LABA= Long acting beta$_2$ agonists, LTRA = Leukotriene receptor agonists.

4.10.2 Independent predictors of HRQoL

Logistic regression analysis was performed to identify variables that are independent predictors of HRQoL in the cohort (Table 4.16). On age, young adults category was found to be an independent predictor of HRQoL on bivariate (cOR= 4.77; 95% CI 1.21-18.78; p= 0.025) but not on multivariate analysis. Occupational risk and cigarette smoking were shown to be important predictors of asthma-HRQoL in this population. On bivariate analysis, both variables did not show independent effects on HRQoL (occupational risk cOR=0.53; 95% CI 0.26-1.09; p= 0.084 and cigarette smoking cOR= 0.65; 95% CI 0.32-1.33; p= 0.237). However, on multivariate regression analysis, occupational risk (aOR= 0.35; 95% CI 0.13-0.89; p= 0.029) and cigarette smoking (aOR= 0.32; 95% CI 0.11-0.89; p= 0.029) proved to be important predictors of HRQoL in the population under study.

Presence of a respiratory tract infection (cOR= 0.36; 95% CI 0.13-0.94; p=0.036) was associated with asthma-HRQoL in the cohort, an effect that was lost on multivariate logistic regression analysis (aOR= 0.31; 95% CI 0.07- 1.07; p= 0.062). Other variables such as dosage optimality, LTRA usage, treatment choice at severity step and guideline

adherence were shown to have significant impact on HRQoL on bivariate analysis, an effect that was also lost on multivariate logistic regression. All the remaining variables did not show independence in predicting the HRQoL in the population under study. In Table 4.16 reference categories for multi-level variables are each represented by the first level entry.

Table 4.16: Independent predictors of Asthma-HRQoL

Variable	Bivariate analysis		Multivariate analysis	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
Age category:				
Adolescents (13-19)	1		1	
Young adults (20-39)	**4.77[1.21-18.78]**	**0.025**	0	0.991
Middle aged (40-64)	2.67[0.78-09.17]	0.118	0	0.991
Elderly (>65)	3.75[0.44-31.62]	0.224	0	0.989
Gender	1.01[0.46-02.24]	0.972	0.06[0.00-2.21]	0.124
Marital status:	0.71[0.39-1.28]	0.254	0.58[0.18-1.86]	0.357
Minor	1		1	
Single	0.79[0.37-1.74]	0.569	0.91[0.26-3.14]	0.879
Married	0.45[0.12-1.64]	0.224	0	0.991
Residence	1.38[0.60-3.17]	0.447	2.20[0.64-7.47]	0.208
Level of education	0.95[0.47-1.89]	0.880	0.54[0.15-1.92]	0.344
Employment status	1.12[0.54-2.36]	0.748	0.69[0.178-2.67]	0.590
Socioeconomic status	0.98[0.47-2.04]	0.957	1.99[0.51-7.82]	0.324
Age at onset	1.15[0.50-2.64]	0.735	0.76[0.21-2.82]	0.684
Occupational risk	**0.53[0.26-1.09]**	**0.084**	**0.35[0.133-0.89]**	**0.029**
Cigarette smoking	**0.65[0.32-1.33]**	**0.237**	**0.32[0.11-0.89]**	**0.029**
Exercise	0.58[0.29-1.16]	0.122	0.56[0.22-1.42]	0.219
Stress	0.34[0.06-1.80]	0.205	0.12[0.01-1.17]	0.068
Adherence	1.32[0.45-3.86]	0.612	0.99[0.23-4.25]	0.992
Menses	1.29[0.38-4.34]	0.683	5.12[0.81-32.39]	0.082
BMI category:				
Underweight	1		1	
Normal weight	0.35[0.06-1.90]	0.223	0.55[0.05-06.09]	0.624
Overweight	0.42[0.07-2.33]	0.321	1.64[0.15-18.19]	0.687
Obese	0.30[0.05-1.68]	0.171	2.99[0.04-205.5]	0.611
GERD	0.56[0.27-1.17]	0.123	0.48[0.16-1.49]	0.208
Allergy	0.68[0.25-1.87]	0.454	0.43[0.11-1.73]	0.234
Diabetes Mellitus	0.44[0.034-4.94]	0.505	0.27[0.01-5.43]	0.395
Obesity	0.74[0.35-1.56]	0.428	0.71[0.054-9.44]	0.798

HIV positive status	0.89[0.17-4.56]	0.886	0.98[0.09-9.94]	0.989
Cardiovascular disease	0.78[0.31-1.98]	0.603	0.78[0.21-2.99]	0.722
Respiratory infection	**0.36[0.13-0.94]**	**0.036**	0.31[0.07-1.07]	0.062
Relievers	1.35[0.22-8.35]	0.745	3.06[0.28-33.04]	0.357
Controllers:				
Low dose ICS	1		1	
Low dose ICS/LABA	0.49[0.18-1.32]	0.158	4.30[0.44-42.54]	0.212
Medium dose ICS/LABA	0.44[0.11-1.71]	0.234	2.51[0.11-55.42]	0.560
Add-on medications	2.00[0.19-21.4]	0.567	32.44[0.62-1708]	0.085
Corticosteroid type:				
Beclomethasone	1		1	
Budesonide	0.16[0.02-1.45]	0.104	0	0.997
Fluticasone	0.35[0.04-3.28]	0.360	0	0.995
LABA type:				
Formoterol	1		1	
Salmeterol	2.46[0.99-6.08]	0.051	20800000[0]	0.997
None	2.33[0.93-5.79]	0.070	40200000[0]	0.995
Asthma severity(Step):				
Step 1/intermittent asthma	1		1	
Step 2/mild persistent	1.78[0.59-5.35]	0.306	1.06[0.04-23.32]	0.970
Step 3/moderate persistent	1.00[0.43-2.35]	1.000	2.69[0.42-17.04]	0.290
Step 4/severe persistent	1.00		1.00	
Dosage optimality	**8.83[1.91-40.79]**	**0.005**	0	0.990
LTRA	**0.30[0.10-0.88]**	**0.029**	0.36[0.11-1.18]	0.092
Treatment choice at step	**6.43[1.35-30.53]**	**0.019**	0	0.990
Guideline usage	**8.00[1.72-37.24]**	**0.008**	0	0.995

cOR = Crude odds ratio, aOR = Adjusted odds ratio, CI = Confidence interval, BMI = Body mass index, GERD = Gastroesophageal reflux disease, HIV = Human immunodeficiency virus, ICS = Inhaled corticosteroids, LABA= Long acting $beta_2$ agonists, LTRA = Leukotriene receptor agonists.

4.10.3: Independent domain predictors of HRQoL score by the level of asthma control

Logistic regression analysis was conducted to determine the independent domains in the HRQoL significantly impacted by the level of asthma control after controlling for confounding. The symptoms (p= 0.004) and activity limitations (p= 0.007) domains were found to be significantly impacted by the level of asthma control independently (Table 4.17).

Table 4.17: Independent predictor domains of HRQoL score by the level of asthma control

DOMAIN	Bivariate analysis		Multivariate analysis	
	cOR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**
Symptoms	**8.46[3.87-18.49]**	**<0.001**	**3.75[1.54-9.12]**	**0.004**
Activity limitation	**6.96[3.28-14.78]**	**<0.001**	**3.62[1.42-9.24]**	**0.007**
Emotional function	3.38[2.06-5.55]	<0.001	1.73[0.88-3.39]	0.112
Environmental stimulation	1.91[1.46-2.50]	<0.001	0.95[0.60-1.51]	0.836

cOR = Crude odds ratio, aOR = Adjusted odds ratio, CI = Confidence interval.

CHAPTER FIVE: DISCUSSION, SUMMARY, CONCLUSION AND RECOMMENDATIONS.

5.1 Introduction

This chapter discusses the key findings with regard to the study objectives. Differences and similarities of the study findings with other related studies have been discussed. The main study findings have also been summarized and conclusions as well as recommendations drawn from these findings made.

5.2 Discussion

Findings of this study reveal that majority of participants were middle aged with the median age being 45 years. The middle age and the young age categories had higher number of participants in whom asthma control and HRQoL scores were high. Our results were similar to studies conducted in the US and Spain which associated poor asthma control and HRQoL to advanced age. In their population, the elderly age category was noted to have lower income, less education, more obese and likely to be former smokers (42,93). They also had higher odds of having severe asthma (94). Contrary to these findings, a study in Nigeria found no correlation between age and quality of life (95). Factors associated with ageing could explain our findings in that the elderly are likely to have more irreversible airway obstruction, increased air trapping, reduced chest wall compliance and elastic recoil, increased airway hyper-responsiveness, high number of comorbidities and low adherence due to poor cognitive skills. Most participants in our study had late onset asthma (80%) which showed a relationship with neither asthma control nor HRQoL. This was comparable to a study in the USA that showed slightly more than half their population (58%) had late onset asthma. Their cut off age was 16 whereas ours was 12 which explains why they had a lesser proportion to ours (96). Studies elsewhere however, found contrary observations where late onset asthma impacted negatively on HRQoL and was attributed to poor response to corticosteroids (5,53,54).

Our population was largely female dominated (77.1%), a finding that was in line with most other related studies (3,8,42,55,97–99) which suggest that beyond age 16, the number of females with asthma supersedes that of males. This could be attributed to

female sex hormones and obesity. Gender was not significantly associated with either asthma control or HRQoLs, results which mirrored those of a French population where asthma impacted both men and women equally (98). Other studies however reported males having higher HRQoL than females (42,95,100).

More than half our population was married (65%). Studies elsewhere showed similar findings at 74.4% and 76.7% (101,102). We found marital status not having any relationship with asthma control or HRQoL. A study in Morocco found significant association between marital status and asthma control though not an independent predictor (102). Our study was dominated mostly by urban dwellers (80%) a finding that tallies with literature that urban residents have higher prevalence of asthma than rural dwellers. Most studies support our findings in that asthma control and HRQoL were higher in urban asthmatics than their rural counterparts, although the relationship was not significant (42,100,103,104). Most of our participants had low level education up to secondary level (64.3%) again, not significantly associated with asthma control or HRQoL. However, studies in Spain (42), Sweden (105) and others worldwide (100,104) show that low level education negatively impacted asthma control and HRQoL. Non-formal employment and low SES correlated and were high (71.4%) in our cohort though without any significance on asthma control or HRQoL. This observation could be attributed mainly to high levels of adherence, drug-cost subsidization and use of treatment guidelines observed in this study since several studies have shown negative association between SES, unemployment and asthma control or HRQoL (98,100,103,104,106–109).

Over half of the population (61.4%) reported worsening of their asthma symptoms during exercise. However, the impact was not significantly associated with HRQoL or asthma control. Literature has revealed that in up to 30% of asthmatics, exercise causes daily life limitations. A number of studies however show contrary results that indicate, physical exercise resulted in improved lung function, better asthma control and HRQoL (99,110,111). Exacerbation of asthma symptoms was experienced by a few members of our cohort group (7.5%) and was related to low HRQoL in 71.4% of this population. Events such as bereavement, stressful work environment and family conflicts were reported by most participants who had stress. Our results were comparable to those of a

study in Japan which showed that psychological stress resulted more to poor quality of life than asthma severity (112).

Participant responses in the current study showed that majority (89.3%) were adherent to their asthma medications, a fact that may have significantly contributed to the high levels of asthma control observed. This high adherence may have been as a result of adequate patient health education, good healthcare provider-patient relationship and patient satisfaction. Our results differ from those of a UK study where a significant number of participants were non-adherent with most having stopped taking their medication once they felt better. In this UK population 60% of the adults, despite being on ICS/LABA had poorly controlled asthma (20). Our results are similar to those of a study conducted in 12 countries where uncontrolled asthma was found to be low (16.3%) among the non-adherent. Their results, like ours, did not find any significant associations with asthma control (100).

Among the women studied, a small proportion (11.1%) experienced worsening of their asthma symptoms during menses and consequent low HRQoL. This outcome was similar to that observed in a French population (98). Another study where women aged 18-24 years were the most affected by asthma researchers found the association between menses and low HRQoL to be statistically significant (113). These observations were attributed to increased levels of estrogen during that period. The current study found an increased rate of high BMI (overweight and obese) among its participants (60.7%) with the population mean BMI (26.74 kg/m^2) favoring the overweight category. Our results related to those of a Canadian study where 64% were either overweight or obese. Although they had higher asthma control scores than the normal and underweight participants their HRQoL scores were lower. Other studies elsewhere reported that being overweight or obese was associated with worse asthma control and quality of life (100,105,114).

The level of asthma control in the population studied was high with only 20% being uncontrolled and all of them consequently reported low HRQoL. Close to half the cohort including some in whom asthma was controlled were found to have low HRQoL. This relationship between asthma control and HRQoL was statistically significant ($p<0.001$).

Our findings concur with those of several related studies conducted worldwide for instance in Brazilian and United Kingdom, researchers found that the degree to which asthma was controlled had a significant impact on a patient's HRQoL (20,83,97). Asthma control reflects the disease's effect in a patient as captured by fluctuations in their symptoms, limitations in their range of activities, their environmental as well as emotional functioning. In our study, all the HRQoL domains had significant associations with HRQoL ($p<0.001$). The domains that were most negatively impacted by uncontrolled disease were the activity and symptoms domains. Analogously, our results were similar to those of a multicenter study which showed that poor asthma control significantly impaired and predicted HRQoL more than a patient's asthma severity status. It was also strongly associated more with the activity limitation domain than the environmental domain (115).

The relationship between asthma control and HRQoL was also emphasized by the results of an Italian study which found that close to a third of their population had optimal HRQoL and it was neither associated with the duration of severity of asthma nor rhinitis, but the degree of asthma control (116). Another multicenter study identified asthma control to be suboptimal in 56.5% of its study population which consequently led to poor HRQoL (100). Elsewhere, in a France and UK study, it was reported that poor asthma control was the only factor that independently impacted HRQoL (98). These consistent outcomes confirm that asthma control is indeed the single most important determinant factor of an individual's HRQoL. The negative impact of asthma on patients' HRQoL could be reduced if patient care focused on achievement of good control of the disease. To achieve optimal control therefore, variables that significantly impact it in populations need to be identified and addressed, so that patients can live near normal lives.

Our findings indicate that history of occupational risk exposure to asthmagens was positive in 33.6% of the population. Of these 29.8% had poor asthma control that was significantly associated to the exposure even after multivariate logistic regression. Our findings correlate with a similar study in the United States which indicated that individuals with work related asthma were significantly more likely to have poor HRQoL as compared to those with non-work related asthma. The researchers noted that occupations that included agriculture, fishery and crafts trades had more participants

reporting respiratory symptoms. These occupations were noted to have flour, diisocyanates, welding/soldering and vehicle fumes as asthmagens (117). In our setup, participants who were found to have occupational risk exposure worked in either of these occupations farming, bakery, rubber/plastic work, cleaning, spray painting, electronic assembly, food processing, nursing and teaching professions.

The cornerstone of asthma management is inhalational therapy. Thus, correct inhaler technique during administration of asthma medications is critical in controlling symptoms of asthma and preserving lung function. Incorrect inhaler technique negatively affects the pulmonary deposition of the medications to their target site and unsurprisingly poor treatment outcomes result. These are manifested as poor asthma control and low HRQoL. In our study, 4.3% of the population studied demonstrated incorrect inhaler technique and were found to have poor asthma control, an association that was significant. Our results mirrored those of a study in Muscat in which researchers noted that 85% of their patients who demonstrated poor inhalational technique had poorly controlled asthma (118). In another Saudi Arabian study, investigators found that 45% of their population showed improper use of asthma devices and correspondingly had poorly controlled asthma (119). These results imply that all asthmatic patients showing poor asthma control would benefit from re-assessment of their inhaler technique and provided with proper instructions on their inhaler usage to achieve the desired therapeutic goals.

Cigarette smoking has been associated with worse asthma symptoms. Our study was comprised mainly of non-smokers (93.6%) while the rest were ex-smokers. We found that smoking is an independent predictor of asthma-HRQoL in this population. Eosinophil and neutrophil activity in smokers has been shown to be resistant to ICS therapy even at high doses. Smoking cessation is what actually causes reduction in neutrophil counts. Of the ex-smokers, 66.7% had moderate to severe asthma which required control using combination medications. A small proportion of ex-smokers with severe asthma required add-on therapy (tiotropium). We found that for every three non-smokers with severe asthma requiring tiotropium, there were 10 ex-smokers requiring the same. Most ex-smokers were represented at step 4 treatment (33.3%) when compared to the 19.1% of non-smokers at the same step. Our findings relate similarly to a study in

which it was noted that asthmatic smokers had poor disease control when compared to their non-smoker counterparts (101).

Allergy was present in 87.1% of our population and impacted HRQoL more negatively than asthma control, an observation that was similar to results from a multination study (100). Another study reported atopy to be present in 60% of its participants (99). A similar observation was also noted in a Turkey study where results showed that 78.7% of the patients studied had atopy which was not associated with asthma control or HRQoL (120). Literature indicates that atopy is common in the asthmatic population worldwide.

Gastroesophageal reflux disease and asthma are known to often co-exist and in such a setup they negatively and significantly impact a patient's quality of life. Asthma symptoms are aggravated by GERD and vice versa. Studies show that GERD produces permanent histopathological changes and progression to fibrosis in asthmatics- changes which have been associated with decreased patient response to asthma treatment via direct irritation, hypersensitivity of the airway and vagal reflex stimulation that may cause shortness of breath. On the other hand, asthma exacerbations result in negative intrathoracic pressure that could lead to reflux. Medications for management of asthma such as theophylline, beta agonists and steroids decrease the lower esophageal sphincter pressure causing reflux. In our study, 28.6% of the population had comorbid asthma and GERD. Of these, 32.5% were reported to have significant poor asthma control and 57.5% of them had low HRQoL. Our results reflected those of a study in Hong Kong where 40.4% of the participants were found to have GERD that was significantly associated with worse asthma control and HRQoL in all the domains (121). The proper diagnosis and optimal treatment of GERD is therefore paramount in achieving the desired asthma control and improvement in the HRQoL.

The prevalence of Human immunodeficiency virus (HIV) in our study population was 4% which mirrors the literature 2% prevalence among asthmatic patients (122). Our results show that, a HIV positive status had no impact on asthma control or HRQoL of asthmatics. The immunosuppressive disease is known to interact synergistically with other asthma risk factors to lower HRQoL but use of Highly Active Anti-Retroviral Therapy (HAART) has significantly reduced this impact, an observation confirmed by

our study findings (122,123). Cardiovascular disease, hypertension or heart failure was present in 15% of our population and related more negatively with HRQoL than asthma control though not in a significant way. This was similar to other study reported (100,105). The presence of a respiratory tract infection in our population was significantly associated with lower HRQoL scores although it did not stand out as an independent predictor of HRQoL. The coexistence of asthma and diabetes mellitus is known to be rare. Two percent of our population had concomitant asthma and type 2 diabetes mellitus. Studies show that effective treatment of one disease causes exacerbation of the other (98). Optimal dosing of corticosteroids and particularly use of higher doses to achieve and maintain asthma control predisposes patients to the hyperglycemic side effects of the drugs thereby exacerbating pre-existing diabetes whose control becomes a challenge. After multivariate analysis, our study showed that having comorbid diabetes mellitus had a great impact on a patient's asthma-HRQoL. Our results tally with those of a similar study which showed that the impact of asthma on HRQoL was greater when in coexistence with type 2 diabetes mellitus (98).

Close to 100% of our patients were treated (on controller medication) a fact that we attribute to the high degree of asthma control observed in our population. Our findings however, were contrary to those of most studies where a high proportion of asthma sufferers went untreated (20,95,100,103,123,124). We attribute our good results to the fact that, KNH being a referral institution, patients were offered specialized care from the readily available highly trained and knowledgeable human resource, current diagnostic equipment, provision of the recommended medications, adequate patient education and prescriber adherence to current guidelines. Moderately persistent asthma at step 3 of treatment was the commonest level of asthma severity among our participants although this did not have any significant association with asthma control or HRQoL implying that asthma control at any severity level was the most important determinant of HRQoL outcome.

Inhaled corticosteroids are the mainstay of therapy in asthma management. Asthma, being a state of inflammation, results in persistence of symptoms when left untreated. Studies have shown that all ICS can achieve similar clinical efficacy when administered at equipotent dosages. They effectively and reproducibly suppress the inflammatory

processes in most asthmatic patients' airways. The ICS dose-response curve produces a plateau in the low to moderate dose ranges. Once a patient's asthma symptoms are controlled, ICS doses ought to be titrated to the lowest effective doses as per the individual patient's response. Higher ICS doses are usually preserved for temporary treatment such as during an exacerbation. However, a subset of asthmatic patients such as smokers, the obese and those with neutrophilic phenotype, may require higher ICS doses to effectively obtain and maintain control of their symptoms. In our study 87.2% of the patients who had been optimally dosed reported their asthma to be under control while 80% of those sub-optimally dosed had uncontrolled asthma, a relationship which was found significant. This also impacted negatively on their HRQoL as 86.7% of the sub-optimally dosed reported low HRQoL. Our results compare well to those of a study in which ICS doses were increased in a stepwise manner till total control or maximum doses were reached. Their results confirm that optimization of dosage is key to controlling asthma symptoms and attaining high HRQoL scores (83,125).

Prescriber adherence to asthma treatment guidelines during asthma management is critical in meeting the desired goals of therapy. A stepwise approach to treatment in which the dosage of controller medication is increased till asthma control is achieved is recommended. This study found a significant association between asthma control, HRQoL and guideline usage by the prescribers. Of the 10% in whom treatment guidelines were not followed during their management, 85.7% were found to have uncontrolled asthma. Our results were comparable to those of a study based on GINA guidelines where researchers found that well controlled patients who had achieved guideline-based asthma control reported consistently higher overall HRQoL than their uncontrolled counterparts in whom guidelines were not followed. In addition, the mean scores of AQLQ in those well controlled were similar regardless of the severity of asthma or treatment intervention (126). In another cross sectional study where half the treatment regimens were considered non-adherent to guideline recommendations, only those patients in whom treatment was in accordance to guidelines had significantly higher HRQoL. There was a clear distinction in the symptoms and environmental stimulation domains between those with low and those with high HRQoL (127). In our study, of the 90% participants in whom prescribers adhered to guideline recommendations, 86.5% had

controlled asthma. The 10% in whom guidelines were not followed either had their controller medications prescribed once daily, were on SABA only instead of combination with controller medication, or their asthma severity level required step-up to a higher dose or addition of other medications to the ones they had been put on. There is therefore a strong relationship between guideline adherence and asthma control and by extension, HRQoL.

Asthma treatment recommendations follow a stepwise progression based on a patient's asthma severity step as classified in the NEW 2017 GINA report. Treatment for a higher severity step requires addition to a lower severity step treatment of either new medications or by increasing the dose. In our study, 75% of patients whose treatment choice at their severity step was inappropriate, had uncontrolled asthma. This relationship was also significant in terms of their HRQoL. In a related study, researchers showed that combination inhalers improved pulmonary function when compared with their respective ICSs alone (128). A systematic review also showed that the addition of LABA was superior to increasing ICS dose and was most beneficial to patients who experienced frequent exacerbations. The addition of a LTRA to ICS conferred comparable asthma control to doubling the ICS dose (129). In our study the addition of LTRA (montelukast) to ICS/LABA treatment had significant positive outcomes on HRQoL. On the other hand, associations were not found between asthma control or HRQoL and the type of reliever, ICS or LABA a patient was using.

5.2.1 Strengths and Limitations

Our study was real-life and made use of the well validated tools to measure outcomes. The study location being a referral institution was well endowed in terms of resources. In addition, literacy levels among participants were high, a fact that reduced the chances of participants providing wrong responses to questions because of lack of understanding. Some of the responses in the questionnaires were patient subjective reports which could have been biased either by under-reporting or exaggeration. The convenience sampling technique that was non-random could have introduced another source of bias in this study. However, despite these limitations, our study was adequately powered and findings compared well with those of other similar studies conducted worldwide.

5.3 Summary

The study set out to determine the Health Related Quality of Life (HRQoL) and factors that influenced it amongst asthmatic patients who attended Kenyatta National Hospital (KNH) chest clinic for their routine management. In this study, these factors have been explored and discussed. The level of asthma control was found to be the single most important determinant of an individual's HRQoL. Our study did not find any significant association between asthma control, HRQoL and sociodemographic traits of patients such as age, gender, marital status, residence (rural/ urban), level of education and socioeconomic status. Patient specific traits such as age at asthma onset, exercise, stress, adherence, menses and high BMI were also not found to be significantly associated with asthma control or asthma-HRQoL. Of the comorbidities, having a HIV positive status or cardiovascular disease did not impact asthma control or HRQoL significantly. Presence of a respiratory tract infection was significantly associated with lower HRQoL scores although this was not an independent predictor of HRQoL in this population. Associations were also not found between asthma control or HRQoL and the type of reliever, ICS or LABA a patient was on.

Asthma control on the other hand was significantly influenced by various factors which in this population included occupational exposure, correctness of inhaler technique, presence of gastroesophageal reflex disease (GERD), type 2 diabetes mellitus, optimality of dosage of the inhaled corticosteroids, prescriber guideline usage and treatment choice at the asthma severity step. Amongst these variables those that stood out as independent predictors of asthma control and thus HRQoL were occupational exposure to asthmagens, GERD, diabetes mellitus and cigarette smoking status. The symptoms and activity limitation domains of the HRQoL were most significantly impacted by the level of asthma control. Nevertheless, in this population, the level of asthma control was high (80%) which we attribute to the high level of care offered to asthmatic patients in this facility. Guideline adherence by prescribers as well as patient education and satisfaction were high. This might have played a role in patient adherence to therapy as it was found not to have an influence on asthma control.

5.4 Conclusion

Asthma-HRQoL outcome among patients was largely dependent upon the degree to which asthma was controlled. Asthma was controlled in 80% of the participants who slightly over half reported high HRQoL scores (53%). All the 20% participants in whom asthma was uncontrolled had low HRQoL scores. The independent predictors of asthma control and HRQoL included occupational risk exposure, GERD, type 2 diabetes mellitus and cigarette smoking. The symptoms and activity limitation domains of the HRQoL were the most negatively impacted by poorly controlled asthma**.**

5.5 Recommendations

5.5.1 Recommendations for Policy and Practice

1. Incorporation of HRQoL into routine practice as an important measurement for assessing the outcome of asthma therapy.
2. Dissemination and support of adherence to current treatment guideline recommendations to all healthcare facilities for uniformity in asthma care by clinicians.
3. Screening, early diagnosis and prompt treatment of GERD in asthmatic patients.
4. Recheck and re-demonstration of inhaler technique in asthmatic patients at every consultation especially in those with uncontrolled disease.
5. Reduction in occupational exposures to asthmagens by shifting workers affected to departments with less or no exposures. Work-related stress reduction for those working in professions not associated with asthmagens.

5.5.2 Recommendations for Further Research

1. To assess asthma control and HRQoL and their determinants in asthmatic patients on care at lower health facilities that may not have the infrastructure and resources available in higher level facilities.
2. To compare asthma control levels in patients as determined by objective clinical measures (such as spirometry) with subjective patient reported measures (such as ACT) and relate them to the patient's HRQoL.

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7.0 APPENDICES

APPENDIX 1: ETHICAL APPROVAL (PROTOCOL No. P190/03/2018).

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/204

June 8, 2018

KENYATTA NATIONAL HOSPITAL APPROVED 08 JUN 2018 KNH/UoN-ERC P.O. Box 20723-00202 NAIROBI

Dr. Mary Consepta Khacheha Alubisia
Reg. No.U56/87331/2016
Dept of Pharmaceutics and Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Dr.Alubisia

RESEARCH PROPOSAL – HEALTH RELATED QUALITY OF LIFE AND ITS DETERMINANTS IN ASTHMATIC PATIENTS AT KENYATTA NATIONAL HOSPITAL (P190/03/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and approved your above research proposal. The approval period is from 8th June 2018 – 7th June 2019.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. *(Attach a comprehensive progress report to support the renewal).*
f) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chairperson, KNH-UON ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmaceutics and Pharmacy Practice, UoN
Supervisors: Dr.Sylvia Opanga, Dr.George A. Mugendi

APPENDIX 2: INSTITUTIONAL APPROVAL.

KENYATTA NATIONAL HOSPITAL
P. O. Box 20723, 00202 Nairobi

Tel: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/AD-MED/42B/VOL.I/

Date: 12th June 2018

Dr. Mary Consepta Khacheha Alubisia
Department of Pharmaceutics & Pharmacy Practice
School of Pharmacy
College of Health Sciences
University of Nairobi
NAIROBI/

RE:APPROVAL TO CONDUCT A STUDY IN MEDICINE DEPARTMENT

Following approval of your study by the KNH/UoN ERC and completion of the KNH study registration certificate, permission is hereby granted to collect data from Medical Outpatient Clinic (MOPC) to enable you complete your study on "*Health related quality of life and its determinants in asthmatic patient at* Kenyatta National Hospital.

Kindly liaise with the Assistant Chief Nurse in MOPC Department for facilitation.

Dr. K. Ndege

DR. K.NDEGE
AG.HOD - MEDICINE

Copy to: Assistant Chief Nurse - MOPC

Vision: A world class patient-centered specialized care hospital

ISO 9001: 2008 CERTIFIED

APPENDIX 3: LETTER OF PERMISSION TO USE THE ASTHMA QUALITY OF LIFE QUESTIONNAIRE (AQLQ(S)) TOOL.

Elizabeth Juniper, MCSP, MSc.
20 Marcuse Fields, Bosham, West Sussex, PO18 8NA, England
Phone: +44 (0) 1243 572124 Fax: +44 (0) 1243 573680
E-mail: juniper@qoltech.co.uk www.qoltech.co.uk

19th March 2018

Dr Mary Alubisia
Pharmacist
University of Nairobi
Karatina Sub County Hospital
Nyeri Karatina Highway
Karatina Town
Nyeri County
PO Box 133
10101 Kenya
Africa

Dear Dr Alubisia,

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (AQLQ) AND ASTHMA CONTROL QUESTIONNAIRE (ACQ)

I am delighted that you are using the Asthma Quality of Life Questionnaire (AQLQ) and Asthma Control Questionnaire (ACQ) for your non commercial study. I can confirm our permission for you to use the paper versions of the validated and unmodified questionnaires that you have.

I also give you permission to copy and to make paper versions of our questionnaires and instruction sheets if required. You will be aware that all the questionnaires are protected by copyright and must not be altered, sold, translated or adapted for another medium without our permission.

With all good wishes,

Jilly Styles
Director – QOL Technologies Ltd
Tel: + 44 (0) 1243 572124
Fax: + 44 (0) 1243 573680
e:mail: jill@qoltech.co.uk

APPENDIX 4: ELIGIBILITY CRITERIA.

All the participants to be enrolled must meet eligibility criteria based on the inclusion/exclusion criteria detailed in this form.

(I) Study Information

TITLE:	Health related quality of life and its determinants in asthmatic patients at Kenyatta National Hospital.
KNH/UoN-ERC Protocol Number:	P190/03/2018
Principal Investigator:	DR. MARY C. K ALUBISIA

(II) Subject Information:

Subject Name/ID:			
Gender:	Male ☐	Female ☐	

(III) Inclusion/Exclusion Criteria

Inclusion Criteria *(tick as appropriate)*	**Yes**	**No**
1. Has the patient been diagnosed with asthma?		
2. Is the patient aged 13 years and above?		
3. Is the patient on treatment for asthma?		
4. Is the patient enrolled at KNH chest clinic?		
5. Has the patient consented to participate in the study?		

Exclusion Criteria	**Yes** ☐	**No** ☐
1. Does the patient have COPD/TB/Pregnancy or is from vulnerable groups?		
2. Is the patient under 13years of age?		

All subject files must include supporting documentation to confirm subject eligibility. The method of confirmation could include, but is not limited to, laboratory test results, radiology test results, subject self-report, and medical record review.

(IV) Statement of Eligibility

This subject is **ELIGIBLE** ☐ / **NOT ELIGIBLE** ☐ to participate in the study.

Signature:	Date:
Name:	

APPENDIX 5A: CONSENT FORM

Title of the study: Health Related Quality of Life and its determinants in asthmatic patients at Kenyatta National Hospital.

Institution: Department of Pharmaceutics & Pharmacy Practice, School of Pharmacy.

Principal Investigator: Dr. Mary C. K Alubisia.

Supervisors: 1. Dr. Sylvia A. Opanga. 2. Dr. George A. Mugendi.

Department of Pharmaceutics and Pharmacy practice,

University of Nairobi, P.O BOX 30197-00400, Nairobi.

Ethical Approval: This study has the approval of Kenyatta National Hospital/University of Nairobi Ethical and Research Committee (KNH-UoN ERC) Protocol number P190/03/2018.

Introduction

I would like to inform you about a medical research to be conducted by the above mentioned researchers. The importance of having this discussion with you is to give you detailed information on what the research involves so you can make informed decision on whether to take part or not. Please be free to ask any question on what may happen to you should you agree to participate concerning any dangers or risks to you, benefits, your rights or anything you have not understood. After we address your concerns then you will decide whether to take part or not. If you decide to participate, I will ask you to sign the consent form below. You are therefore required to understand the following general principles which apply to all participants in a medical research before we can proceed.

What is the research about?

The reason for doing this research is to find out the well-being of patients who have asthma so as to be able to measure how well the disease has been treated or controlled. The findings of this research will make it possible for doctors to check a patient's response to medical treatment and evaluation of how well the disease has been controlled and its effects on the patient's life that cannot be adequately tested by medical tests alone.

The research therefore aims to assess how well your disease is controlled, your view of benefit from treatment, and your sense of well-being. It also intends to look for factors that are also related to your well-being.

Procedure: With your permission, I will ask you questions on personal information to help us find out which factors are related to your level of asthma control and your view of well-being. All information obtained will be handled secretly. This will take about 30 minutes of your time.

Any Risks involved? In this research, there will be no dangers to your health involved since we will not give you any medicines, only questions.

Benefits: There will be no direct benefits to you but the findings will be shared with your doctor so that your illness can be understood well for you to be treated better.

Assurance of Confidentiality: All information obtained from you will be kept in utmost confidence. At no point will your name be used or mentioned during data handling or in any resulting publication. Serial numbers will be used instead.

Your rights as a participant

I. Your agreement to participate in this study is voluntary.

2. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal and no injustice or loss of benefit will be meted out on you.

3. Your refusal to participate in the research will not affect the services you are entitled to in this health facility or any other.

4. After you have read the explanation you can ask any questions that will enable you to clearly understand the nature of the study.

5. We will give you a copy of this form for your records.

Contacts: If you have any questions about your rights as a research participant, please get in touch with any of the following using the contacts given;

1. Dr. Mary Alubisia, P.O BOX 133-10101, Karatina. Tel: 0726285431.

   Email: *maryalubisia@gmail.com*

2. Lead Supervisor: 1. Dr. Sylvia A. Opanga. Tel: 0721296448.

   Department of Pharmaceutics and Pharmacy practice

   University of Nairobi, P.O BOX 30197-00400, Nairobi.

3. The Chairperson, KNH-UoN ERC Committee, P.O BOX 20723-00100, Nairobi. Tel 2726300/2716450 Ext 44102. Email: *uonknh-erc@uonbi.ac.ke*.

You will be refunded back any airtime money you may spent when making any call that concerns this research.

I now request you to sign the attached consent form below.

CONSENT TO PARTICIPATE IN THE STUDY.

I have read and also been explained to the information in this consent form and have fully understood. My questions and concerns have been addressed. The risks and benefits have been explained to me. I understand that my participation is voluntary and I can withdraw from the study any time without injustice or loss of any benefit. I also know that all efforts will be made to keep information regarding my personal identity confidential.

Name of participant _____ Date _____

Signature of participant _____

Researcher statement

I confirm that I have explained the details of the research to the participant and that he/she has understood.

Name of researcher _____ Date _____

Signature of researcher _____

APPENDIX 5B: RIDHAA YA KUSHIRIKI KATIKA UTAFITI.

Kichwa cha Utafiti:

Hali ya maisha kiafya na mambo yaaamuayo miongoni mwa wagonjwa wanaougua ugonjwa wa pumu katika Hospitali ya Kitaifa ya Kenyatta.

Taasisi:

Idara ya mazoezi ya Famasia, Shule ya Famasia, Chuo Kikuu cha Nairobi,

Mtafiti Mkuu:

Dkt. Mary C.K Alubisia.

Watafiti Wengine pia Wasimamizi:

1.[Sylvia A.Opanga - Mhadhiri, 2. Dkt. George A. Mugendi] - Wahadhiri

Idara ya mazoezi ya Famasia, Shule ya Famasia, Chuo Kikuu cha Nairobi, S.L.P 30197-00400, Nairobi.

Idhini ya Idara ya Adili:

Utafiti huu umeidhinishwa na Hospitali ya Kitaifa ya Kenyatta ikishirikiana na Kamati ya Adili naUtafiti ya Nairobi. Nambari ya Itifaki P190/03/2018.

Utangulizi:

Ningependa kukujulisha kuhusu utafiti huu utakaofanywa na waliotajwa hapo juu. Umuhimu wa mazungumzo haya ni kukufahamisha zaidi ili uweze kufanya uamuzi wa hekima kushiriki au kutoshiriki katika utafiti huu.

Una uhuru wa kuuliza maswali yoyote kuhusu kitakachofanyika utakapokubali kushiriki, madhara yanayoweza kutokea, manufaa ya utafiti huu, haki zako kama mshiriki na maswali yoyote kuhusu lolote ambalo hulielewi. Tutakapo jibu maswali yako yote, basi utaamua kushiriki au la. Ukikubali kushiriki, nitakuuliza utie sahihi na majina yako kwa ukurasa hapo chini. Unahitajika kuelewa maelezo yafwatayo kuhusu nguzo muhimu ambazo zinalinda washiriki wote katika ufatiti wa sayansi ya afya kabla ya tuendelee.

Utafiti huu unahusu nini?

Sababu ya kufanya utafiti huu ni kuweza kutambua hali ya maisha kiafya ya walioadhiriwa na ugojwa wa pumu ndiposa tuweze kupima ni kwa kiwango gani ugojwa huu umeweza kuthibitika. Matokeo ya utafiti huu yataweza kufahamisha madaktari jinsi waadhiriwa wanavyotibika kwa dawa na pia kujua kiwango ugonjwa huo umethibitiwa na madhara yake kwa mhasiriwa yenye haiwezi pimika kikamilifu kwa vipimo vya kisayansi vya matibabu.

Kwa hivyo utafiti huu unalenga kupima ni kwa kiwango gani ugonjwa wako wa pumu umeweza kuthibitiwa, maoni yako kuhusu faida ya matibabu na jinsi unavyojihisi kiafya. Vile vile, utafiti huu unanuia kupambanua mambo yanayohusiana na uzima wako kiafya.

Mtindo:

Ukinipa ruhusa, nitaweza kukuuliza maswali yanayohusu hahari yako binafsi ndiposa tuweze kupambanua mambo yanayohusiana na kiwango chako cha uthibiti wa pumu na maoni yako kuhusu uzima wako kiafya. Habari zote utakazotueleza zitalindwa kisiri. Tutakuwa nawe katika mahojiano hayo kwa muda wa dakika kama thelathini.

Hatari yoyote?

Hakuna hatari yoyote utakayoponzwa nayo maana hakuna matibabu washiriki watapewa. Ni maswali tu utakayoulizwa.

Manufaa:

Hakuna manufaa mshiriki atapokea moja kwa moja bali matokeo ya utafiti kwako utajadililiwa pamoja na madaktari wanaokutibu ili ugonjwa wako ueleweke kwa undani ndiposa upate kutibiwa vyema zaidi.

Dhibitisho la usiri:

Habari zote utakazotueleza zitalindwa kwa siri kuu. Hakutakuwepo wakati wowote ambapo jina lako litatumika au kutajwa wakati wa kutayarisha matokeo ya utafiti huu. Badala ya jina la mshiriki, nambari tambulishi ndio itakayotumika.

Haki zako kama mshirika:

1. Kushiriki kwako kwa utafiti huu ni kwa hiari.

2. Unaweza kujiondoa wakati wowote bila kushurutishwa kutoa maelezo ya kufanya hivyo.

3. Kutoshiriki kwako katika utafiti huu hakutaathiri huduma unazopaswa kupata kwa hosipitali hii au ingineyo iwayo.

4. Una uhuru wa kuuliza swali lolote baada ya kusoma na kuelewa ujumbe huu ili upate habari kamili kuhusu utafiti wenyewe.

5. Tutakupa nakala yako ili ujiwekee kwa manufaa yako binafsi.

Nambari ya mawasiliano ya baadaye:

Ukiwa na swali lolote baadaye kuhusu haki zako kama mshiriki, tafadhali wasiliana na:

1. Dkt. Mary C.K Alubisia. S.L.P 133 Karatina. Nambari ya simu: 0726285431.
   Tovuti: *maryalubisia@gmail.com*
2. Mwenyekiti,
   Hospitali ya Kitaifa ya Kenyatta ikishirikiana na
   Kamati ya Adili na Utafiti ya Nairobi, S.L.P 2073-00100, Nairobi. Nambari ya simu- 2726300/2716450 kiendelezi 44102.Tovuti: uonknh-erc@uonbi.ac.ke.

Utarudishiwa ada ya mazungumzo kupitia laini hizi kama mazungumzo yenyewe yanahusu utafiti huu.

Sasa, ninakualika kushiriki katika utafiti huu kwa kutia sahihi yako kwa ridhaa hii.

FOMU YA RIDHAA

Nimesoma na pia kupokea maelezo katika ridhaa hii na nimeyaelewa kikamilifu. Maswali na haja zangu kuhusu huu utafiti yamejibiwa. Manufaa na pia hatari zozote nimepata kuelezwa. Nimefahamu ya kwamba kushiriki kwangu ni kwa hiari na nina uhuru wa kujiondoa bila thuluma au kuathirika kwa huduma ninazopaswa kupokea kwa hosipitali hii au ingine iwayo. Nimefahamu tena ya kwamba, juhudi zote zitafanywa kuweka habari zote kunihusu siri.

Jina la mshiriki: _____Tarehe: _____

Sahihi ya mshiriki: _____

Andiko la Mtafiti Mkuu

Nadhibitisha ya kwamba nimemueleza mshiriki habari zote anapaswa kujua kuhusu utafiti huu na amepata kufahamu.

Jina la Mtafiti mkuu: _____ Tarehe: _____

Sahihi ya Mtafiti mkuu: _____

APPENDIX 6A: ASSENT FORM (13-17 year old), Parent/Guardian consent.

Project Title: Health Related Quality of Life and its determinants in asthmatic patients at Kenyatta National Hospital.

Institution: Department of Pharmaceutics & Pharmacy Practice, School of Pharmacy.

Principal Investigator: Dr. Mary C. K Alubisia.

Supervisors: 1. Dr. Sylvia A. Opanga. 2. Dr. George A. Mugendi.

Department of Pharmaceutics and Pharmacy practice

University of Nairobi, P.O BOX 30197-00400, Nairobi.

Introduction

We are doing a research study the well-being of patients who have asthma so as to be able to measure how well the disease has been treated or controlled. Permission has been granted to undertake this study by Kenyatta National Hospital- University of Nairobi Ethics and Research Committee (KNH-UoN ERC Protocol Number- P190/03/2018.

The findings of this research will make it possible for doctors to check a patient's response to medical treatment and evaluation of how well the disease has been treated and its effects on the patient's life that cannot be fully tested by medical tests alone. At least fifty children will be participating in this research study with you.

If you decide that you want to be part of this study, we will ask you questions on personal information to help us find out which factors are related to your level of asthma control and your view of well-being. All information obtained will be handled secretly. This will take about 30 minutes of your time.

There are some things about this study you should know. These are:

Any Risks involved? In this research, there will be no dangers to your health involved since we will not give you any medicines, only questions.

Benefits: There will be no direct benefits to you but the findings will be shared with your doctor so that your illness can be understood better for you to be treated properly. You will also know if your disease has been controlled well.

When we are finished with this study we will write a report about what was learnt. This report will not include your name or that you were in the study.

You do not have to be in the study if you do not want to be. If you decide to stop after we begin, that's ok too. Your parents know about the study too.

If you decide you want to be in the study, please sign your name.

I _____ want to be in the research study.

Signature _____ Date _____

Parent/Guardian consent

I have been informed about the study my child will participate in and I have agreed.

Name of parent/guardian _____ Signature _____ Date _____

Researcher statement

I confirm that I have explained the details of the research to the participant and his/her parent/guardian and that they have understood.

Name of researcher _____ Signature _____ Date _____

APPENDIX 6B: RIDHAA YA KUSHIRIKI KATIKA UTAFITI (Umri miaka 13-17), MZAZI/MLEZI.

Kichwa cha Utafiti:

Hali ya maisha kiafya na mambo yaaamuayo miongoni mwa wagonjwa wanaougua ugonjwa wa pumu katika Hospitali ya Kitaifa ya Kenyatta.

Mtafiti Mkuu:

Dkt. Mary C.K Alubisia.

Watafiti Wengine pia Wasimamizi:

1. [Dkt. Sylvia A.Opanga 2. Dkt. George A. Mugendi]- Wahadhiri.

Idara ya mazoezi ya Famasia, Shule ya Famasia, Chuo Kikuu cha Nairobi, S.L.P 30197-00400, Nairobi.

Idhini ya Idara ya Adili:

Utafiti huu umeidhinishwa na Hospitali ya Kitaifa ya Kenyatta ikishirikiana na Kamati ya Adili naUtafiti ya Nairobi. Nambari ya Itifaki P190/03/2018.

Utangulizi:

Ningependa kukujulisha kuhusu utafiti huu utakaofanywa na watafiti waliotajwa hapo juu. Sababu ya kufanya utafiti huu ni kuweza kutambua hali ya maisha kiafya ya walioadhiriwa na ugojwa wa pumu ndiposa tuweze kupima ni kwa kiwango gani ugojwa huu umeweza kuthibitika.

Matokeo ya utafiti huu yataweza kufahamisha madaktari jinsi waadhiriwa wanavyotibika kwa dawa na pia kujua kiwango ugonjwa huo umethibitiwa na madhara yake kwa mhasiriwa yenye haiwezi pimika kikamilifu kwa vipimo vya kisayansi vya matibabu.

Vile vile, utafiti huu unanuia kupambanua mambo yanayohusiana na uzima wako kiafya.

Kadri ya watoto hamini wengine watashiriki kwa huu utafiti pamoja nawe.

Mtindo:

Ukinipa ruhusa, nitaweza kukuuliza maswali yanayohusu hahari yako binafsi ndiposa tuweze kupambanua mambo yanayohusiana na kiwango chako cha uthibiti wa pumu na maoni yako kuhusu uzima wako kiafya. Habari zote utakazotueleza zitalindwa kisiri. Tutakuwa nawe katika mahojiano hayo kwa muda wa dakika kama thelathini.

Hatari yoyote?

Hakuna hatari yoyote utakayoponzwa nayo maana hakuna matibabu washiriki watapewa. Ni maswali tu utakayoulizwa.

Manufaa:

Hakuna manufaa mshiriki atapokea moja kwa moja bali matokeo ya utafiti kwako utajadililiwa pamoja na madaktari wanaokutibu ili ugonjwa wako ueleweke kwa undani ndiposa upate kutibiwa vyema zaidi.

Tutakapokamilisha utafiti huu, tutaandika ripoti kuhusu yale tumesoma. Ripoti hii haitakua na jina lako na hakuna mahali tutaandika mahali kwamba ulishiriki.

Una uhuru wa kukataa kujiunga kwa utafiti ikiwa hutaki. Ukiamua kutoka baada ya utafiti kuanza, pia umeruhusiwa. Wazazi wako wamejulishwa kuhusu utafiti huu pia.

Sasa, ninakualika kushiriki katika utafiti huu kwa kutia sahihi yako kwa ridhaa hii.

Mimi _____nakubali kushiriki katika utafiti huu.

Sahihi: _____Tarehe: _____

Ridhaa ya mzazi/mlezi

Nimejulishwa kuhusu utafiti mwanangu atahusika nami nimeelewa kwa hivyo, ninampa ruhusa kushiriki.

Jina la mzazi/mlezi_____Sahihi _____Tarehe _____

Andiko la Mtafiti Mkuu

Nadhibitisha ya kwamba nimemueleza mshiriki pamoja na mzazi/mlezi wake habari zote wanapaswa kujua kuhusu utafiti huu na wamepata kufahamu.

Jina la Mtafiti mkuu: _____ Sahihi _____ Tarehe:_____

APPENDIX 7: ASTHMA CONTROL TEST (ACT).
Please tick the most appropriate option that the participant describes.

1. In the past four weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home *(WORKDONE*)*? SCORE: ☐

1. All of the time	2. Most of the time	3. Some of the time	4. A little of the time	5. None of the time

2. During the past four weeks how often have you had shortness of breath *(SOB*)?* SCORE: ☐

1. More than once a day	2. Once a day	3.3-6 times a day	4. Once or twice a week	5. Not at all

3. During the past four weeks how often did your asthma symptoms (wheeze, coughing, and shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning *(NIGHTss*)?* SCORE: ☐

1. 4 or more nights a week	2. 2-3 nights a week	3. Once a week	4. Once or twice	5. Not at all

4. During the past four weeks, how often have you used your rescue inhaler or nebulizer medication *(RESCUE*)*? SCORE: ☐

1. 3 or more time times a day	2. 1 or 2 times per day	3. 2 or 3 times per week	4. once a week or less	5. Not at all

5. How would you rate your asthma control during the past four weeks *(CONTROLRATING*)*? SCORE: ☐

1. Not controlled at all	2. Poorly controlled	3. Somewhat controlled	4. Well controlled	5. Completely controlled

TOTAL SCORE: ☐

KEY: (ITALICS*) = Codes used on Epi Info Ms Excel Data sheet.

APPENDIX 8: ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S).

ASTHMA QUALITY OF LIFE QUESTIONNAIRE WITH STANDARDISED ACTIVITIES (AQLQ(S))

SELF-ADMINISTERED

(>12 years)

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APRIL 2008

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AQLQ(S) ≥12 years SA North American English Version

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID: _____

SELF-ADMINISTERED DATE: _____

Please complete **all** questions by circling the number that best describes how you have been during the **last 2 weeks as a result of your asthma.**

HOW **LIMITED** HAVE YOU BEEN **DURING THE LAST 2 WEEKS** IN THESE ACTIVITIES **AS A RESULT OF YOUR ASTHMA**?

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
1. STRENUOUS ACTIVITIES (such as hurrying, exercising, running up stairs, sports)	1	2	3	4	5	6	7
2. MODERATE ACTIVITIES (such as walking, housework, gardening, shopping, climbing stairs)	1	2	3	4	5	6	7
3. SOCIAL ACTIVITIES (such as talking, playing with pets/children, visiting friends/relatives)	1	2	3	4	5	6	7
4. WORK/SCHOOL-RELATED ACTIVITIES* (tasks you have to do at work/in school)	1	2	3	4	5	6	7
5. SLEEPING	1	2	3	4	5	6	7

*If you are not employed or self-employed, these should be tasks you have to do most days.

HOW MUCH **DISCOMFORT OR DISTRESS** HAVE YOU FELT **DURING THE LAST 2 WEEKS**?

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
6 How much discomfort or distress have you felt over the last 2 weeks as a result of CHEST TIGHTNESS?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID: _____

SELF-ADMINISTERED DATE: _____

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
7. Feel CONCERNED ABOUT HAVING ASTHMA?	1	2	3	4	5	6	7
8. Feel SHORT OF BREATH as a result of your asthma?	1	2	3	4	5	6	7
9. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO CIGARETTE SMOKE?	1	2	3	4	5	6	7
10. Experience a WHEEZE in your chest?	1	2	3	4	5	6	7
11. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF CIGARETTE SMOKE?	1	2	3	4	5	6	7

HOW MUCH **DISCOMFORT OR DISTRESS** HAVE YOU FELT **DURING THE LAST 2 WEEKS?**

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
12. How much discomfort or distress have you felt over the last 2 weeks as a result of COUGHING?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
13. Feel FRUSTRATED as a result of your asthma?	1	2	3	4	5	6	7
14. Experience a feeling of CHEST HEAVINESS?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID: _____

SELF-ADMINISTERED DATE: _____

IN GENERAL, **HOW MUCH** OF THE TIME **DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
15. Feel CONCERNED ABOUT THE NEED TO USE MEDICATION for your asthma?	1	2	3	4	5	6	7
16. Feel the need to CLEAR YOUR THROAT?	1	2	3	4	5	6	7
17. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO DUST?	1	2	3	4	5	6	7
18. Experience DIFFICULTY BREATHING OUT as a result of your asthma?	1	2	3	4	5	6	7
19. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF DUST?	1	2	3	4	5	6	7
20. WAKE UP IN THE MORNING WITH ASTHMA SYMPTOMS?	1	2	3	4	5	6	7
21. Feel AFRAID OF NOT HAVING YOUR ASTHMA MEDICATION AVAILABLE?	1	2	3	4	5	6	7
22. Feel bothered by HEAVY BREATHING?	1	2	3	4	5	6	7
23. Experience asthma symptoms as a RESULT OF THE WEATHER OR AIR POLLUTION OUTSIDE?	1	2	3	4	5	6	7
24. Were you WOKEN AT NIGHT by your asthma?	1	2	3	4	5	6	7
25. AVOID OR LIMIT GOING OUTSIDE BECAUSE OF THE WEATHER OR AIR POLLUTION?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
26. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7
27. Feel AFRAID OF GETTING OUT OF BREATH?	1	2	3	4	5	6	7
28. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7
29. Has your asthma INTERFERED WITH GETTING A GOOD NIGHT'S SLEEP?	1	2	3	4	5	6	7
30. Have a feeling of FIGHTING FOR AIR?	1	2	3	4	5	6	7

HOW **LIMITED** HAVE YOU BEEN **DURING THE LAST 2 WEEKS**?

	Severely Limited Most Not Done	Very Limited	Moderately Limited Several Not Done	Slightly Limited	Very Slightly Limited Very Few Not Done	Hardly Limited At All	Not Limited I Have Done All Activities
31. Think of the OVERALL RANGE OF ACTIVITIES that you would have liked to have done during the last 2 weeks. How much has your range of activities been limited by your asthma?	1	2	3	4	5	6	7

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID: _____

SELF-ADMINISTERED DATE: _____

HOW LIMITED HAVE YOU BEEN **DURING THE LAST 2 WEEKS?**

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
32. Overall, among ALL THE ACTIVITIES that you have done during the last 2 weeks, how limited have you been by your asthma?	1	2	3	4	5	6	7

DOMAIN CODE:

Symptoms: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 29, 30
Activity Limitation: 1, 2, 3, 4, 5, 11, 19, 25, 28, 31, 32
Emotional Function: 7, 13, 15, 21, 27
Environmental Stimuli: 9, 17, 23, 26

BMI KEY

Body Mass Index in kg/m^2.

Underweight = <18.5

Normal weight = 18.5-24.9

Overweight = 25- 29.9

Obesity= ≥30

APPENDIX 9: DETERMINANTS OF ASTHMA CONTROL AND HRQoL QUESTIONNAIRE

BIODATA

Patient's unique key……. Study number: P190/03/2018.

Patient's Initials..…….. Date of enrollment ……

KEY: (*ITALICS**) = Codes used on Epi Info Ms Excel Data sheet.

PATIENT FACTORS

1. What is your age *(AGE*)*?_____ (years)

2. Patient's age category *(AGECAT*)*:

(0) Adolescent 13-19 (1) Young adult 20-39 (2) Middle aged 40-64 (3) Elderly>65

3. Patient's gender *(GENDER*)*: (0) Female (1) Male

4. What is your marital status *(MARITAL*)*: (0) Minor (1) Single 2) Married

5. Level of education *(EDU*)*: 0) Low (None, primary, secondary) 1) High (Tertiary)

6. Where do you live *(RESIDENCE*)*? 0) Rural 1) Urban

7. What is your employment status *(EMPL*)*? 0) Non-formal 1) Formal

8. Patient/Parent's SES category based on employment status *(SES*):*

0) Low SES (1) High SES

9. When do you suffer from asthma symptoms most? 0) When at work/school (1) At home

10. What is your occupation?

Occupation		**Occupation**		**Occupation**	
0	Student	7	Nursing profession	14	Saw mill work
1	Farming	8	Cleaning	15	Food processing
2	Laboratory work	9	Spray painting	16	Hairdressing
3	Bakery	10	Wood work	17	House wife
4	Chemical processing	11	Electronic assembly	18	Other:
5	Rubber/Plastic work	12	Tobacco processing		
6	Printing	13	Metal treatment work		

11. Does the patient's occupation pose a risk to asthma development *(OCCUPRISK*)*? 0) NO 1) YES

12. What age were you when the asthma diagnosis was made?

0) < 12 year old 1) >12years old

13. Asthma onset category *(ASTHMAONST*)*: 0) Early onset 1) Late onset

14. Cigarette smoking status *(CIGARETTE*):*

0) Non-smoker 1) Current smoker 2) Former smoker

15. Do you develop asthma symptoms during exercise *(EXER*)*? 0) NO 1) YES

16. Females: Are your asthma symptoms worse just before and or during your menses *(MENSES*)*? 0) NO 1) YES

17. BMI measurements:

i) Weight (kg)…… ii) Height (cm)…… iii) Age (13-20yr)……..

(BMI*)……

18. BMI categories *(BMICAT*):*

0) Underweight 1) Normal weight 2) Overweight 3) Obese

COMMORBIDITIES/MEDICAL STATES

What other comorbidities/health conditions does the patient have?

19. Does the patient have GERD *(GERD*)?* 0) NO 1) YES

20. Does the patient have Allergy (Allergic rhinitis, atopy, eczema) *(ALLERGY*)?*

0) NO 1) YES

21. Does the patient have Obesity *(OBESE*)*? 0) NO 1) YES

22. Does the patient have Diabetes Mellitus *(DM*)?* 0) NO 1) YES

23. Does the patient have Retroviral disease *(RVD*)*? 0) NO 1) YES

24. Does the patient have Cardio-vascular disease *(CVS*)?* 0) NO 1) YES

25. Upper respiratory tract infection *(URTI*)* 0) NO 1) YES

26. Has the patient undergone any stressful event in their life over the last 4 weeks *(STRESS*)?*

0) NO 1) YES

27. Demonstration of inhaler technique *(CORRECTINHTECHN*):*

0) Incorrect 1) Correct

PATIENT COMPLIANCE/ADHERENCE

28. For how long have you been on asthma medication *(MEDyrs*)?*

0) <1 year 1) 1-5 years 2) 5-10 years 3) >10 years

29. How many days in the past 28 days have you missed to take your asthma medications *(DAYMISS*)*? ……

*Adherence computation: (number of days medication not missed /28)*100.*

30. Patient's adherence score *(ADH*):* 0) <75%- poor 1) ≥75%-good

Reasons for missing to take asthma medication(s):

31. Did not miss to take *(NOTMISS*)* 0) NO 1) YES

32. Cannot afford to buy *(UNAFFORD*)* 0) NO 1) YES

33. Prefers not to take *(PREFERNOT*)* 0) NO 1) YES

34. Drug product unavailable *(UNAVAIL*)* 0) NO 1) YES

35. Forgets to take *(FORGETS*)* 0) NO 1) YES

36. Side effects *(SE*)* 0) NO 1) YES

37. Are you taking other medications other than for asthma treatment? 0) NO 1) YES

38. Which other classes of medications other than for asthma are you taking?

Class of medicine		**Types**	***Class of Medicine***		**Types**	***Class of Medicine***		**Types**
0	None		8	Antibacterials				
1	Cardiovascular system		9	Antivirals				
2	Digestive system		10	Antifungals				
3	Liver		11	Joint/musculoskeletal				
4	CNS		12	Supplements				
5	Ocular (Eye)		13	Antineoplastics				
6	Endocrine		14	Renal				
7	Dermatology		15	Blood				

39. What is the total number of all the various types of the medications (asthma included) the patient is taking *(PILLBURDEN*)?* _____

HEALTH CARE PROVIDER FACTORS

40. Are you and your family satisfied with the asthma care services offered to you *(SATISF*)?* 0) NO 1) YES

41. How can you describe your working relationship with the health care providers who treat you *(RLSHIP*)?* 0) POOR 1) GOOD

42. Have you been given health education concerning your illness on what things to avoid, about asthma medications and their use and what to do when you get an attack *(INFO*)?* 0) NO 1) YES

43. How would you rate the services offered to you by your health care providers *(SERVRATE*)?*

0) POOR 1) FAIR 2) SATISFACTORY 3) EXCELLENT

ASTHMA TREATMENT FACTORS

What medications have been prescribed for the management of the patient's asthma?

44. Relievers *(RELIEVERS*):*

0) SABA name……..…….

1) Low dose ICS/formoterol name/dose ……..

45. Controllers *(CONTROLLERS*):*

0) Low dose ICS: name/dose.....Otheroptions……

1) Low dose ICS/LABA: name/dose...…….Other options …….

2) Medium dose ICS/LABA: name/dose ……Other options……..

3) Add-on therapy: name/dose…….....

KEY: INHALED CORTICOSTEROID DOSES (mcg) ……*(New GINA 2018 Report).*

DRUG	**Low dose**	**Medium dose**	**High dose**
Beclomethasone dipropionate *(CFC)	200-500	>600-1000	>1000
Beclomethasone dipropionate *(HFA)	100-200	>200-400	>400
Budesonide *DPI	200-400	>400-800	>800
Ciclesonide HFA	80-160	>160-320	>320
Fluticasone furoate DPI	100	n.a	200
Fluticasone propionate DPI	100-250	>250-500	>500
Fluticasone propionate HFA	100-250	>250-500	>500
Mometasone furoate	110-220	>220-440	>440
Triamcinolone acetonide	400-1000	>1000-2000	>2000

*CFC=chlorofluorocarbon propellant. *DPI= dry powder inhaler. *HFA= hydrofluroalkane propellant

46. Corticosteroid type *(ICStype*):* 0) Beclomethasone 1) Budesonide 2) Fluticasone

47. Long acting beta agonist type *(LABA*):* 0) Formoterol 1) Salmeterol 3) None

48. Uses Leukotriene receptor agonists *(LTRA*)?* 0) NO 1) YES Name _____

The patient is considered treated if he is on Controller medication and not treated if he is on Reliever medication only.

49. Is the patient treated *(TREATED*)?* 0) NO 1) YES

50. What treatment step/severity class is the patient's disease (refer to response to question 45 above) *(TRSTEP*)?*

0) Step 1/intermittent asthma 1) Step 2/mild persistent

2) Step 3/moderate persistent 3) Step 4/severe persistent 4) Step 5/severe persistent

51. Is the patient receiving appropriate treatment for their asthma severity *(APPTX*)?*

0) NO 1) YES

52. Level of patient's asthma treatment *(LEVELTx*):* 0) Optimal 1) Sub-optimal

53. Does the patient's pharmacotherapy comply with the recommended treatment guidelines *(GUIDELN*)?* 0) NO 1) YES

54. Asthma Control Test score (from ACT tool) *(ACT*):* _____

55. Patient's asthma control category based on ACT score *(ACTscore*):*

0) Uncontrolled (≤19) 1) Controlled (>19)

56. HRQoL SCORE: Overall Mean HRQoL score (from AQLQ(S) tool) *(HRQoL*):* _____

57. Patient's HRQoL category based on the HRQoL score *(HRQoLCAT*):*

0) Low (<6) 1) High (≥6)

HRQoL DOMAIN SCORES:

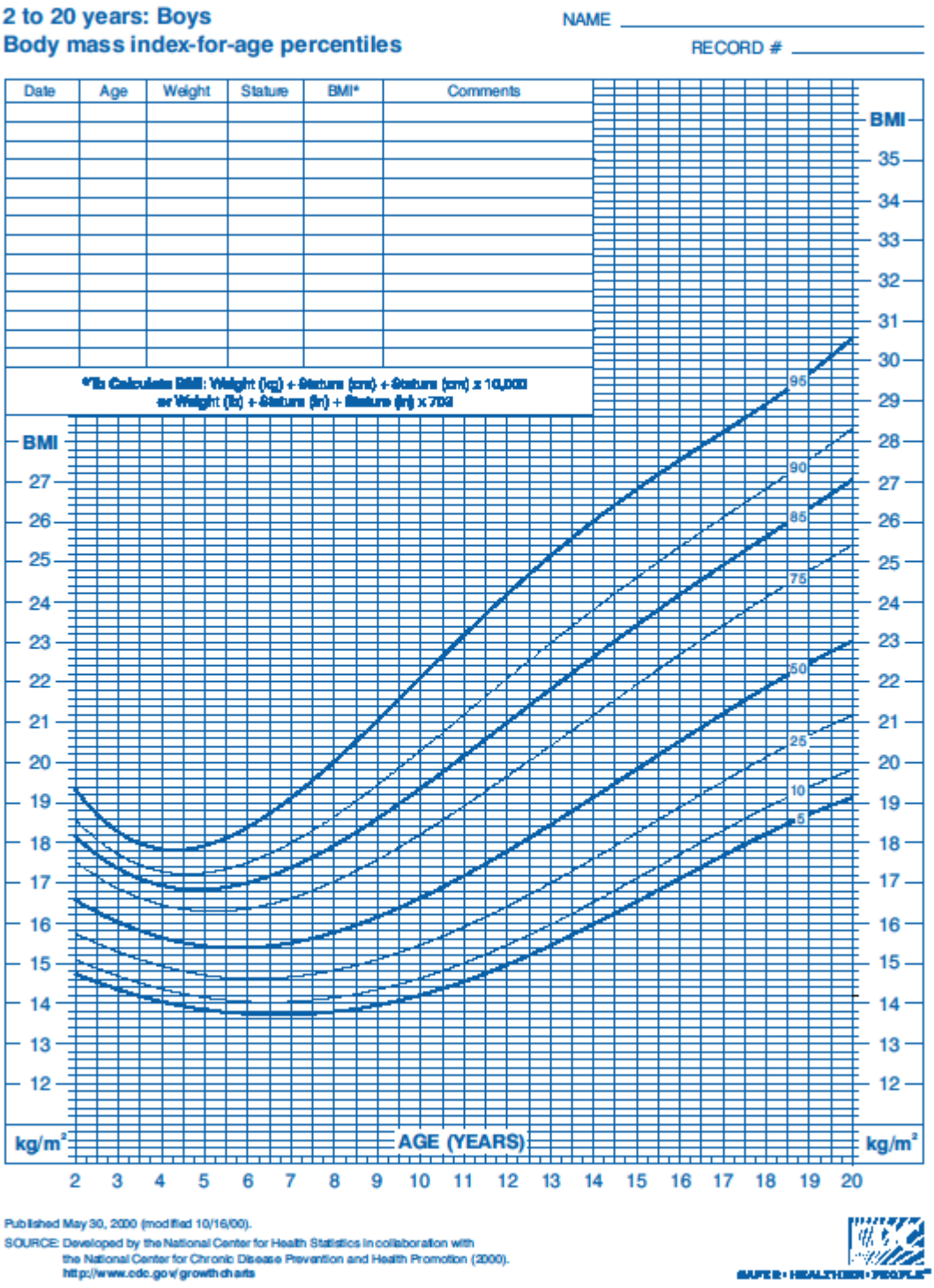
58. Symptoms mean score *(SYMPTOMS*)* ……

59. Activity limitation mean score *(ACTLMT*)* …….

60. Emotional function mean score *(EMFx*)*……..

61. Environmental stimuli mean score *(ENVstm*)*…….

APPENDIX 10A: BMI CHART FOR BOYS' AGE PERCENTILES.



APPENDIX 10B: BMI CHART FOR GIRLS' AGE PERCENTILES.