# A PSYCHOMETRIC ASSESSMENT OF THE IMPACT OF PHARMACEUTICAL CARE INTERVENTION ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ASTHMA

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# DECLARATION

I hereby declare that this submission is my own work and that to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University, except where due acknowledgement has been made in the text.

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# ABSTRACT

## Background

For chronic health conditions, the traditional measures of disease impact such as prevalence, mortality and hospitalization rates may be inadequate in understanding the extent of the impact of the disease on the individual. Measuring Health-related Quality of Life (HRQoL) has a role in describing health outcomes, guiding and assessing clinical management, predicting health outcomes, formulating clinical policy and allocating health resources. Pharmaceutical care delivery stands a good chance of positively impacting the HRQoL of patients' significantly. This must however be accompanied by appropriate prescribing and the care delivery must be oriented around the chronic model of care.

## Objectives

This study assessed the content and outcomes of counselling and education delivered by pharmaceutical service providers to patients, reviewed prescribing patterns of asthma medications and evaluated the impact of pharmaceutical care provision on HRQoL of patients with asthma.

## Methods

A 26-item interviewer-administered questionnaire was used to collect patient pharmacy-exit data on 388 prescription encounters. Patient data were separated into chronic and acute health conditions groups and the content and outcomes of their counseling and education at the pharmacy were assessed in phase I of this study.

In Phase II, 409 prescriptions were retrospectively reviewed against the recommendations of the national standard treatment guidelines from 4 health care facilities around the country. Prescriptions on previous visits were selected with a developed tool just before participants were seen by their physicians and reviewed for conformity with the recommendations of national treatment guidelines.

In phase III, a prospective pre/post- intervention study of a cohort of 77 adult out-patients visiting specialist asthma clinics were assessed for HRQoL and peak expiratory flow rates one month after a pharmaceutical care intervention. The Pharmaceutical care intervention included education on the health condition, pharmacotherapy and self-management including correction of inhaler-use technique, where necessary and self-referral.

**Results**

Participants with chronic health conditions were not provided with the same counseling and education as their counterparts with acute health conditions. Less than 20% of participants from the two disease condition groups received precautionary information. Close to 15% of the participants in the chronic health group were informed about what to do in case they felt bad or reacted to any of their medications as against 10% of participants in the acute health group. Prescribing patterns for asthma medications indicated widespread discrepancies. Many patients were on step III medications, an indication that most of the asthma patients had moderate persistent condition. About 46% of participants on inhaled Salmeterol/Fluticasone combination therapy were on dosage regimens not recommended in the standard treatment guidelines.

The Pharmaceutical care intervention led to a significant improvement in asthma specific quality of life and peak flow rates. The mean paired difference of the HRQoL for the patients with asthma post- pharmaceutical care intervention was $0.697 \pm 0.89$. A t-test analysis of the means at 95% CI, yielded a $t= 6.85$ ($p<0.05$). The mean paired difference for peak expiratory flow rate post intervention was $17.533 \pm 63.705$ and a $t=2.384$ ($p=0.02$ at 95% CI).

**Conclusion**

The contents and outcomes from patient education and counseling at the pharmacies did not reflect any discrimination between acute and chronic health conditions. Prescriptions for pharmacologic therapy of asthma contained widespread inconsistent patterns as compared to those in the standard treatment guidelines. At one month after pharmaceutical care intervention, patients with asthma showed significant improvements with regard to asthma-specific quality of life, peak flow and knowledge.

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## List of Abbreviations

| | |
|---|---|
| **AIDS** | Acquired Immuno-Deficiency Syndrome |
| **AIWA** | Australian Institute of Health and Welfare |
| **AME** | Adverse Medical Event |
| **AQLQ** | Asthma Quality of Life Questionnaire |
| **ASHP** | American Society of Health-system Pharmacists |
| **ASUI** | Asthma Symptom Utility Index |
| **BDP** | Beclomethasone Dipropionate |
| **BP** | Blood Pressure |
| **CDC** | Centres for Disease Control and Prevention |
| **COAD** | Chronic Obstructive Airways Disease |
| **COPD** | Chronic Obstructive Pulmonary Disease |
| **CORE** | Centre for Outcome Research and Education |
| **CV** | Construct Validity |
| **DPI** | Dry Powder Inhaler |
| **EBC** | Exhaled Breath Condensate |
| **ECHO** | Economic, Clinical an Humanistic Outcomes |
| **ECP** | Eosinophilic Cationic Protein |
| **ED** | Emergency Department |
| **EIB** | Exercise-induced Bronchospasm |
| **EPR** | Expert Panel Report |
| **EuroQol** | European Quality of Life |
| **$FEV_1$** | Forced Expiratory Volume in one second |
| **FIP** | International Pharmaceutical Federation |
| **FVC** | Forced Vital Capacity |
| **GINA** | Global Initiative for Asthma |
| **HALex** | Health and Activities Limitations Index |
| **HIV** | Human Immuno-deficiency Virus |
| **HRQoL** | Health Related Quality of Life |
| **HUI** | Health Utility Index |
| **PEFR** | Peak Expiratory Flow Rate |
| **IC** | Internal Constitency |

| | |
|---|---|
| **ICS** | Inhaled Corticosteroids |
| **ICU** | Intensive Care Unit |
| **IFN-γ** | Interferon-gamma |
| **Ig E** | Immunoglobulin E |
| **IL** | Inter-leukine |
| **LABA** | Long-acting Beta-agonist |
| **L/T ratio** | Lung/Total Systemic availability |
| **LTRA** | Leuktotriene Receptor Antagonist |
| **LWAQ** | Living With Asthma Questionnaire |
| **MDI** | Metered Dose Inhaler |
| **MEMS** | Medication Event Monitoring System |
| **MLHFQ** | Minnesota Living with Heart Failure |
| **MMAS** | Morisky Medication Adherence Scale |
| **MMD** | Mean Median Diameter |
| **NAEP-EPP** | National |
| **NCD** | Non-communicable Disease |
| **NEI** | National Eye Institute |
| **PEF** | Peak Expiratory Flow |
| **QWBS** | Quality of Well Being Scale |
| **RB** | Respondent Burden |
| **SABA** | Short-acting Beta-agonist |
| **SF** | Short Form |
| **SGRQ** | St. George's Respiratory Questionnaire |
| **Th** | T helper |
| **T-R** | Test-retest Repeatability |
| **VFQ** | Visual Function Questionnaire |
| **WHO** | World Health Organization |
| **WHO-ICCC** | World Health Organization-Innovative Care for Chronic Conditions |
| **WHOQOL** | World Health Organization Quality of Life |

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# CHAPTER 1 INTRODUCTION

## 1. General Introduction

One of the greatest challenges health care professionals, organizations and systems will be confronted with in the twenty-first century is the dramatic increase in the number of patients suffering from one or more chronic diseases (Yach, 2002; Nolte & McKee, 2008). In relation to the aging rate of the population and the growing longivity of people with many chronic health conditions, the number of persons with chronic conditions is growing at an astonishing rate. (Wagner *et al,* 2001). This challenge will require that healthcare professionals and systems make the necessary adjustments to adequately cope with this situation effectively and efficiently. This will further require that patients with chronic diseases get the needed support to play active roles in the management of their chronic conditions. This notwithstanding, the current health care system is still largely organized around an acute, episodic model of care, which does not meet the needs of chronically ill patients.

Chronic health problems are enduring, necessitating a care strategy that reflects a protracted time frame and clarifies for patients their roles and responsibilities in managing their health problems. The World Health Organisation has noted that even though appropriate clinical care is necessary; it is not sufficient to achieve optimal health outcomes. To successfully manage their conditions, patients with chronic diseases will have to make changes in their lifestyles, must develop new skills, and must learn to interact with health care organizations (WHO-ICCC, 2002). According to Bodenheimer and colleagues patients with chronic health conditions will need a model of care that will attention to issues of self-management, prevention and continuity of care, which has not received attention in the acute care models (Bodenheimer *et al,* 2002).

The acute care models were not designed to handle chronic conditions. The current care systems, according to Wagner and colleagues (2001) have been designed to quickly manage efficiently acute illnesses and injuries that presented at the health facility. The focus here was the definition of the condition, elimination other serious diagnoses, and the quick provision of professional management of the acute condition. The patient played a passive role because the condition lasted for only a few days or weeks and the need for the development of self-management roles with the patient was not necessary (Wagner *et al*, 2001).

Wagner and colleagues (2001) have argued about the challenges and difficulties that many chronically ill persons go through with demands of their illness. They claim there is often no help for the chronically ill persons to manage the psychological, physical and social demands of their condition, and many a time the help they received did not match demands needed to make the patient an effective self-managers of their health condition (Wagner *et al*, 2001).

In recognition of these challenges, the WHO in its first key component of a three-pronged strategy to improve the prevention and management of chronic conditions in the healthcare systems developed the document, "Innovative Care for Chronic Conditions: Building Blocks for Action", to alert decision-makers throughout the world about the important changes in global health, and to present health care solutions for managing this rising burden.

The WHO-ICCC document (2002) took note of the growing evidence from around the world that suggested that when patients receive effective treatments, self-management support, and regular follow-up, they do better. Further evidence also suggested that organized systems of care, not just individual health care workers, were essential in producing positive outcomes (WHO-ICCC, 2002).

Wagner and colleagues (2001) also believe that multi-tasking and the delegation of care by the physician to other health professionals in an environment that enables adequate and

productive interactions will be an effective healthcare delivery system for the management of chronic conditions.

It is against this background that this project sought to generally review the type of care approach used to deliver pharmaceutical services in healthcare facilities and also to explore what contributions pharmaceutical service could provide towards effective and efficient management of patients with asthma, where the ultimate goal of treatment from various policy guidelines (GINA, 2006; EPR-3, 2007) is to minimize symptoms regardless of severity, continuously monitor the level of control and make the necessary adjustments to therapy. Ultimately for any substantial positive outcomes, the components of management of asthma under the chronic care model will include self-management by patients (EPR-3, 2007), making the issues of patient-education and adherence eminent.

Over the years various attempts have been made to develop ways of ensuring that patients with chronic illness continue to their therapies for a long period of time. These initiatives considered the patient as the probable cause of non-compliance but later, the role of the care provider had to be addressed as well. The current thinking in this endeavour now points to a systems approach (WHO, 2003). Irrespective of the blame games associated with compliance, the main concept of adherence comes in its wake the need relevant changes in the roles various over time to ensure optimal health in patients with chronic conditions (WHO, 2003).

From the foregone discuss, it therefore important that any strategic choice of a measure for the approximation of adherence behaviour should consider all the issues above. Most importantly, the strategies employed must meet basic psychometric standards of acceptable reliability and validity (Numally & Berstein, 1994).

Bateman and colleagues (2004) have noted in most asthma cases, clinical control can be achieved and maintained (Bateman *et al*, 2004). Vollmer and colleagues (1999) have also noted that, since 'control' is intended as a predictor of asthma outcomes, it would be expected that during periods of poor asthma control, health related quality of life (HRQoL) would be poorer (Vollmer *et al*. 1999). However, according to Juniper *et al* (2004), HRQoL is not the same as asthma severity or asthma control (Juniper *et al*, 2004). HRQoL can be regarded as a broad-ranging, but not all encompassing, outcome of asthma. However, recent studies have also shown that the HRQoL of patients with asthma is closely correlated with the level of their asthma control and this remains a very distinct component of the overall asthma status (Juniper *et al*, 2004).

Controlled trials of asthma education delivered by pharmacists have shown mixed results (Bynum *et al*, 2001; Cordina *et al*, 2001; Stergachis *et al*, 2002; Barbanel *et al*, 2003; McLean *et al*, 2003; Saini *et al*, 2004; Basheti*et al*, 2005; ). This project therefore used internally controlled cohort rather than case-controlled methodology to evaluate the contributions made by pharmacist to improve asthma care.

To explore the above issues further, this project reviewed relevant information in the literature, guided by the keywords: Adherence; Asthma control; Self-management education; Pharmaceutical care; Health-related quality of life. The project considered various systematic reviews, randomised control studies, clinical case-studies and cohort studies from the Cochrane library, Pubmed in Medline and various other sources to identify works done, existing knowledge and gaps in this area.

### 1.1. Patient Adherence in Chronic Conditions

The WHO (2003) has noted that often the effectiveness of treatment is severely compromised due to poor adherence to long-term therapies and therefore adherence is an important issue from various perspectives (health economics and health-related quality of life) in population. Therefore interventions that are aimed at improving patient adherence would obviously generate a significant positive impact on health investments by the possible prevention of risk factors associated with chronic conditions and subsequent prevention of any adverse health outcomes (WHO, 2003).

In developed countries, adherence among patients suffering chronic diseases averages only 50% (Haynes, 2001). It is however believed that the situation adherence may be worse in developing countries because of weaknesses in the healthcare structures and challenges of access healthcare services (Sabate, 2003). The issues of patient adherence are also of importance especially in the management of chronic diseases to ascertain therapeutic efficacies of various medicines as demonstrated in clinical trials.

Currently, strong evidence shows a relationship between the challenges with recommended regimens and sub-optimal clinical benefits, implicating adherence in illness control (Dunbar-Jacob *et al*, 2000; Rybacki, 2002*)*.

The World Health Organisation reported that (WHO) reported that non-communicable diseases (NCDs), mental health disorders (NCD), HIV/AIDS and tuberculosis in combination accounted for more than a half of all diseases worldwide in year 2001 (WHO, 2002), and this according to Murray and Lopez may exceed 65% of the global disease burden by 2020 (Murray & Lopez, 1996). In developing countries, non-communicable diseases and mental health problems are also prevalent and, represented almost one half the total number of

disease for the year 2001 (WHO, 2002). This situation has also been predicted to rise to 56% by the year 2020 (Murray & Lopez, 1996). Patient adherence in long-term chronic disease management therefore represents a major global challenge that should adequately engage the attention of the healthcare system.

The Ghana health report (MoH, 2011), admits that NCD did not receive much attention at the regional and district level even though some important activities have been carried out at central level, including development of the national policy for prevention and control of NCD. The report further acknowledges that the prevalence of NCDs is alarming and that the lack of focus on NCDs reflects a continuous bias towards communicable over non communicable disease by both political and professional actors in the health sector (MoH, 2011).

### 1.1.1. Definition of Patient Adherence

Adherence has been defined differently and with various words that implies how the issues are being considered. While some believe that it is an issue of poor patient attitude, others also perceive it as instructions that patients must follow at all cost. Whichever way the term "adherence" is perceived defines the approach to developing interventions that seeks to improve the situation.

In one definition, adherence is defined as:

*"The extent to which a patient's behaviour (in terms of taking medication, following a diet, modifying habits, or attending clinics) coincides with medical or health advice"* (Haynes, 2002).

However, the use of the term *"medical"* in the above definition is deemed insufficient in describing the range of interventions that are used to treat chronic diseases, whereas the term

*"instructions",* that has been used in some other definitions of adherence may also imply a very passive patient who is not actively involved in the treatment processes but only receives advice from the professional expert.

Adherence has therefore been defined as:

*"The extent to which patient behaviour corresponds with recommendations from a health care provider"* (Vitolins *et al*, 2000).

In these simple broad definitions of adherence lie the numerous difficulties that many medical regimens present for the patient. A WHO adherence meeting participants, in 2001, recognized that adherence is a behavioural issue with various components.

The components of these behaviours ranges from the way patients seek medical attention for their conditions, the way they fill their prescriptions, the way they take their medications, the way they obtain immunizations and attend follow-up appointments, and how they execute modifications that seeks to address personal hygiene, self-management of chronic conditions among others. (Sabate, 2001). The regimen usually described for type 2 diabetes mellitus include a special diet, increased exercise, smoking cessation, oral hypoglycaemic drugs, and risk factor management, that may also involve addition of more drugs. Such regimens, according to McDonald *et al* (2002), may only fulfil theoretical, physiological, and empirical considerations about optimal care, but technically ignores practical patient-centred concerns, such as the nature, nurture, culture, and stereotyping of the patient, and the inconvenience, cost, and adverse effects of the treatment on the patient (McDonald *et al*, 2002).

Obviously, the patient would need support to adjust to new behaviours and be made capable of adhering to the various requirements at one level or the other. Many a time, patients are pushed into behavioural adjustments without sufficient support to make them capable of doing so. A clear reflection of these is the way adherence is sometime perceived and also assessed.

### 1.1.2. Relevance of Patient Adherence to Treatment

Adherence, in a WHO report, is further referred to as the main determinant that ascribes the effectiveness of any treatment (WHO Report, 2002) because poor patient adherence tends to attenuate the optimum clinical benefit (Dunbar-Jacob *et al*, 2000). According to Haynes, (2001) evidence is emerging that suggests that because of the alarmingly low patient adherence rates, paying attention to interventions effectively directed towards patient adherence may yield better impact on the health of the population than any improvement in specific medical treatments (Haynes, 2001). It is of note that relapses related to poor patient adherence to prescribed medication can be more severe than those that occur while the patient is adherent to recommended regimens. It can therefore be suggested that when persistently a patient remains non-adherent, the overall course of the illness may become worse and eventually reduce the response to treatment (Weiden, 2002).

Suffering from a chronic disease condition also implies that patients may have to adopt new health behaviours or adapt their existing health behaviours and may need also to engage in a number of activities to promote physical and psychosocial well-being; interact with health care professionals; adhere to treatment regimens; monitor their health status and make associated care decisions; and manage the impact of their chronic health condition on physical, psychological and social functioning (Nolte & McKee, 2008). This type of self-management by the patient involves the various actions they have to perform for themselves in daily life to manage their illness and the treatment thereof, while avoiding functional and health deterioration (Bodenheimer *et al*, 2002; Yach, 2002; Pruitt & Epping-Jordan, 2005).

Non-adherence to medication treatment can have serious consequences in chronically ill patient populations. These consequences may include increased cost of care, higher re-

admission rates to hospital and inadequate expected clinical outcomes (Haynes *et al*, 2008; Burman *et al*, 2008; Pinsky, 2009). A meta-analysis of patient adherence studies indicated that patients who were adherent were 26% more likely to have a good clinical outcome compared to patients who did not adhere to their overall treatment regimens (not only medication adherence) (DiMatteo *et al*, 2002). The economic implication of non-adherence is enormous and has been reported to cost the US health care system an estimated $100 billion annually in direct costs, whereas indirect costs exceed $1.5 billion in lost patient earnings and $50 billion in lost productivity (Peterson *et al*, 2003).

Considering the consequences and the implications of patient medication adherence, it stands to reason not to overlook such an issue and more so, when evidence abounds that with the right interventions it is possible to maximise the levels of adherence, thereby improving health outcomes whilst reducing cost.

### 1.1.3. Assessment of Patient Medication Adherence

Patient medication adherence is referred to the aspect of the various health management behaviours that relates directly to medication usage. Patient medication adherence has been expressed in various ways: as the extent to which a recommended regimen is followed and expressed as a ratio, making adherence a categorically good or bad phenomena, or as a score that reflects multiple behaviours. However, the WHO (2003) report noted that, the type of treatments that patients with chronic conditions are usually required to follow for self-management tend to vary according to the demands imposed on them by these treatment regimens and these may be relatively simple or very complex in nature (WHO, 2003).

Usually, the levels of medication adherence for individual patients are reported as an expression of the percentage between the doses of the medication actually administered to the

patient and the doses prescribed over a specified period. Others have however, refined medication adherence by including data on dose-taking (administering the recommended number of pills each day) and the regimens of doses (administering the dose within a recommended period of time) (Osterberg & Blaschke, 2005).

Wetzels and colleagues (2004) reviewed 30 studies on patient compliance. The various studies used varied methods to quantify patient compliance. In 20 of these studies, medication-administering compliance and/or correct dosing were employed. The average value for medication-taking compliance for regimens administered once a day was 94.0 +/- 4.4% and 88.2 +/- 6.5% for those administered twice a day. The average estimated value for correct dosing was 85.0 +/- 8.7% for a once a day regimen and 75.3 +/- 6.5% for twice a day regimen. Only five (5) studies provided the proportions of the patients with medication-administering compliance or correct dosing</= 80% and these ranged between 9 and 37% (Wetzels *et al*, 2004).

In studies, where monitoring of patients for compliance went beyond 6 months, there were clear demonstrations of decreasing compliance. Inconsistent reports were reported for studies that looked at the association between patient blood pressure control and patient compliance. In this review Wetzels *et al* (2004), concluded that, poor patient compliance may be responsible the inadequate blood pressure control reported, even though no empirical evidence exist to support this relationship (Wetzels *et al*, 2004). It is therefore obvious that patient non-adherence alone can only take part of the blame that may come with the attainment of inadequate health outcomes. The healthcare provider's adherence to relevant protocols and guidelines as well as the quality, currency and reliability of the various guidelines and protocols may also need some consideration in determining the levels of adherence.

There seem however to be no consensual standard for what constitutes adequate adherence. Some trials consider adherence rates of greater than 80% to be acceptable, whereas others consider rates of greater than 95% (Chesney, 2003) to be mandatory for adequate adherence. What therefore constitutes patient adherence may vary from one management or treatment to the other. It may therefore be necessary to identify the critical extent and the relevance of patient adherence to various management issues and therapies. The over-arching concept of patient pill-counts or extent of therapies administered may not be suitable for all conditions. Whereas the administration of some oral therapies may not necessarily meet the criteria for adequate adherence because of timing of administration, poor inhalation technique may also not meet the adherence criteria for inhalers.

Various methodologies have been used by researchers to measure adherence. These include the Medication Event Monitoring System (MEMS), patient self-report, patient pill-counts, pharmacy databases or refill rates, and blood level assessments. The MEMS uses a microprocessor technology that has been embedded in the cap of a container to record time and date the container with medication was opened (Aslani & Krass, 2009). Using the MEMS can generate incorrect results from patients who may remove more than the single recommended dose or may not remove a dose at all when they opened the bottle. (Aslani & Krass, 2009; Carter *et al*, 2010). Using a different device for each medication makes the use of the MEMS a very expensive means of monitoring adherence in clinical care.
(Morisky *et al*, 2008; Aslani & Krass, 2009; Carter *et al*, 2010).

On the contrary, the use of prescription filling history from pharmacy databases can be used to check the patient prescription filling activities. However, prescription filling may not

necessarily imply usage by the patient. Further to this the patient may fill the prescription at different pharmacies thereby making data capturing a difficult one and incomplete.

Biochemical measurement is another method for assessing patient adherence behaviours. Here, the presence of a non-toxic biological marker can be investigated in the blood or urine of a patient who has recently administered a dose of a medication containing the marker. The drawback for this assessment approach may be the influences of the individual patient pharmacokinetic systems on the medication and the marker.

Patient self-report may probably be the easiest way to determine their adherence, but there are some obvious problems with this approach as well. Patients in an attempt to impress their care-providers, tend to report medication-administration than it is in reality.

Further to this, many a time, patient self-reported questionnaires are not open-ended and to allow for further information from the patient. The Morisky's Medication Adherence Scale (MMAS) in Table 1.1 was designed to differentiate between adherence levels of patients on anti-hypertensive regimens. The MMAS consists of questions that address various reasons for non-adherence. These questions have been phrased in a way to avoid the bias of patients giving positive answers to please their providers and each of these questions measure a specific medication-taking behaviour and not patient adherence or compliance behaviour.

**Table 1.1:** Morisky Medication Adherence Scale *(Morisky et al, 2008)*

| | |
|---|---|
| 1 | Do you sometimes forget to take your high-BP pills? |
| 2 | Over the past 2 weeks, were there any days that you did not take your high-BP medication? |
| 3 | Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it? |
| 4 | When you travel or leave home do you sometimes forget to bring your medication? |
| 5 | Did you take your high-BP medication yesterday? |
| 6 | When you feel your BP is under control, do you sometimes stop taking your medication? |
| 7 | Taking medication every day is a real inconvenience for some people. Do you ever feel haled about sticking to your BP treatment plan? |
| 8 | How often do you have difficulty remembering to take your BP medication? |

A baseline interview was conducted in about 1,300 hypertensive patients in the Morisky *et al* (2008), study to assess demographic characteristics, medical history, health behaviours, appointment-keeping, and medication adherence. The blood pressure (BP) of these participants was subsequently measured at the various health facilities over the next 6 months. A systolic BP $\geq$140 and diastolic BP $\geq$ 90 denoted uncontrolled hypertension. The correlation between high scores on the adherence scale and low BP mean values was reported as statistically significant. The variables that associated well with medication adherence were patient satisfaction, patient knowledge, patient coping skills, patient stress level, and complexity of medication regimen (Morisky *et al*, 2008). MMAS correlated with pharmacy fill rates. The MMAS had 93% sensitivity (identifying non-adherent patients), but only 53% specificity (identifying adherent patients). The MMAS has drawbacks in identifying adherent patients whose BP remain uncontrolled (Morisky *et al*, 2008).

### 1.1.4. Global Perspective on Adherence

The global status report on non-communicable diseases (NCDs) indicates that NCDs kill more people annually than all other causes combined (WHO- GSR-NCDs, 2010). It noted that on the contrary to popular opinion 80% of NCD deaths occur in the low and middle-income countries and that much of the human and social impact caused annually by NCD-related deaths could be averted through well-understood, cost-effective and feasible interventions (WHO- GSR-NCDs, 2010).

Haynes and colleagues (2008) reported that patients who are prescribed self-administered medications usually take less than half the prescribed doses (Haynes *et al*, 2008).

Sub-optimal adherence to inhaled medicines for COPD and asthmatic conditions are reported by Mika colleagues (2013), to be associated with poor symptom control and reductions in health-related quality of life, in addition to a higher healthcare utilization and cost (Mika *et al*, 2013).

Spector *et al* (1986), in a study of 19 adult patients with asthma, monitored adherence to their MDI medications using an electronic medication monitor. They followed the patients for 12 weeks to examine the anti-inflammatory drug usage. The patients also in addition to the monitoring maintained asthma diaries as part of the studies. The results of the study indicated patient adherence rate range of 4.3% to 95%. Patients over-reported in diaries more than 50% their appropriate use of medications.

Similarly, Mawhinney *et al* (1993) followed adult asthmatic patients over a 3–4 week period. They observed an average adherence rate of 37% of the days to the medications prescribed and under-use on more than 38% of the days monitored (Mawhinney *et al*, 1993).

Yeung *et al* (1994), in another study used an electronic monitor to follow the use of inhaled corticosteroid over a period of 2–3 weeks. Their findings indicated higher adherence when patients were aware they were being monitored as compared when they were unaware of any monitoring (Yeung *et al*, 1994).

In another study, Celano and colleagues (1998) observed in African American children low MDI adherence rates (44%) to anti-inflammatory medications. Adherence estimates were derived by weighing MDI canisters and then calculating the ratio of the number puffs used over the review period to the number of puffs on the recommended regimen. In all, 12% of all the children had MDI adherence rates exceeding 75% (Celano *et al*, 1998).

In the United Kingdom, Coutts *et al* (1992) observed underuse of inhaled Corticosteroids on 55% of study days in children aged 9-16 years who were electronically monitored in addition to their asthma diaries for 2 to 6 months (Coutts *et al*, 1992).

In a randomized, double-blind clinical trial, Jonasson *et al* (1999) using a breath-driven inhaler studied adherence in 163 children who have been diagnosed with mild asthma.

Though they encountered a high MDI adherence rate of 77%, the asthma diaries indicated a mean adherence rate of 93%. (Jonasson *et al*, 1999).

Williams *et al* (2004), in the United States, used medical records and pahramcy claims to estimated adherence rates in 405 adults. The study reported adherence rates of approximately 50 % and significantly negative correlationships between adherence to ICS and emergency department visits, number of fills of oral corticosteroids and the total days' supply of oral corticosteroid (Williams *et al*, 2004).

Their results indicate the impact of poor adherence on asthma-related outcomes.

In a systematic review of empirical studies in adults published between 1999 and 2009 conducted in France by Charles and colleagues (2011), to investigate the associations between perceptions of asthma and treatment beliefs and also adherence to inhaled corticosteroids. They noted that better adherence rates were associated with perception of the chronicity of asthma and its consequences on daily life, as well as the concept that it is necessary to continue treatment in the absence of symptoms. On the contrary, poor adherence rates were associated with the fear of side effects and the belief that treatment is ineffective in controlling symptoms (Charles *et al*, 2011).

In Brazil Lasmar *et al* (2009) in a cohort concurrent study, followed 122 asthmatic patients, aged 3-12 years for 12 months. The study objective was to assess the association between patient adherence rates to Beclomethasone dipropionate (BDP) and the degree of asthma control. Patient adherence rates were verified by pharmacy records and clinical control of asthma was assessed through a scoring system four domain variables (nocturnal and morning symptoms, limitation of physical activities and exacerbations). Patients were grouped those considered as controlled (score $\leq$ 2), and uncontrolled (score $\geq$ 3). Patients were considered as controlled when spirometry results indicated a forced expiratory volume in 1 second ($FEV_1$) was $\geq$ 80% of the predicted value, and uncontrolled when their $FEV_1$ < 80%.

In this study, Lasmar *et al* (2009) noted that fewer than half (40.3%) of the 122 patients maintained asthma control. The median patient adherence rate of groups 1 and 2 were reported as 85.5% and 33.8%, ($P < 0.001$) in the 4th month, 90.0% and 48.0% ($P < 0.001$) in the 8th month and 84.4% and 47.0% in the 12th month ($P < 0.001$), respectively (Lasmar *et al*, 2009). In conclusion, the study suggested that optimal asthma control entailed patient adherence rate higher than 80% (Lasmar *et al*, 2009).

In another study, Roy *et al* (2011) using a standardize checklist for user inhaler-use technique and the Medication Adherence Report Scale (MARS) for adherence reviewed adherence for 270 adults with asthma. Participants were using either metered-dose inhaler (MDI) or dry powder inhaler (DPI).

There were no differences found in user inhaler-use technique scores between the groups (p=0.46) (Roy *et al*, 2011).

Even though some of the authors of these studies are of the opinion that the levels of non-adherence in many of these patients may be an indication misunderstandings or concerns related to the side-effects of the medications, the WHO report on adherence is of the opinion that high levels of patient adherence to treatment and physician adherence to best-practice protocols are important co-determinants of treatment outcome (Sabate, 2003).

It is important at this point to consider what influences patient adherence or otherwise from the literature.

#### 1.1.4.1. Predictors of Adherence

According to WHO (2003) review, a considerable amount of empirical, descriptive, research had identified correlates and predictors of adherence and non-adherence that include aspects of the complexity and duration of treatment, characteristics of the illness, iatrogenic effects of treatment, costs of treatment, and characteristics of health service provision, interaction between practitioner and patient, and socio-demographic variables (WHO, 2003). However a lot of these variables according Sabaté (2003) are not dynamic issues and somehow static, and may not be easily amenable to intervention (Sabaté, 2003). There are several other relatively important variables (behaviours of health care providers, health-system factors and attributes of patients) in existence that are mostly behavioural in nature and are also dynamic, and therefore more amenable to intervention (Sabaté, 2003).

The review further noted that, health-care providers in practice provide limited information to chronic patients in their bid to motivate them and to improve their behavioural skills to improve their health. But the care providers themselves lack skills in motivational enhancement, and lack knowledge and also experience frustration in teaching patients behavioural skills (WHO, 2003).

In relation to the health-system, the WHO has suggested that it is rather the functioning of the health-system that influences patients' behaviour by: regulating patient contact times with providers; by determining reimbursements and/or fee structures that do not provide financial coverage for patient counselling and education; by determining continuity of care that dissociates patients from their regular care-providers; by directing information sharing that limits clinics and pharmacies to share information regarding patients' behaviour towards prescription refills; and also by determining the level of communication with patients (WHO, 2003).

To reach successful behavioural change, it is important that the patient is motivated; Alemi *et al* (2000) emphasizes the importance of the system (an individual's environment) in promoting the change. The process of accounting for the influence of various people, circumstances and historical choices on the behaviour that is to be modified is called system thinking or ecological thinking (Alemi *et al*, 2003; Alemi *et al*, 2011). This concept of ecology originates from public health and psychology (Glanz *et al*, 2002). The WHO-ICCC (2002) identifies 3 levels (micro-, meso- and macro-) within the ecological frame as factors contributing to patient behaviour:

*Micro-level factors* encompass factors related to the interpersonal or face-to-face relationships with health care professionals, as well as social support (Yach, 2002). Examples are the quality of communication between the health care professionals and patients and the degree of trust the patient has in the health care professional.

*Meso-level factors* refer to the practice patterns or the characteristics of the health care organization where the patient is being treated (Yach, 2002). Examples of a health care organization characteristic or a practice pattern is the time available for consultation or the interventions implemented in daily clinical practice to enhance patients' medication adherence.

*Macro-level factors* include the characteristics of the health care system in which a patient lives (Yach, 2002). This level includes local, state, and national laws and policies related to health (e.g., insurance coverage and regulations on reimbursement for medication).

For the patient, the WHO review noted that illness-relevant cognitions, perceptions of disease factors, and beliefs about treatment have stronger relationships to adherence. It noted that, in particular, factors such as perceived susceptibility to illness, perceived severity of illness, self-efficacy and perceived control over health behaviours appear to correlate and that, for adherence to occur, the symptoms must be sufficiently severe to arouse the need for adherence, and be perceived as being resolvable and acute, and that the remedial action must effect a rapid and noticeable reduction in symptoms (WHO, 2003).

The review also considered providers and noted that since they have a significant role in adherence, designing interventions to influence their behaviour seems a reasonable strategy. However, few investigations on this subject have been reported in the literature. Training providers in patient-centred methods of care may be effective, but the strongest effects of such training appear to be on patient satisfaction with treatment. Some recent studies have

suggested that adherence interventions based on behavioural principles can be successfully implemented by social workers and nurses (Rock & Cooper, 2000; De los Rios & Sanchez-Sosa, 2002). Studies of physicians trained to use goal-setting, feedback and on-going education also revealed better patient outcomes, though such studies have seldom measured adherence as an outcome.

Many other studies have been done to determine whether pharmacist interventions can lead to improved adherence and treatment outcomes. In a large meta-analysis conducted to determine medication adherence (along with several other outcomes), pharmacist interventions were found to improve medication adherence (P = 0.001) (Chisholm-Burns, 2010).

A systematic review of 15 studies of hypertensive patients was conducted to determine adherence and BP control as a result of pharmacist interventions (Molgado *et al*, 2011). The interventions were medication management (regimen simplification, resolving adverse drug reactions, and monitoring or adjusting drug therapy); patient education (on hypertension and lifestyle modification or BP self-monitoring); BP self-monitoring and documentation, including education, encouragement, and validation; medication reminders (adherence aids or telephone- or computer-based appointment reminders); improved administration system (MEMS or blister packs); increased follow-up appointments or contacts; HCP (e.g., physician or nurse practitioner) educational interventions; and visits with a clinical pharmacist. Significant improvements in clinical outcomes (systolic, diastolic, or controlled BP) occurred in 88% of studies; however, only 44% had significant increases in adherence. The difference in improved adherence and improved clinical outcomes was proposed to be due to medication adjustments made by pharmacists; if a regimen was improved, BP could be improved without a change in adherence (Molgado et al, 2011). This project reviewed pharmaceutical care impact on the health outcomes of patients with asthma.

## 1.2. Asthma

### 1.2.1. Global Burden of Asthma

Asthma prevalence rates continue to rise significantly in Africa, Central and South America, Asia and the Pacific Basin. The GINA Asthma Burden report indicated that in South and Central America more than 40 million cases are reported, with prevalence rates of 13%, 11.9%, 11.4% and 8.2% in Peru, Costa Rica, Brazil and Ecuador respectively. Some 50 million cases of asthma are believed to prevail in Africa, with South Africa alone having a prevalence rate of about 8.1% (GINA-Asthma Burden Report, 2003).

Findings of the ISAAC report (2007) indicated that international difference in asthma symptom prevalence have generally reduced, particularly in the 13-14 year age group and with decreases in prevalence in Western Europe. The results however indicated increases in prevalence in regions where prevalence was previously low, such as in Africa and parts of Asia. (Pearce *et al*, 2007).

The prevalence rates in the United Kingdom and the Republic of Ireland averages 16.1% of the total population, making the region have one of the highest prevalence rates of asthma in the world. There are about 20,000 first or new cases of asthma present each week to general practitioners in the region and over 75,000 emergency hospital admissions due to asthma each year, a quarter of which are in children below 4 years of age (GINA-Asthma Burden Report, 2003).

According to Simpson and Sheikh (2009), who reviewed the asthma prevalence rates in England, the number of adults with lifetime asthma diagnosis continues to rise, while the incidence rate of asthma is declining in all groups of asthma patients especially in pre-school children (Simpson & Sheikh, 2009). The GINA report (2003) indicated that over 1,500

people die from asthma each year within the region probably due to suboptimal routine care, delay in obtaining help during the final attack, and poor adherence to medication.(GINA-Asthma Burden Report, 2003).

The mean prevalence of clinical asthma in the Scandinavian and Baltic states are about 4.9% of the total population. Asthma mortality rates are reported to have declined markedly over the last 10 years in Scandinavian countries, a trend which has been attributed to improvements in asthma management, including the increased use of inhaled corticosteroid therapy. These countries have amongst the lowest case fatality rates worldwide and indicate the potential that exists to reduce asthma mortality in other countries (GINA, 2003).

Carlsen and colleagues (2006) reported an increasing prevalence of asthma in Oslo in comparison with previous studies. Their findings were consistent with findings to similar surveys carried in other parts of Norway. The findings indicated a lifetime prevalence of asthma of 20.2%; a current asthma prevalence of about 11%; a doctor diagnosis of 16% and wheeze ever in 30% of children in a 10 year follow up of a birth cohort study (Carlsen *et al*, 2006).

A Swedish study also found increased prevalence of physician diagnosed asthma and an unchanged prevalence of most respiratory symptoms over an 11 year period that concluded that social awareness and changes in physician diagnostic practices may be the possible causes of increasing asthma reporting (Ekerljung *et al*, 2011).

In the republics of Eastern Europe, the prevalence of asthma is generally low at about 3.7%, making the countries in this region some of the lowest asthma regions worldwide; however, high case fatality rates are also reported in this region (GINA, 2003).

The prevalence of asthma is generally low within the Middle East, although high rates have been recorded in the Kingdom of Saudi Arabia, Kuwait, Lebanon, and Israel. The prevalence of asthma in migrant communities often differs from that in the resident population in countries in the region. In Israel the prevalence of asthma is three times greater among adults of Ethiopian origin compared with the general population. In contrast, in the Kingdom of Saudi Arabia asthma is less common in the non-Saudi population. Children from refugee camps in the Occupied Territory of Palestine appear to be at greater risk of asthma than children from neighbouring villages and cities. This observation adds further evidence of the major adverse health and socioeconomic conditions present within this community. The burden of severe asthma is considerable within the Middle East, with hospital admission rates in excess of 150-200 per 100,000 per year in some of the 'high prevalence' countries. For example, in Israel, one in five asthmatic children visit the emergency room per year, and one in ten asthmatic children is hospitalized in the same period due to severe asthma (GINA-Asthma Burden Report, 2003).

In a review of studies on asthma prevalence in Africa over two decades, Adeloye and colleagues (2013) estimated 74 million cases of asthma in 1990; 94.8 million cases in 2000 and 119.3 million cases in 2010 The prevalence of asthma is higher in Southern Africa than in many other regions in Africa.

In Zimbabwe the prevalence of exercise-induced asthma is 25 times higher in urban compared with rural communities, where asthma is rare. Asthma is a common cause of admission to hospital in the region, particularly in children. In the case of South Africa, asthma is the third most common cause of hospital admission in children, after pneumonia and gastroenteritis (GINA-Asthma Burden Report, 2003).

Despite progressive reductions in asthma prevalence over the last few decades, asthma mortality remains high within the region. For example, in South Africa among 5- to 34-year-olds the asthma mortality rate has decreased by 0.13 deaths per 100,000 per year over recent decades, however at 1.5 it still represents a relatively high rate internationally and is associated with the fifth-highest case fatality rate in the world (GINA-, 2003).

The report of the third phase of the ISAAC study (2007) indicated asthma prevalence rates of 11.2% in Ethiopia, 21.2% in Kenya, 13.0% in Nigeria, and 25.0% in South Africa among participants of the study in some English-speaking African countries. The asthma prevalence rates from some of the French-speaking were 10.3% in Algeria, 17.7% in Tunisia, 20.9% in Ivory Coast, 18.5% in Togo among participants (Ait-Khaled *et al*., 2007).

The prevalence of asthma is generally low within countries in West Africa. The prevalence of asthma has increased over recent decades, having previously been rare within the countries that make up this region. With increasing urbanization and lifestyle changes it is likely that the prevalence of asthma will increase further in West Africa over the next decade (GINA-Asthma Burden Report, 2003).

In Ghana, data on non-communicable diseases are scattered and not representative (WHO, 2005), however the WHO (2009) estimated an asthma country incidence rate of 1.5/1000 per year for Ghana (WHO, 2009).

While communicable diseases remain the major public health problems within the West African region, certain non-communicable diseases including asthma are increasingly recognized as contributing significantly to the overall burden of disease. A major barrier to effective management of asthma in the region is the cost and availability of medications.

Whereas in many of the countries in the various regions, reduction in case fatality rates have been associated to improved management, including the use of inhaled corticosteroids, in a

few countries challenges with regards to improving case management remains a major barrier (GINA-Asthma Burden Report, 2003).

### 1.2.2. Definition of Asthma

An international consensus report defined asthma as a *"common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyper-responsiveness, and an underlying inflammation"* (EPR-3, 2007).

Airway narrowing is the final common pathway leading to symptoms and physiological changes in asthma. Several factors contribute to the development of airway narrowing in asthma (McParland *et al*, 2003; Hirst *et al*, 2004; Black, 2004). These various factors captured in Table 1.2 may influence the risk of asthma. They are divided into those that cause the development (host factors) of asthma and those that trigger (environmental factors) asthma symptoms, even though it is also believed that some do both (Busse & Lemanske, 2001 ).

**Table 1.2:** Factors Influencing the Development and Expression of Asthma

| **Factors Influencing the Development and Expression of Asthma** | |
|---|---|
| Host Factors | Environmental Factors |
| Genetic-<br>*genes predisposing to atopy*<br>*genes predisposing to airway hyper-sensitivity*<br>Obesity | Allergens – *indoor* (domestic mites, furred animal, cockroach allergen, fungi, moulds, yeast); outdoor (pollens, fungi, moulds, yeasts)<br>Infections – predominantly viral |
| Sex | Occupational sensitizers<br>Tobacco smoke – passive/active smoking<br>Outdoor/indoor air pollution<br>Diet |

As the various environmental factors interact with the host factors by a mechanism that has not yet been fully elucidated, airway inflammation that is associated with hyper-responsiveness is induced, leading to recurrent episodes of wheezing, breathlessness, chest

tightness and night or early morning coughing. These episodes are usually associated with widespread, but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment.

The NAEPP-EPR has also provided a working definition of asthma to guide the description and identification of treatment directions which states that:

*Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role: in particular, mast cells, eosinophils, T lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyper-responsiveness to a variety of stimuli. Reversibility of airflow limitation may be incomplete in some patients with asthma* (EPR–2, 1997; EPR-3, 2007).

This working definition and its recognition of key features of asthma was derived from the way airway changes in asthma relate to the various factors; such as allergens, respiratory viruses, and some occupational exposures, are associated with the development of airway inflammation and recognition of genetic regulation of these processes. According to the EPR (2007), it from these descriptive approaches of asthma definition that a more comprehensive understanding of asthma pathogenesis, the processes involved in the development of persistent airway inflammation, and the significant implications that these immunological events have for the development, diagnosis, treatment, and possible prevention of asthma has evolved (EPR-3, 2007).

### 1.2.3. Pathogenesis of Asthma

What initiates the inflammatory process in the first place and makes some persons susceptible to its effects is an area of active investigation. There is not yet a definitive answer to this question, but new observations suggest that the origins of asthma primarily occur early in life. The expression of asthma is a complex, interactive process that depends on the interplay between two major factors—host factors (particularly genetics) and environmental exposures that occur at a crucial time in the development of the immune system.

#### 1.2.3.1. Host Factors

There is considerable interest in the role of innate and adaptive immune responses associated with both the development and regulation of inflammation (Eder et al. 2006).

The current "hygiene hypothesis" of asthma illustrates how this cytokine imbalance may explain some of the dramatic increases in asthma prevalence in westernized countries. This hypothesis is based on the assumption that the immune system of the newly born is skewed toward Th2 cytokine generation. Following birth, environmental stimuli such as infections will activate Th1 responses and bring the Th1/Th2 relationship to an appropriate balance. Evidence indicates that the incidence of asthma is reduced in association with certain infections (*M. tuberculosis*, measles, or hepatitis A), exposure to other children (e.g., presence of older siblings and early enrolment in childcare), and less frequent use of antibiotics (Horwood *et al*, 1985; Gern *et al*, 1999; Gern and Busse 2002; Sears *et al*, 2003; Eder *et al*, 2006). Furthermore, the absence of these lifestyle events is associated with the persistence of a Th2 cytokine pattern. Under these conditions, the genetic background of the child who has a cytokine imbalance toward Th2 will set the stage to promote the production of IgE antibodies to key environmental antigens, such as house-dust mite, cockroach, *Alternaria*, and possibly cat. Therefore, a gene-by-environment interaction occurs in which

the susceptible host is exposed to environmental factors that are capable of generating IgE, and sensitization occurs. Precisely why the airways of some individuals are susceptible to these allergic events has not been established.

There also appears to be a reciprocal interaction between the two subpopulations in which Th1 cytokines can inhibit Th2 generation and vice versa. Allergic inflammation may be the result of an excessive expression of Th2 cytokines. Alternatively, recent studies have suggested the possibility that the loss of normal immune balance arises from a cytokine dys-regulation in which Th1 activity in asthma is diminished. The focus on actions of cytokines and chemokines to regulate and activate the inflammatory profile in asthma has provided ongoing and new insight into the pattern of airway injury that may lead to new therapeutic targets.

It is well recognized that asthma has an inheritable component to its expression, but the genetics involved in the eventual development of asthma remain a complex and incomplete picture (Holgate, 1999; Ober, 2005). To date, many genes have been found that either are involved in or linked to the presence of asthma and certain of its features. The complexity of their involvement in clinical asthma is noted by linkages to certain phenotypic characteristics, but not necessarily the pathophysiologic disease process or clinical picture itself. The role of genetics in IgE production, airway hyper-responsiveness, and dysfunctional regulation of the generation of inflammatory mediators (such as cytokines, chemokines, and growth factors) has appropriately captured much attention. In addition, studies are investigating genetic variations that may determine the response to therapy. The relevance of polymorphisms in the beta-adrenergic and corticosteroid receptors in determining responsiveness to therapies is of

increasing interest, but the widespread application of these genetic factors remains to be fully established.

In early life, the prevalence of asthma is higher in boys. At puberty, however, the sex ratio shifts, and asthma appears predominantly in women (Horwood *et al*, 1985). How specifically sex and sex hormones, or related hormone generation, are linked to asthma has not been established, but they may contribute to the onset and persistence of the disease.

#### 1.2.3.2. Environmental Factors

Two major environmental factors have emerged as the most important in the development, persistence, and possibly severity of asthma: airborne allergens and viral respiratory infections. In the susceptible host, and at a critical time of development (e.g., immunological and physiological), both respiratory infections and allergens have a major influence on asthma development and its likely persistence. It is also apparent that allergen exposure, allergic sensitization, and respiratory infections are not separate entities but function interactively in the eventual development of asthma.

The role of allergens in the development of asthma has yet to be fully defined or resolved, but it is obviously important. Sensitization and exposure to house-dust mite and *Alternaria* are important factors in the development of asthma in children. Early studies showed that animal dander, particularly dog and cat, were associated with the development of asthma.

Recent data suggested that, under some circumstances, dog and cat exposure in early life may actually protect against the development of asthma. The determinant of these diverse outcomes has not been established. Studies to evaluate house-dust mite and cockroach

exposure have shown that the prevalence of sensitization and subsequent development of asthma are linked (Sporik *et al*, 1990; Wahn *et al*, 1997; Huss *et al*, 2001). Exposure to cockroach allergen, for example, a major allergen in inner-city dwellings, is an important cause of allergen sensitization, a risk factor for the development of asthma (Rosenstreich *et al*, 1997).

In addition, allergen exposure can promote the persistence of airway inflammation and likelihood of an exacerbation.

During infancy, a number of respiratory viruses have been associated with the inception or development of the asthma. In early life, respiratory syncytial virus (RSV) and para-influenza virus in particular, cause bronchiolitis that parallels many features of childhood asthma (Sigurs *et al*, 2000; Gern and Busse, 2002). A number of long-term prospective studies of children admitted to hospital with documented RSV have shown that approximately 40 percent of these infants will continue to wheeze or have asthma in later childhood (Sigurs *et al*, 2000).

Symptomatic rhinovirus infections in early life also are emerging as risk factors for recurrent wheezing. On the other hand, evidence also indicates that certain respiratory infections early in life—including measles and even RSV (Stein *et al*, 1999) or repeated viral infections (other than lower respiratory tract infections) (Shaheen *et al*, 1996; Illi *et al*, 2001)—can protect against the development of asthma.

The "hygiene hypothesis" of asthma suggests that exposure to infections early in life influences the development of a child's immune system along a "non-allergic" pathway, leading to a reduced risk of asthma and other allergic diseases. Although the hygiene

hypothesis continues to be investigated, this association may explain observed associations between large family size, later birth order, day-care attendance, and a reduced risk of asthma (Illi *et al*, 2001; Eder *et al*, 2006).

The influence of viral respiratory infections on the development of asthma may depend on an interaction with atopy. The atopic state can influence the lower airway response to viral infections, and viral infections may then influence the development of allergic sensitization. The airway interactions that may occur when individuals are exposed simultaneously to both allergens and viruses are of interest but are not defined at present. Tobacco smoke, air pollution, occupations, and diet have also been associated with an increased risk for the onset of asthma, although the association has not been as clearly established as with allergens and respiratory infections (Strachan & Cook, 1998; Malo *et al*, 2004).

In utero exposure to environmental tobacco smoke increases the likelihood for wheezing in the infant, although the subsequent development of asthma has not been well defined. In adults who have asthma, cigarette smoking has been associated with an increase in asthma severity and decreased responsiveness to inhaled corticosteroids (ICSs) (Dezateux *et al*, 1999).

The role of air pollution in the development of asthma remains controversial and may be related to allergic sensitization (ATS, 2000). One recent epidemiologic study showed that heavy exercise (three or more team sports) outdoors in communities with high concentration of ozone was associated with a higher risk of asthma among school-age children (McConnell *et al*, 2002). The relationship between increased levels of pollution and increases in asthma exacerbations and emergency care visits has been well documented.

An association of low intake of antioxidants and omega-3 fatty acids has been noted in observational studies, but a direct link as a causative factor has not been established.

Increasing rates of obesity have paralleled increasing rates in asthma prevalence, but the interrelation is uncertain (Ford, 2005). Obesity may be a risk factor for asthma due to the generation of unique inflammatory mediators that lead to airway dysfunction.

Understanding of asthma pathogenesis and underlying mechanisms now includes the concept that gene-by-environmental interactions are critical factors in the development of airway inflammation and eventual alteration in the pulmonary physiology that is characteristic of clinical asthma.

### 1.2.4. Pathophysiology of Asthma

Airflow limitation in asthma is recurrent and caused by a variety of changes in the airway. Changes in airway activities are defined by the processes of broncho-constriction, airway oedema, airway hypersensitivity and airway remodelling. These various processes when in place tend to limit the amount of airflow during the breathing process in patients with asthma. These processes may present at any time as individual processes or in various combinations.

#### 1.2.4.1. Broncho-constriction

Broncho-constriction is the dominant physiological event leading to clinical symptoms in airway narrowing and a subsequent interference with airflow. In acute exacerbations of asthma, bronchial smooth muscle contraction (broncho-constriction) occurs quickly to narrow the airways in response to exposure to a variety of stimuli including allergens or irritants.

According to Busse and Lemanske (2001), allergen-induced acute broncho-constriction results from an IgE-dependent release of mediators from mast cells that includes histamine,

tryptase, leukotrienes, and prostaglandins that directly contract airway smooth muscle (Busse & Lemanske, 2001).

Aspirin and other non-steroidal anti-inflammatory drugs can also cause acute airflow obstruction in some patients, and the evidence indicates that this is non-IgE-dependent response even though it also involves mediator release from airway cells (Stevenson & Szczeklik, 2006). In addition to these, other stimuli (including exercise, cold air, and irritants) can also cause acute airflow obstruction. Even though the mechanisms regulating the airway response to these factors are less well defined, the intensity of the response is believed to be related to underlying airway inflammation.

Stress is also believed to play a role in precipitating asthma exacerbations and even though the mechanisms involved here are also yet to be established, it is believed that they may include enhanced generation of pro-inflammatory cytokines (EPR-3, 2007).

#### 1.2.4.2. Airway Oedema

The process of airway oedema is believed to set in at a later stage of the processes that limits airflow in patients with asthma. As the disease become more persistent and inflammation more progressive; oedema, mucus hyper-secretion and the formation of inspissated mucus plugs, as well as structural changes including hypertrophy and hyperplasia of the airway smooth muscle also tend to further limit the airflow. However, these latter changes may not respond to usual treatment (Holgate & Polosa, 2006).

#### 1.2.4.3. Airway Hypersensitivity

Airway hyper-sensitivity or hyper-responsiveness is an exaggerated bronchial response to a wide variety of stimuli that leads to broncho-constriction. The degree to which airway hyper-responsiveness can be defined by contractile responses to challenges with methacholine correlates with the clinical severity of asthma. Various processes are implicated in the mechanisms that influence airway hyper-responsiveness and these may include but not limited to inflammation, dysfunctional neuro-regulation, and structural changes. However, inflammation appears to be a major factor in determining the degree of airway hyper-responsiveness. Treatment directed toward reducing inflammation can reduce airway hyper-responsiveness and improve asthma control.

#### 1.2.4.4. Airway Remodelling

Changes in the airway structures do occur with time in patients with asthma. In some patients with asthma, airflow limitation may be only partially reversible. Permanent structural changes can occur in the airway and these are associated with a progressive loss of lung function that is not prevented by or fully reversible by current therapy. Airway remodelling involves an activation of many of the structural cells, with consequent permanent changes in the airway that increase airflow obstruction and airway responsiveness and render the patient less responsive to therapy (Holgate & Polosa, 2006). These structural changes can include thickening of the sub-basement membrane, sub-epithelial fibrosis, airway smooth muscle hypertrophy and hyperplasia, blood vessel proliferation and dilation, and mucous gland hyperplasia and hyper-secretion. Regulation of the repair and remodelling process is not well established, but both the process of repair and its regulation are likely to be key events in explaining the persistent nature of the disease and the limitations to a therapeutic response.

Though airway remodelling and airway oedema may not respond to current treatment options, inflammation which is implicated in both broncho-constriction and airway hyper-sensitivity responds to therapy.

### 1.2.5. Development of Airway Inflammation

Inflammation has a central role in the pathophysiology of asthma. As noted in the definition of asthma, airway inflammation involves an interaction of many cell types and multiple mediators with the airways that eventually results in the characteristic pathophysiological features of the disease: bronchial inflammation and airflow limitation that result in recurrent episodes of cough, wheeze, and shortness of breath.

The processes by which these interactive events occur and lead to clinical asthma are still under investigation (EPR-3, 2007). Moreover, although distinct phenotypes of asthma exist (e.g., intermittent, persistent, exercise-associated, aspirin-sensitive, or severe asthma), airway inflammation remains a consistent pattern. The pattern of airway inflammation in asthma, however, does not necessarily vary depending upon disease severity, persistence, and duration of disease. The cellular profile and the response of the structural cells in asthma are quite consistent (EPR-3, 2007).

#### 1.2.5.1. Inflammatory Cells Involved in Airway Inflammation

Activities of various cells are implicated in the inflammatory processes in clinical asthma. These include the lymphocytes, mast cells, eosinophils, neutrophils, dendritic cells, resident cells of the airways, epithelial cells and the macrophages.

*Lymphocytes:* An increased understanding of the development and regulation of airway

Inflammation in asthma followed the discovery and description of sub-populations of lymphocytes, T helper 1 cells and T helper 2 cells (Th1 and Th2), with distinct inflammatory mediator profiles and effects on airway function. After the discovery of these distinct lymphocyte sub-populations in animal models of allergic inflammation, evidence emerged that, in human asthma, a shift, or predilection, toward the Th2-cytokine profile resulted in the eosinophilic inflammation characteristic of asthma (Cohn *et al*, 2004). In addition, generation of Th2 cytokines (e.g., interleukin-4 (IL-4), IL-5, and IL-13) could also explain the over-production of IgE, presence of eosinophils, and development of airway hyper-responsiveness. There also may be a reduction in a sub-group of lymphocytes, regulatory T cells, which normally inhibit Th2 cells, as well as an increase in natural killer (NK) cells that release large amounts of Th1 and Th2 cytokines (Larche *et al*, 2003; Akbari *et al*, 2006). T lymphocytes, along with other airway resident cells, can also determine the development and degree of airway remodelling (Barnes, 2002; Zimmermann *et al*, 2003).

*Mast cells:* Activation of mucosal mast cells releases broncho-constrictor mediators (histamine, cysteinyl-leukotrienes, prostaglandin D2) (Boyce, 2003; Robinson, 2004; Galli *et al*, 2005). Although allergen activation occurs through high-affinity IgE receptors and is likely the most relevant reaction, sensitized mast cells also may be activated by osmotic stimuli to account for exercise-induced bronchospasm (EIB). Increased numbers of mast cells in airway smooth muscle may be linked to airway hyper-responsiveness (Brightling *et al*, 2002). Mast cells also can release a large number of cytokines to change the airway environment and promote inflammation even though exposure to allergens is limited.

*Eosinophils:* Increased numbers of eosinophils exist in the airways of most, but not all persons who have asthma (Sampson, 2000; Chu & Martin, 2001; Williams, 2004). These

cells contain inflammatory enzymes, generate leukotrienes, and express a wide variety of pro-inflammatory cytokines. Increases in eosinophils often correlate with greater asthma severity. In addition, numerous studies show that treating asthma with corticosteroids reduces circulating and airway eosinophils in parallel with clinical improvement (Leckie *et al*, 2000). However, the role and contribution of eosinophils to asthma is undergoing a re-evaluation based on studies with an anti-IL-5 treatment that has significantly reduced eosinophils but did not affect asthma control (Leckie *et al*, 2000). Therefore, although the eosinophil may not be the only primary effector cell in asthma, it likely has a distinct role in different phases of the disease.

*Neutrophils:* Neutrophils are increased in the airways and sputum of persons who have severe asthma, during acute exacerbations, and in the presence of smoking. Their pathophysiological role remains uncertain; they may be a determinant of a lack of response to corticosteroid treatment (Fahy *et al*, 1995). The regulation of neutrophil recruitment, activation, and alteration in lung function is still under study, but leukotriene B4 may contribute to these processes (Wenzel *et al*, 1997; Jatakanon *et al*, 1999; Wenzel, 2006).

*Dendritic cells:* These cells function as key antigen-presenting cells that interact with allergens from the airway surface and then migrate to regional lymph nodes to interact with regulatory cells and ultimately to stimulate Th2 cell production from naïve T cells (Kuipers & Lambrecht, 2004).

*Macrophages:* Macrophages are the most numerous cells in the airways and also can be activated by allergens through low-affinity IgE receptors to release inflammatory mediators and cytokines that amplify the inflammatory response (Peters-Golden, 2004).

*Resident cells of the airway:* Airway smooth muscle is not only a target of the asthma response (by undergoing contraction to produce airflow obstruction) but also contributes to it (via the production of its own family of pro-inflammatory mediators). As a consequence of airway inflammation and the generation of growth factors, the airway smooth muscle cell can undergo proliferation, activation, contraction, and hypertrophy—events that can influence airway dysfunction of asthma (EPR-3, 2007).

*Epithelial cells:* Airway epithelium is another airway lining cell critically involved in asthma (Polito & Proud, 1998). The generation of inflammatory mediators, recruitment and activation of inflammatory cells, and infection by respiratory viruses can cause epithelial cells to produce more inflammatory mediators or to injure the epithelium itself. The repair process, following injury to the epithelium, may be abnormal in asthma, thus furthering the obstructive lesions that occur in asthma.

#### 1.2.5.2. Inflammatory Mediators in Airway Inflammation

Various inflammatory mediators (chemokines, cytokines, immunoglobulin E, cystienyl-leukostrienes and nitric oxide) have been identified to be at play within the inflammatory activities of the airways. Understanding of the interplay of these mediators and the inflammatory cells in the development of airway inflammation has implications for the therapeutic management of asthma. Chemokines are important in recruitment of inflammatory cells into the airways and are mainly expressed in airway epithelial cells (Zimmermann *et al*, 2003).

The cytokines are believed to direct and modify the inflammatory response in asthma and likely determine its severity. Th2-derived cytokines include IL-5, which is needed for eosinophil differentiation and survival, and IL-4, which is important for Th2 cell

differentiation and with IL-13, is important for IgE formation. Key cytokines include IL-1β and tumor necrosis factor-α (TNF-α), which amplify the inflammatory response, and granulocyte-macrophage colony-stimulating factor (GM-CSF), which prolongs eosinophil survival in airways.

The Cysteinyl-leukotrienes are potent broncho-constrictors derived mainly from the mast cells. They are the only mediator whose inhibition has been specifically associated with an improvement in lung function and asthma symptoms (Busse, 1996; Leff, 2001). Recent studies have also shown leukotriene B4 can contribute to the inflammatory process by recruitment of neutrophils (Gelfand & Dakhama, 2006).

Nitric oxide (NO) is produced predominantly from the action of inducible NO synthase in airway epithelial cells; it is a potent vasodilator (Deykin *et al,* 2002; Strunk *et al,* 2003). Measurements of fractional exhaled NO (FeNO) may be useful for monitoring response to asthma treatment because of the purported association between FeNO and the presence of inflammation in asthma (Green *et al,* 2002).

Immunoglobulin E (IgE) is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic diseases and the development and persistence of inflammation. IgE attaches to cell surfaces via a specific high-affinity receptor. The mast cell has large numbers of IgE receptors; these, when activated by interaction with antigen, release a wide variety of mediators to initiate acute bronchospasm and also to release pro-inflammatory cytokines to perpetuate underlying airway inflammation (Sporik *et al,* 1995; Boyce, 2003). Other cells, basophils, dendritic cells, and lymphocytes also have high-affinity IgE receptors.

The development of monoclonal antibodies against IgE has shown that the reduction of IgE is effective in asthma treatment (Busse *et al*, 2001; Holgate *et al*, 2005). These clinical observations further support the importance of IgE to asthma.

#### 1.2.5.3. Implications of Airway Inflammation for Therapy

Scientific investigations have focused on translating the increased understanding of the inflammatory processes in asthma into therapies targeted at interrupting these processes (Barnes, 2002). Some investigations have yielded promising results, such as the development of leukotriene modifiers and anti-IgE monoclonal antibody therapy (Wenzel, 2003; O'Bryne, 2009). Other studies, such as those directed at IL-4 or IL-5 cytokines, underscore the relevance of multiple factors regulating inflammation in asthma and the redundancy of these processes (Foster *et al*, 2001; Hart *et al*, 2002).

Some clinical studies have indicated that phenotypes of asthma exist, and these phenotypes may have very specific patterns of inflammation that require different treatment approaches (Foster *et al*, 2001; Hart *et al*, 2002; Wenzel, 2003; O'Bryne, 2009). Current studies are investigating novel therapies targeted at the cytokines, chemokines, and inflammatory cells farther upstream in the inflammatory process (Barnes, 2002; Thornburn & Hansbro, 2010). For example, drugs designed to inhibit the Th2 inflammatory pathway may cause a broad spectrum of effects such as airway hyper-responsiveness and mucus hyper-secretion. Further research into the mechanisms responsible for the varying asthma phenotypes and appropriately targeted therapy may enable improved control for all manifestations of asthma, and, perhaps, prevention of disease progression (Barnes, 2002; Thornburn & Hansbro, 2010).

### 1.2.6. Components of Asthma Management

Four components are generally recommended for the management of asthma. These are the:

- Measures of assessment and monitoring, which are obtained by objective tests, physical examination, patient history and patient report, to diagnose and assess the characteristics and severity of asthma and also to monitor whether asthma control is achieved and maintained.
- Education for a partnership in asthma care
- Control of environmental factors and co-morbid conditions that affect asthma
- Pharmacotherapy

The functions of assessment and monitoring are closely linked to the concepts of severity, control, and responsiveness to treatment:

***Severity:*** the intrinsic intensity of the disease process. Severity is most easily and directly measured in a patient who is not currently receiving long-term control treatment.

***Control:*** the degree to which the manifestations of asthma (symptoms, functional impairments, and risks of untoward events) are minimized and the goals of therapy are met.

***Responsiveness:*** the ease with which control is achieved by therapy.

An important point linking asthma severity, control, and responsiveness is that the goals are identical for all levels of baseline asthma severity. A patient who has severe persistent asthma compared to a patient who has mild persistent asthma, or a patient who is less responsive to therapy may require more intensive intervention to achieve well-controlled asthma; however, the goals are the same: in well-controlled asthma, the manifestations of asthma are minimized by therapeutic intervention (EPR-3, 2007).

Although the severity of disease is most accurately assessed in patients before initiating long-term control medication, many patients are already receiving treatment when first seen by a new health care provider. In such cases, severity can be inferred from the least amount of treatment required to maintain control. This approach presumes that the severity of asthma is closely related to its responsiveness to treatment. Although this assumption may not be true for all forms of asthma and all treatments, it does focus attention on what is important in managing patients who have asthma: achieving a satisfactory level of control.

Both asthma severity and asthma control can be broken down into two domains: impairment and risk. Impairment is an assessment of the frequency and intensity of symptoms and functional limitations that a patient is experiencing or has recently experienced. Risk is an estimate of the likelihood of either asthma exacerbations or of progressive loss of pulmonary function over time.

An assessment of the impairment domain for determining the severity of disease (in patients on no long-term-control treatment before treatment is initiated) or the level of control (after treatment is selected) usually can be elicited by careful, directed history and lung function measurement. Standardized questionnaires like the Asthma Control Test (ACT) (Nathan *et al*, 2004), the Childhood Asthma Control Test (Liu *et al*, 2007), the Asthma Control Questionnaire (Juniper *et al*, 1999a), the Asthma Therapy Assessment Questionnaire (ATAQ) control index (Vollmer *et al,* 1999), and others have been developed to facilitate and standardize the assessment of the impairment domain of asthma control.

Some patients, however, appear to perceive the severity of airflow obstruction poorly (Kikuchi *et al,* 1994; Bijl-Hofland *et al*, 2000). These patients may have unconsciously become accommodated to their symptoms, or perhaps they have mistakenly attributed these

symptoms to other causes, like aging, obesity, or lack of fitness, so that they do not report them readily. For these patients, some other measures, such as spirometry, may identify that the degree of airflow obstruction is poorly recognized or perceived by the patient. A trial of therapy can be initiated and lead to unexpected improvement in quality of life.

Assessment of the risk domain for adverse events in the future, especially of exacerbations and of progressive, irreversible loss of pulmonary function seems to be more problematic. Some assessment of the risk of exacerbations can be inferred from the medical history. Patients who have had exacerbations requiring emergency department (ED) visits, hospitalization, or intensive care unit (ICU) admission, especially in the past year, have a great risk of exacerbations in the future (Lieu *et al*, 1998; Adams *et al*, 2000; Eisner *et al*, 2001). Conversely, the achievement of good control of asthma symptoms and airflow obstruction from treatment with inhaled corticosteroids (ICS) lowers the risk for asthma exacerbations in the future (Bateman *et al*, 2004).

It is not known, however, whether the minimum treatment to control symptoms necessarily reduces the risk of exacerbations. Some patients who have few current symptoms or impairment of quality of life may still be at grave risk of severe, even life-threatening exacerbations (Ayres *et al*, 2004).

Finally, little is known about the prevalence of a heightened risk of progressive loss of pulmonary function among patients who have asthma or whether any current treatment can prevent it.

Most frequently spirometry is used to assess any risk of possible future adverse events. The forced expiratory volume in 1 second ($FEV_1$) is expressed expressed as a proportion of forced vital capacity (FVC) and expressed as $FEV_1$/FVC. The use of biomarkers may however be a more accurate, simple and easily applied test. Biomakers may present a better correlation the severity of any future risk (Szefler *et al*, 2012).

Various biomarkers may be considered for this assessment they have to be associated with activities in the airways. These may include but not limited to mediators of inflammation, exhaled nitric oxide concentration (FeNO), sputum or blood eosinophils and serum immunoglobulin among others (Wadworth *et al*, 2011).

Future estimations of the correlation between the various historical features and those of the biomarkers may serve as determinants of possible risks of adverse events. These notwithstanding, the best means of measuring asthma control are those of quality of life over time, frequency and severity of symptoms and exacerbations (EPR-3, 2007).

A patient's response to therapy is also very important, except for a clearer definition for what constitutes the response

Bates and colleagues (2004) observed in their randomized control trial that asthma control correlates with a composite definition of a responder (Bateman *et al*, 2004).

An editorial review by Stempel and Fuhlbrigge (2005) draws attention to variations in in statistical significance when pre- or post-bronchodilator $FEV_1$ are used for assessment of response to therapy. Studies that depended solely on the $FEV_1$ to assess response to therapy may also face the challenges posed by the influences disease activities that are independent of ongoing intervention.

According to them, it may necessary to take note of other relevant responses that affects airways activities, such as night-time awakenings associated to asthma, airway responses to methacholine challenge, and the frequency of asthma exacerbations (Stempel & Fuhlbrigge, 2005).

It is now obvious that some agreement would be needed on what clinically significant outcomes characterize the responses to therapy. In addition, some agreement would also be needed on timelines in the assessment of response to generate similar information about response to asthma interventions (Zhang *et al,* 2002), but the timelines may have to relate to the type of treatment used in the intervention. The timelines for long-acting agents that influence frequency of exacerbations may vary from those of rapid –acting agents with acute action, such as bronchodilator medicines (Bousquet *et al,* 2004).

#### 1.2.6.1. Asthma Self-management Education

Evidence is now abundant that in the management of chronic asthma, self-management education impacts positively on improving outcomes (Gibson *et al,* 2003; Morgan *et al*, 2004; Krieger *et al*, 2005; GINA, 2012). Improved outcomes are a result of modified behaviours that can be derived from the self-management skills acquired through patient education. Improvement in outcomes is not only a function of expert care and the number of reviews by healthcare professionals, but also a function appropriate behavioural change derived from patient education towards self-management (EPR-3, 2007). Active patient participation through self-management involving the control of environment trigger-factors and therapy adjustments strategies can improve disease control.

The shared goal for both the health professional and the patient is adequate response to management or control (EPR-3, 2007).

The benefits to be derived from adequate self-management skills may save the patient and the health care system the costs of hospitalization and management of asthma exacerbations (Cowie *et al*, 1997; Madge *et al*, 1997; Wesseldine *et al*, 1999; Bartholomew *et al*, 2000; Gibson *et al*, 2000; Cordina *et al*, 2001; Guevara *et al*, 2003; Krishna *et al*, 2003; MeGhan *et al*, 2003; Powell & Gibson 2003; Morgan *et al*, 2004; Cicutto *et al*, 2005; Krieger *et al*, 2005; Teach *et al*, 2006).

Other valuable benefits from the implementation of adequate self-management strategies for the patient will be lesser frequency of asthma symptoms, increased activity, improvement in quality of life among others (Christiansen *et al*, 1997; Evans *et al*, 1999; Bonner *et al*, 2002; Perneger *et al*, 2002; Janson *et al*, 2003; McLean *et al*, 2003; Thoonen *et al*, 2003; Clark *et al*, 2004; Saini *et al*, 2004).

Various cost-analysis studies have demonstrated the cost-effective impact of asthma education on asthma morbidity, especially in patients who are rated high-risk (Kattan *et al*, 1997; Gallefoss & Bakke, 2001; Schermer *et al*, 2002; Sullivan *et al*, 2002; Powell & Gibson, 2003).

Self-management strategies may employ the use peak-flow-meter or symptoms assessments alongside written instructions to guide decision-making. The written instructions will contain clear decision-making points on worsening condition and medication adjustments.

Some studies have demonstrated the equivalence of impact on emergency department (ED) visits from methods that employed peak-flow monitoring and those using symptoms assessments. However another study found the peak-flow monitoring more effective. Than the symptoms assessment on ED visits (Powell & Gibson, 2003).

All patients are likely to benefit from asthma plans that clearly provide instructions on the day to day management actions that the patient need to follow and also information to help with early detection and management of a worsening asthma condition. This plan must also emphasis self-adjustment in medication regimens where necessary. Asthma action plans are more relevant for patients who have challenges with asthma control and those whose conditions have been rated as moderate or severe. Patients known for severe asthma exacerbations may also benefit from the action plans.

Patient education must comprise the provision of information as well as training in self-management skills to reduce frequent hospitalizations, loss of productivity, hospital visits whilst improving medication use and lung function (Gibson *et al,* 2002).

Randomised control trials (Wilson *et al,* 2005; 2006) used the context of the patient-clinician partnership to test the impact of shared decision-making about asthma treatment, compared to guideline-based clinician decision-making and usual care, in adults who had poorly controlled asthma. Clinician care managers (nurse practitioners, pharmacists, respiratory therapists) met with the patients to adjust therapy in two visits, 1 month apart, followed by three brief telephone calls (at 3, 6, and 9 months) to assess patients' progress in both intervention groups. The unique features of shared decision-making included identifying patients' goals and preferences regarding treatment and negotiating a treatment regimen to accommodate best each patient's goals and preferences. Establishing rapport, providing educational information, teaching inhaler technique, writing the prescription, and preparing a written asthma action plan for the patient occurred in both the guidelines and shared-decision groups. The shared-decision group had significantly greater adherence to long-term control medication compared to the guidelines group, and both interventions produced significantly better adherence to asthma control medications than usual care over 12 months of follow-up.

Controlled trials of asthma education delivered by pharmacists have shown mixed results (Bynum *et al*, 2001; Cordina *et al*, 2001; Stergachis *et al*, 2002; Barbanel *et al*, 2003; McLean *et al*, 2003; Basheti *et al*, 2005; Saini *et al*, 2004). Four of these RCTs recruited community pharmacies, provided training for their pharmacists, and evaluated the impact of pharmacist teaching on patient outcomes (Cordina *et al*, 2001; Stergachis *et al*, 2002; McLean *et al*, 2003; Saini *et al*, 2004). All of these studies involved repeated contacts with patients. One study showed reduced hospitalizations and improved inhaler technique (Cordina *et al*, 2001). A second study found reduced asthma severity, better lung function, less use of albuterol, and better perceived control of asthma (Saini *et al*, 2004). The third study showed reductions in daytime and night-time symptoms, use of short-acting beta-agonist (SABA), and doctor visits, as well as improvements in PEF and quality of life (McLean *et al*, 2003). The fourth study found no differences between intervention patients and controls on any measure (Stergachis *et al*, 2002).

In their assessment of a Community Pharmacy-Based Program for Patients with Asthma Cordina and McElnay (2001), in a prospective, randomized, controlled trial in Malta, patients were provided a comprehensive asthma education and monitored. Intervention patients received verbal counselling, an educational video, an information leaflet, and subsequent monitoring with reinforcement, while control patients received routine dispensing services. Patients were then assessed at baseline and at 4, 8, and 12 months for health-related quality of life, peak expiratory flow (PEF), inhaler technique, compliance with therapy, hospitalization rates, days lost from work, asthma symptoms, and patient satisfaction.

Their findings indicated improved HRQoL at 12 months ($p=0.009$), while in the same period PEF significantly decreased in control patients compared with intervention patients ($p=0.009$)

whereas inhaler technique improved in the intervention group (p=0.021). There were also significantly fewer self-reported hospitalizations in intervention patients.

The EPR-3 (2007) recommends against these various background that with the support of clinicians, effective educational interventions should be provided at points of care outside the traditional health care setting, including schools (Christiansen *et al*, 1997; Clark *et al*, 2004; MeGhan *et al*, 2003; Butz *et al*, 2005; Cicutto *et al*, 2005), pharmacies (Cordina *et al*, 2001; McLean *et al*, 2003; Saini *et al*, 2004), and homes. For example, pharmacy-based education directed toward understanding medications and teaching inhaler skills as well as home-based interventions to increase patient and family capacity to control allergen and irritant exposure (Custovic *et al*, 2000; Morgan *et al*, 2004; Eggleston *et al*, 2005; Klinnert *et al*, 2005; Krieger *et al*, 2005; McConnell *et al*, 2005) are strategies that are believed will enhance overall asthma self-management support.

Written asthma actions plans are also recommended to support patients make decision outside the clinical facilities. The two important elements of the asthma actions plans are guides for daily management (what medicine to take daily, including the specific names of the medications and what actions to take to control environmental factors that worsen the patient's asthma) and how to recognise and handle worsening asthma (what signs, symptoms, and PEF measurements (if peak flow monitoring is used) indicate worsening asthma, what medications to take in response to these signs, what symptoms and PEF measurements indicate the need for urgent medical attention, emergency telephone numbers for the physician, emergency department, and person or service to transport the patient rapidly for medical care) (EPR-3, 2007; GINA, 2012).

#### 1.2.6.2. Medications for the Management of Asthma

In recent years asthma is no longer thought of as a collection of intermittent symptoms but as a chronic syndrome (GINA, 2006). This shift in reference has changed the way the disease is treated. The idea of controlling asthma and preventing acute exacerbations has taken centre stage and reflects today's treatment. The goal of asthma treatment is to achieve and maintain clinical control with treatment medications usually referred to as "controllers" and "relievers" (EPR-3, 2007; GINA, 2006).

Medicines are used to prevent and control asthma symptoms, improve quality of life, reduce the frequency and severity of asthma exacerbations, and reverse airflow obstruction.

Scientifically asthma is a chronic disorder that is characterized with re-occurring episodes of reversible airway obstructions, mucous production and coughs and with varying degrees of severity.

Generally there are two broad categories of asthma medications, those referred to as preventers or long-term control medications and relievers or quick-relief medications. Preventers or long-term control medications are used by patients group in the class of those with persistent asthma to achieve and maintain control, whilst the reliever or quick-relief medication as used in the acute situation to reverse air-way constrictions.

#### 1.2.6.3. Long-term Control Medications

Various long-term asthma-control medications or preventers are currently in use to control asthma. The preventers are grouped by pharmacologic class into inhaled corticosteroids (ICS), inhaled long-acting bronchodilators, immunomodulators leukotriene modifiers, mast-cell stabilizers, and xanthine-oxidase inhibitors.

Due to the presence of lymphocytic and eosinophilic types of inflammation in the mucosa of the airways, the most commonly used and effective preventers are those that potentially block the inflammatory processes (Kerrebijn *et al*, 1987; Haahtela *et al*, 1991; Van Essen-Zandvliet *et al*, 1992).

Anti-inflammatory medications are those that cause a reduction in the markers of airway inflammation in airway tissue or airway secretions (e.g., eosinophils, mast cells, activated lymphocytes, macrophages, and cytokines; or ECP and tryptase; or extra-vascular leakage of albumin, fibrinogen, or other vascular protein) and thus decrease the intensity of airway hyper-responsiveness. Because many factors contribute to the inflammatory response in asthma, many drugs may be considered anti-inflammatory. It is not yet established, however, which anti-inflammatory actions are responsible for therapeutic effects, such as reduction in symptoms, improvement in expiratory flow, reduction in airway hyper-responsiveness, prevention of exacerbations, or prevention of airway wall remodelling (EPR-3, 2007).

#### 1.2.6.4. Quick-Relief Medications

Quick-relief medications are acute attacks to provide prompt relief from asthma symptoms and broncho-constriction of the airways. The current reliever medications in use are the short-acting beta-agonists (Salbutamol) and anti-cholinergics (Ipratropium bromide). Systemic corticosteroids with slower onset of action (>4 hours), are also used in the short-term management of moderate or severe exacerbations to prevent progression of the exacerbation, to increase speed to recovery, and prevent possible relapses (EPR-3, 2007; GINA, 2006).

### 1.2.7. Therapeutic Principles in the Management of Asthma

The goal of therapy for asthma as previously mentioned is to achieve and maintain asthma control with the minimum amount of asthma medications to avert the possible risk for adverse effects (EPR-3, 2007; GINA, 2012). Asthma control implies predominately reducing the impairment and risks associated with the asthma condition and its management with medicines.

The GINA (2006) guidelines contained an important change in approach to asthma management, placing the emphasis on assessing, treating, and monitoring patients based on level of *asthma control* rather than asthma severity (GINA, 2006). This has led to classification of asthma as "Controlled", "Partly Controlled", or "Uncontrolled" as presented in the table 1.3.

**Table 1.3:** Classification of Asthma by Level of Control (GINA, 2006)

| **Characteristics** | **Controlled (all of the following)** | **Partly Controlled (any measure present in any week)** | **Uncontrolled** |
|---|---|---|---|
| *Daytime symptoms* | *None (twice or less/week)* | *More than twice/week* | *Three or more feature of partly controlled asthma present in any week* |
| *Limitations of activities* | *None* | *Any* | |
| *Nocturnal symptoms/awakening* | *None* | *Any* | |
| *Need for reliever/rescue treatment* | *None (twice or less/week)* | *More than twice/week* | |
| *Lung function (PEF or $FEV_1$) ‡* | *Normal* | *<80% predicted or personal best (if known)* | |
| *Exacerbations* | *None* | *One or more/year** | *One in any week†* |

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

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

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

#### 1.2.7.1. Reducing Asthma-related Impairment

Asthma is associated with various impairments that affect the quality of life of patients. It is these components that are used to assess the levels of control as referred to in the GINA (2006) recommendations.

- Prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the daytime, in the night, or after exertion)
- Require infrequent use (≤2 days a week) of SABA for quick relief of symptoms
- Maintain (near) normal pulmonary function
- Maintain normal activity levels (including exercise and other physical activity and attendance at work or school)
- Meet patients' and families' expectations of and satisfaction with asthma care.

#### 1.2.7.2. Reducing the Risk Components of Asthma

Reducing risk implies the prevention of future events that may occur as a result of various interactions between the environmental factors, the genetic inherent factors and the application of medications (Agertoft & Pederson, 2000; CAMP, 2000). The therapeutic options for treatment should consider reducing the risk components of the disease condition:

- Prevent recurrent exacerbations of asthma and minimize the need for emergency department visits or hospitalizations
- Prevent progressive loss of lung function; for youths, prevent reduced lung growth
- Provide optimal pharmacotherapy with minimal or no adverse effects

Usually a step-by-step increase in pharmacologic therapy is recommended to achieve and maintain asthma control in both the impairment and risk domains (GINA, 2012):

— Asthma severity is considered when initiating therapy, and also in the determination of which medications and regimens to use in the achievement and maintenance of control

— Therapy step-down in medications and their regimens are recommended to maintain adequate control.

#### 1.2.7.3. Initiating Asthma Therapy

Based on the individual patient measurements of Asthma condition severity, in terms of impairment and risk, the appropriate treatment is selected to correspond to patient's level of severity (EPR-3, 2007; GINA, 2012).

#### 1.2.7.4. Monitoring and Follow-ups on Asthma Therapy

Monitoring of treatment is undertaking at 2- to 6-week intervals after initiating therapy, to ensure that asthma control is achieved (EPR-3, 2007; GINA, 2012).

- A regular review of condition at 1- to 6-month intervals is recommended to ensure maintenance of control and for adjustments in therapy where necessary.
- For an anticipated step down in therapy, 3-month intervals are considered.

#### 1.2.7.5. Adjusting Asthma Therapy

It is recommended that, a patient therapeutic decision is based solely on the level of the individual patients level of asthma control (Aburuz *et al*, 2005; EPR-3, 2007).

The current level of asthma control is generally classified by the most severe indicator of impairment or risk.

- If the patient's asthma is not well controlled:

  Identify the patient's current treatment step, based on what he or she is actually taking. In general, step up one step for patients whose asthma is not well controlled.

For patients who have very poorly controlled asthma, consider increasing by two steps, a course of oral corticosteroids, or both. Before increasing pharmacologic therapy, consider poor inhaler technique, adverse environmental exposures, poor adherence, or co-morbidities as targets for intervention.

- If the office spirometry suggests worse control than does the assessment of impairment based on other measures, (1) consider fixed airway obstruction as the explanation (Aburuz *et al*, 2005) and use changes from percent personal best rather than percent predicted to guide therapy; (2) reassess the other measures of impairment; and (3) if fixed airway obstruction does not appear to be the explanation, consider a step up in therapy, especially if the patient has a history of frequent moderate or severe exacerbations.
- If the history of exacerbations suggests poorer control than does the assessment of impairment, (1) reassess impairment; (2) review control of factors capable of making asthma worse (e.g., lack of adherence, adverse environmental exposure, or co-morbidities); (3) review the written action plan, and be sure it includes oral prednisone for patients who have histories of severe exacerbations; and (4) consider a step up in therapy, especially if the patient has reduced $FEV_1$.
- For troublesome or debilitating side effects, explore a change in therapy. In addition, confirm maximal efforts to control factors capable of making asthma worse.
- After treatment is adjusted, re-evaluate in 2–6 weeks, depending on the level of control.

#### 1.2.7.6. Assessing Asthma Control

In assessing asthma control, both the impairment and the risk domains must be considered, just like for the asthma severity. This ensures that the two domains are appropriately and

adequately addressed in the selection of therapy that is also based on the severe indicators of the impairment and the risk (Nathan *et al*, 2004; EPR-3, 2007).

#### 1.2.7.6.1. Assessing the Impairment Domain in Asthma Control

The multi-factorial components of the impairment domain manifestations differently in asthma and are not necessarily correlated with each other. Assessment of these components are derived from the frequency of the various asthma symptoms, the need or use reliever medication (SABA), pulmonary function test and the use of validated asthma specific questionnaires.

**Symptoms:** Activity limitation, asthma-related night-time awakening and symptom frequency assessment generates relevant information regarding asthma control (Vollmer *et al*, 1999; Fuhlbrigge *et al*, 2002; Nathan *et al*, 2004). However, the rate of occurrence of shortness of breath in a patient more reliably related to asthma control (Nathan *et al*, 2004) and the patients' health-related quality of life (Moy *et al*, 2001).

**Short-acting beta-agonist (SABA) use:** Assessment of the rate of SABA usage or need provides historical information of asthma control in either in the past month (Vollmer *et al*, 1999; Nathan *et al*, 2004) or the past year (Schatz *et al*, 2006). However the assessment must clearly separate quick relief usage from prophylactic usage of SABA.

**Pulmonary function:** Asthma control in treated patients may also be assessed with the use an office spirometry or a home peak expiratory flow meter prior to bronchodilator usage (Juniper *et al*, 1999a; Juniper *et al*, 2001; Bateman *et al*, 2004). However, it must be noted

that these measurements poorly correlates with asthma symptoms (Stahl, 2000; Shingo *et al*, 2001).

**Validated questionnaires:** Asthma control can also be assessed by various asthma-specific validated instruments (Juniper *et al*, 1999a; Vollmer *et al*, 1999; Nathan *et al*, 2004) which can further categorize the levels of asthma control.

#### 1.2.7.6.2. Assessing the Risk Domain of Asthma Control

The occurrence of treatment-related adverse effects and the frequency and severity of exacerbations constitutes the main components of the risk domain. Severe asthma exacerbations may be experienced by patients at any level of control of impairment. Asthma exacerbations leading to patient admission or emergency room visit may significantly increase the risk of future exacerbations (Lieu *et al*, 1998; Adams *et asthma al*, 2000; Cowie *et al*, 2001; Eisner *et al*, 2001; Yurk *et al*, 2004). A patient asthma-related hospitalization history is therefore very vital information. In addition, increasing exacerbation rates are noted with decreasing $FEV_1$ categories >80 percent, 60–79 percent, and <60 percent predicted (Fuhlbrigge *et al*, 2001, Kitch *et al*, 2004; Fuhlbrigge *et al*, 2006).

There seem not to be any association between the controls of impairment and the risk of exacerbations as may be generally envisaged (Vollmer *et al*, 1999; Schatz *et al*, 2005). However, some studies has demonstrated that control based on bronchial hyper-reactivity (Sont *et al*, 1999), sputum eosinophilia (Green *et al*, 2002), or possibly fractional exhaled nitric oxide (FeNO) (Smith *et al*, 2005) is more effective in reducing exacerbations than control based on clinical markers alone.

### 1.2.8. Asthma Drug Delivery Devices

Asthma management requires the use of drug delivery devices to deliver both reliever and preventer medicines in small quantities to their points of pharmacologic effect. These medicines are delivered in the form of aerosols by devices such as nebulizers, pressurized metered-dose inhalers or by dry-powder inhalers.

#### 1.2.8.1. Aerosol Inhalation Therapy

Aerosol inhalation therapy allows an almost ideal benefit to risk ratio to be achieved because very small doses of inhaled medication provide optimal therapy with minimal adverse effects (Taburet & Schmit, 1994). The aerosolized drugs are frequently able to control all but the most severe forms of asthma without the need for oral medication (Newhouse & Dolovich, 1986). However, the therapeutic efficacy of drugs administered by aerosolization depends on not only the pharmacological properties of the inhaled drug, but also the characteristics of the delivery device which influences the amount of drug deposited in the lungs and the pattern of drug distribution in the airways. Poor patient inhalation technique can further limit the amount of drug reaching the point of pharmacologic effect and therefore reduce the impact of action.

#### 1.2.8.2. Lung Deposition of Aerosol

The aerosol released on actuation of a metered dose inhaler (MDI) has a high initial velocity of 30-50 m/sec. (Atkin, 1992; Berg, 1995) and the droplets have an initial mean median diameter (MMD) of approximately 30 μm (Berg, 1995).

High aerosol velocity and the droplet size in relation to the shortness and small size of the natural mouth are most likely to cause the droplets to impact in the mouth and upper airway of the patient.

If drugs are to be effective when given by inhalation then it is essential that they are delivered to the correct site of action. The efficacy of a drug when given by the inhaled route will depend either upon the total amount of the drug deposited in the lungs or upon the regional site of the deposition within the lungs. In contrast, the systemic side effects of a drug are dependent on the amount of drug that is deposited in the lungs and the oropharynx, and the absorption of the drug into systemic circulation via these routes (Newman, 1995). Lung deposition from a MDI is therefore dependent upon both the physicochemical nature of the aerosol formulation and the patient's inhalation technique.

#### 1.2.8.3. Lung Availability /Total Systemic Availability Ratio

The relationship between the desired local effects and the unwanted systemic effects of inhaled therapy can be quantified in the lung availability / total systemic availability ratio (L/T ratio) (Borgstrom, 1991). This ratio allows a valid comparison to be made between different inhaler systems for the same drug when the following assumptions are made: the desired therapeutic effects are mainly exerted by locally available drug in the lungs; that no metabolism or inactivation takes place in the lungs; that the unwanted side effects are systemically mediated.

### 1.3. Pharmaceutical Care Concept

The term pharmaceutical care may have been used in published articles by Brodie to explain the concept pharmaceutical services in the light of medication-use services and control (Brodie, 1973; Brodie *et al,* 1980).

Hepler and Strand in 1990 defined pharmaceutical care as 'the responsible provision of drug therapy for the purpose of achieving definite outcomes which improve a patient's Quality of Life" (Helper & Strand, 1990).

The American Health System Pharmacist Association has further adapted the definition developed by Hepler and Strand to define Pharmaceutical care as "the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life".

The International Pharmaceutical Federation of (FIP) in a policy statement in 1998 defined pharmaceutical care as the responsible provision of pharmaco-therapy for the purpose of achieving definite outcomes that improve or maintain a patient's quality of life. And further suggests, "It is a collaborative process that aims to prevent or identify and solve medicinal product and health related problems". This is a continuous quality improvement process for the use of medicinal products (FIP Statement, 1998).

These guiding principles of practice are conceptual and may vary at length within various practice settings, but remain what can be delivered within the healthcare system if required.

### 1.3.1. Pharmaceutical Care - A Paradigm of Pharmacy Practice

The principal elements of pharmaceutical care in these definitions are that, it is *medication related*; it is *care* that is *directly provided* to the patient; it is provided to produce *definite outcomes*; these outcomes are intended to improve the patient's *quality of life*; and the provider accepts personal *responsibility* for the outcomes (ASHP Statement, 1993).

***Medication Related:*** Pharmaceutical care involves not only medication therapy (the actual provision of medication) but also decisions about medication use for individual patients. As appropriate, this includes decisions *not* to use medication therapy as well as judgments about medication selection, dosages, routes and methods of administration, medication therapy monitoring, and the provision of medication-related information and counselling to individual patients.

***Care:*** Central to the concept of care is caring, a personal concern for the well-being of another person. Overall patient care consists of integrated domains of care including (among others) medical care, nursing care, and pharmaceutical care. Health professionals in each of these disciplines possess unique expertise and must cooperate in the patient's overall care. At times, they share in the execution of the various types of care (including pharmaceutical care). To pharmaceutical care, however, the pharmacist contributes unique knowledge and skills to ensure optimal outcomes from the use of medications.

At the heart of any type of patient care, there exists a one-to-one relationship between a caregiver and a patient.

In pharmaceutical care, the irreducible "unit" of care is one pharmacist in a direct professional relationship with one patient. In this relationship, the pharmacist provides care directly to the patient and for the benefit of the patient. The health and well-being of the patient are paramount.

The pharmacist makes a direct, personal, caring commitment to the individual patient and acts in the patient's best interest. In a bid to improve the quality of life of the patient, the pharmacist cooperates directly with other the other health care team members as well as the patient and designs for implementation and monitoring, a plan of the therapy with an intention to achieve specific measurable outcomes.

***Outcomes:*** It is the goal of pharmaceutical care to improve an individual patient's quality of life through achievement of definite (predefined), medication-related therapeutic outcomes. The outcomes sought are (ASHP Statement, 1993):

- Cure of a patient's disease.
- Elimination or reduction of a patient's symptomatology.
- Arresting or slowing of a disease process.
- Prevention of a disease or symptomatology.

This, in turn, involves three major functions: (1) identifying potential and actual medication-related problems, (2) resolving actual medication-related problems, and (3) preventing potential medication-related problems.

### 1.3.2. Medication-related Problems in Drug Therapy

A medication-related problem is an event or circumstance involving medication therapy that actually or potentially interferes with an optimum outcome for a specific patient.

There are at least the following categories of medication-related problems (Helper & Strand, 1990):

- *Untreated indications.* The patient has a medical problem that requires medication therapy (an indication for medication use) but is not receiving a medication for that indication.
- *Improper drug selection.* The patient has a medication indication but is taking the wrong medication.
- *Sub-therapeutic dosage.* The patient has a medical problem that is being treated with too little of the correct medication.
- *Failure to receive medication.* The patient has a medical problem that is the result of not receiving a medication (e.g., for pharmaceutical, psychological, sociological, or economic reasons).
- *Over-dosage.* The patient has a medical problem that is being treated with too much of the correct medication (toxicity).
- *Adverse drug reactions.* The patient has a medical problem that is the result of an adverse drug reaction or adverse effect.
- *Drug interactions.* The patient has a medical problem that is the result of a drug–drug, drug–food, or drug– laboratory test interaction.
- *Medication use without indication.* The patient is taking a medication for no medically valid indication.

Patients may possess characteristics that interfere with the achievement of desired therapeutic outcomes. Patients may be noncompliant with prescribed medication use regimens, or there may be unpredictable variations in patients' biological responses. Thus, in an imperfect world, intended outcomes from medication-related therapy are not always achievable.

Patients bear a responsibility to help achieve the desired outcomes by engaging in behaviours that will contribute to—and not interfere with—the achievement of desired outcomes.

Pharmacists and other health professionals have an obligation to educate patients about behaviours that will contribute to achieving desired outcomes.

### 1.3.3. Responsibility of Pharmaceutical Care-Provider

The fundamental relationship in any type of patient care is a mutually beneficial exchange in which the patient grants authority to the provider and the provider gives competence and commitment to the patient (accepts responsibility) (Hepler & Strand, 1990). Responsibility involves both moral trustworthiness and accountability.

In pharmaceutical care, the direct relationship between an individual pharmacist and an individual patient is that of a professional covenant in which the patient's safety and well-being are entrusted to the pharmacist, who commits to honouring that trust through competent professional actions that are in the patient's best interest. As a responsible member of the health-care team, the pharmacist must document the care provided (Penna, 1990; APhA Statement, 1990; Galinsky & Nickman, 1991; Angaran, 1991). The pharmacist is personally accountable for patient outcomes (the quality of care) that ensue from the pharmacist's actions and decisions (Brodie, 1973).

## 1.4. Health-related Quality of Life

Health is one important domain of the overall quality of life concept, but complexity of it measurement may be related to spirituality, culture and social values of a setting (The WHOQOL Group, 1998). Scientists have over the years developed techniques that cater for the complexities and capture the various relationships.

Since the 1980s, the determinants of health of the concept of health-related quality of life (HRQoL) have been identified and shown to impact on health—either physical or mental (McHorney, 1999; CDC, 2000; Gandek *et al*, 2004; Selim *et al*, 2009).

There is a general believe that the individual patients perception of the functional impact his or her health condition and therapeutic management constitutes the HRQoL for the said patient (Cela, 1995; Schipper *et al*, 1996). The basis therefore of measuring HRQoL is to capture in a responsible but valid ways, the extent of the impact of these components of health and its management. The Centre for Outcomes Research and Education (CORE, 2013) likens the modern concept of HRQoL as a direct descendent of the World Health Organization definition; in that HRQoL is now thought to encompass three fundamental domains: *biological functioning, psychological functioning, and social functioning*, and that a balanced measure of HRQoL captures all of these domains and summarizes them in a single metric (CORE, 2013).

On the individual level, HRQoL includes physical and mental health perceptions and their correlates—including health risks and conditions, functional status, social support, and socioeconomic status. On the community level, HRQoL includes resources, conditions, policies, and practices that influence a population's health perceptions and functional status (WHOQOL Group, 1998; Kindig *et al*, 2010).

The components of HRQoL engulf a broader stakeholder involvement and bring together for public policy development various players from within wider circle health-related partners. This ensures a collaborative partnership between the health care services, the business groups, the social agencies as well as community planner among others (Kindig *et al,* 2010).

The various domains of the overall general HRQoL are considered valid indicators of service and outcomes measure in health surveillance (Dominick *et al,* 2002). Compared to other objective measures of health, the patient self-assessment of their health status tend to provide a more in-depth information on morbidity and mortality (Dominick *et al,* 2002; DeSalvo *et al,* 2006)

The assessments and interpretations of HRQoL offers a more scientific way of measuring the impact of health on people's quality of life far more than exist previously.

### 1.4.1. Importance of Tracking HRQoL

Studying HRQoL can serve as a supplement to traditional public health measures of morbidity and mortality and also as a rallying point for stakeholder collaboration between the health, mental and social services (CDC, 2000).

The main functions for which HRQoL measures are used may be classified as discrimination, evaluation and prediction (Kirshner & Guyatt, 1985).

Feeny and colleagues (1999) describe the purposes of population monitoring in asthma as to discern subgroups of the population who have greater or lesser impacts attributable to asthma (Feeny *et al,* 1999). This requires an instrument that can discriminate between groups with a

higher burden of disease. High burden subgroups identified in this way may then be targeted for specific interventions or further investigation into the causes (e.g. environmental, economic or cultural) of the observed disparities (AIHW, 2004).

The evaluative measure of the HRQoL is useful in assessing the impact of various health interventions (clinical trials, programs or management guidelines) by tracking change in outcome sover time (AIHW, 2004).The key attributes of these measurement instruments is that they are valid measures of change in HRQoL and that they are responsive to within-subject change in the HRQoL attributes (Kirshner & Guyatt, 1985).

Predictive instruments are used in HRQoL measurement either to predict the result in another measure or to forecast an outcome at a future time (Feeny *et al*, 1999). These can be useful for assisting in decision making processes, classifying individuals entering a study or identifying those who are likely to develop a particular outcome (Kirshner & Guyatt, 1985).

Predictive HRQoL measures might be used to predict future health needs and economic impacts. For example, Eisner *et al* (2002) conducted a prospective cohort study aiming to determine the effectiveness of HRQoL measures for identifying those at risk of adverse health outcomes. This study measured HRQoL using the Short-Form 12 questions (SF-12) and the Integrated Therapeutics Group Asthma Short Form (ITG-ASF) battery measurement instruments to test HRQoL as a predictor of future health care utilisation based upon the subjects' current asthma status and known risk factors for health care utilisation. It found that people with better baseline asthma-specific HRQoL scores had a significantly lower risk of all cause hospitalisation.

The focus of the content within a HRQoL instrument may be on impacts that are relevant to a specific disease or, alternatively, on impacts that are relevant to a broad range of health conditions. Both generic and disease-specific instruments have a role in the assessment of HRQoL. Generic questionnaires aim to assess the impact of any and all adverse health states on HRQoL, without reference to the impacts of any specific disease. Disease-specific HRQoL instruments measure the specific impacts of the target disease (AIHW, 2004).

Studying HRQoL can provide insight on the extent diseases and disabilities as well as the relationships between HRQoL and possible risk factors.

HRQoL surveillance data can also provide information on subgroups within society with poor perception of health and also help with the resolution of these health problems before they become complicated. This can serve as a guide for broader community intervention strategies and monitoring, the basis for health policy formulation and implementation and resource allocation to address unmet needs of society.

For the elderly and in consideration of increasing life expectancy, HRQoL studies comes in as a handy public health tool to help address the goals of improving health irrespective of the impact of health effects on aging (CDC, 2000).

### 1.4.2. Health-related Quality of Life and Asthma

Even though there are no generally agreed definition of ‘control’ or ‘severity’ in relation to asthma, severity is often regarded as an inherent abnormality, which when modified by variable environmental exposures and by treatments, results in a given level of ‘control’ (AHIW, 2004). This implies that control is inherently modifiable but ‘severity’ is not. According to this framework, it is virtually impossible to measure the ‘severity’ of asthma in

the real world since the expression of the disease will almost always be modified by environmental and/or treatment factors.

HRQoL is an outcome of asthma. People with inherently severe asthma can be expected, on average, to have worse outcomes and, hence, worse HRQoL than people with less severe disease. Similarly, since 'control' is intended as a predictor of asthma outcomes, it would be expected that during periods of poor asthma control, HRQoL would be poorer (Vollmer *et al*, 1999). However, as noted above, HRQoL is not the same as asthma severity or asthma control (Juniper *et al*, 2004). HRQoL can be regarded as a broad-ranging, but not all encompassing, outcome of asthma.

### 1.4.3. Health-related Quality of Life Measures

Standardization of HRQoL measures for use in studies is essential, especially for the evaluation of health goals in the population, assessment disparities within the population and the measurement of the effectiveness of interventions to address age-related diseases.

There are generic HRQoL instruments in use for the purposes of general summaries of the the health of the population and there also specific HRQoL instruments for issues related to single disease conditions, patient groups or certain areas of function.

### 1.4.4. Generic Health-related Quality of Life Instruments

Generic HRQoL instruments profiles the health of a population or generates information on health utilities. The information generated from these instruments may be suitable for different circumstances and they may also have different strengths and weaknesses.

#### 1.4.4.1. The Short Form-36v2

The Short-form 36 (SF-36) is an 8-scale multi-purpose survey instrument with 36 questions. It profiles psychometrically-based mental and physical health summaries in addition to preference-based health utility index. It comes as a respondent-based or interviewer-based instrument. The SF-36 has been used in studies involving general and specific populations, and for comparative assessment disease burden and health benefits within various sub-groups. The SF-36v2 is the new version of the instrument that was designed to cater for the shortcomings of the original version and to expand the responses options of some the scales and to improve the instructing and wording of some of the items in the instrument (Ware *et al*, 2000; Ware & Kosinki, 2001).

#### 1.4.4.2. The European Quality of Life-5D

The EQ-5D instrument was developed to serve as a generic tool by a multi-disciplinary group from Western Europe. The EuroQol group formed in 1987, comprise of researchers Finland, England, the Netherlands, Norway and Sweden. approach most commonly used in the European community is the EQ-5D. The instrument has 14 health states in 5 different domains. The domains are self-care, activity, mobility, anxiety or depression and pain (The EuroQol Group, 1990).

#### 1.4.4.3. The Quality of Well-Being Scale

The Quality of Well-Being Scale (QWB) has been used in numerous clinical trials and studies over the years to evaluate medical and surgical therapies in conditions.

The instrument is available in two forms; as a self-administered tool (QWB-SA) or as an interviewer- administered (QWB) tool. The two tools have been found to shown high correlation to each other and retain its psychometric properties.

Functioning is assessed by a series of questions designed to record functional limitations over the previous three days, within three separate domains (mobility, physical activity, and social activity). The four domain scores are combined into a total score that provides a numerical point-in-time expression of well-being that ranges from zero (0) for death to one (1.0) for asymptomatic optimum functioning (ATS, 2007; Anderson & Kaplan, 2008).

#### 1.4.4.4. The Health Utility Index

The Health Utilities Index (HUI) is a family of generic health status and health related quality of life measures developed at McMaster University in Canada over the last 30 years. The HUI has been applied by hundreds of researchers around the world. Questionnaires which provide sufficient information to describe the health status of a subject at a point in time for both the HUI2 and HUI3 systems have been developed. The HUI2 was initially developed to assess outcomes among childhood cancer survivors. The attributes measured by the HUI2 are sensation (vision, hearing, and speech), mobility, emotion, cognition, self-care, pain, and fertility. The HUI3 was originally developed for the 1990 Statistics Canada Ontario Health Survey, and measures eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain). Multiplicative multi-attribute utility functions for the HUI2 and HUI3 translate categorical data on health status collected in the questionnaires into interval scale single attribute utility scores and overall utility scores, reflecting overall health related quality of life. While there is some overlap between HUI2 and HUI3, in other ways the two systems complement each other. HUI2 has been extensively used in clinical

studies, providing useful benchmark results for comparisons. HUI3 has been used in four major Canadian population health surveys, providing extensive data on population norms (Feeny *et al*, 1996).

#### 1.4.4.5. The Health and Activities Limitations Index

The Health and Activities Limitations Index (HALex) was initially developed for use in the National Health Interview Survey, conducted by the National Centre for Health Statistics in the 1980s and 1990s. The version of the measurement tool being used for this program of research was adapted from the original version, specifically to be used for telephone interview surveys conducted for the Behavioural Risk Factor Surveillance Survey (BRFSS) by the Centre for Disease Control and Prevention (CDC), for calculating Healthy People 2000 Years of Healthy Life. This measurement instrument focuses on obtaining information on how health problems may inhibit or limit people in performing work-related functions or daily activities of life (Erickson, 1998).

### 1.4.5. Asthma-specific Health-related Quality of Life Measures

The disease-specific measures for asthma that have been used in population surveys are mainly single item, single dimension measures such as ‘sick days due to asthma’ and ‘nights woken due to asthma’, but these cannot be considered holistic measures of asthma-related quality of life. Asthma monitoring surveys can best be accomplished by including multi-item, multi-dimensional measures such as the Asthma Quality of Life Questionnaire (McMaster) (AQLQ-McMaster), the Mini Asthma Quality of Life Questionnaire (McMaster) (Mini-AQLQ-McMaster), the Standardised Asthma Quality of Life Questionnaire (McMaster) (AQLQ(S)-McMaster), the Sydney Asthma Quality of Life Questionnaire (AQLQ-

Sydney),the Asthma Symptom Utility Index(ASUI), Integrated Therapeutics Group Asthma Short Form (ITG-ASF), the Living with Asthma Questionnaire (Hyland) (LWAQ), the Quality of Life for Respiratory Illness questionnaire (QoLRIQ), or the St George's Respiratory Questionnaire (SGRQ).

#### 1.4.5.1. The Asthma Quality of Life Questionnaire (McMaster)

The Asthma Quality of Life Questionnaire (AQLQ) (McMaster) was developed to measure the functional problems (physical, emotional, social and occupational) that are most troublesome to adults (17-70 years) with asthma. There are 32 questions in the AQLQ and they are in 4 domains (symptoms, activity limitation, emotional function and environmental stimuli). The AQLQ questionnaire has a time specification of two weeks and patients are to recall their experiences during the previous 14 days. In the original AQLQ-McMaster, five of the activity questions in the activity domain are patient-specific, which means that each participant in a study identifies and scores five activities in which they are limited by their asthma. In follow-up studies, it becomes impractical, since participants tend to change their activities over time and it is also difficult to convince staff not to change the list. Therefore the development of a standardized version AQLQ(s) (McMaster) with five formulated generic items to replace the five patient-specific items in the AQLQ-McMaster. In a comparative study by Juniper and colleagues (1999b) to validate the standardize version of the AQLQ, five formulated generic activities (strenuous exercise, moderate exercise, work-related activities, social activities, and sleep) replaced the five patient-specific activities in the AQLQ to generate AQLQ(s). In a 9-week observational study, they compared the AQLQ with the AQLQ(S) and examined their measurement properties. Forty symptomatic adult asthma patients completed the AQLQ(S), the AQLQ, the Medical Outcomes Survey Short Form 36, the Asthma Control Questionnaire, and spirometry at baseline, 1, 5, and 9 weeks.

Their findings revealed that activity domain scores (mean +/- SD) were lower with the AQLQ (5.7 +/- 0.9) than with the AQLQ(S) (5.9 +/- 0.8; p = 0.0003) and correlation between the two was moderate (r = 0.77). However, for overall scores, there was minimal difference (AQLQ, 5.4 +/- 0.8; AQLQ(S), 5.5 +/- 0.8; r = 0.99). Reliability (AQLQ intra-class correlation coefficient, 0.95; AQLQ(S) intra-class correlation coefficient, 0.96) and responsiveness (AQLQ, p < 0.0001; AQLQ(S), p < 0.0001) were similar for the two instruments. Construct validity (correlation with other measures of health status and clinical asthma) was also similar for the two instruments. They concluded that the choice of instrument should depend on the task at hand (Juniper *et al,* 1999b).

#### 1.4.5.2. The Mini Asthma Quality of Life Questionnaire (McMaster)

In response to a demand for a shorter, quicker version for large clinical trials and for managed care monitoring, Juniper and colleagues (1999c) developed and fully validated the Mini-AQLQ (McMaster). This instrument has 15 questions in the same domains as the original AQLQ (symptoms, activities, emotions and environment) and takes 3-4 minutes to complete. The Mini-AQLQ has very good reliability, cross-sectional validity, responsiveness and longitudinal validity. However, as might be expected with a shorter questionnaire, none of these properties are quite as good as those of the original AQLQ and the AQLQ(S). Like the AQLQ and the AQLQ(S), a change in score of greater than 0.5 can be considered clinically important (Juniper *et al,* 1999c).

In a comparative study to develop a mini-instrument to meet the needs of large clinical trials and long-term monitoring of asthma, where efficiency may take precedent over precision of measurement, Juniper and colleagues (1999c) tested the Mini-AQLQ in a 9-week observational study of 40 adults with symptomatic asthma. Patients completed the Mini-

AQLQ, the AQLQ, the Short Form (SF)-36, the Asthma Control Questionnaire and spirometry at baseline, 1, 5 and 9 weeks. In patients whose asthma was stable between clinic visits, reliability was very acceptable for the Mini-AQLQ (intra-class correlation coefficient (ICC)=0.83), but not quite as good as for the AQLQ (ICC=0.95). Similarly, responsiveness in the Mini-AQLQ ($p=0.0007$) was good but not quite as good as for the AQLQ ($p<0.0001$). Construct validity (correlation with other indices of health status) was strong for both the Mini-AQLQ and the AQLQ. Criterion validity showed that there was no bias between the instruments ($p=0.61$) and the correlation between them was high ($r=0.90$). They concluded that the Mini Asthma Quality of Life Questionnaire has good measurement properties but they are not quite as strong as those of the original Asthma Quality of Life (Juniper *et al*, 1999c).

#### 1.4.5.3. The St. George's Respiratory Questionnaire

The St George's Respiratory Questionnaire (SGRQ) is a standardized self-completed questionnaire for measuring impaired health and perceived well-being ('quality of life') in airways disease. It has been designed to allow comparative measurements of health between patient populations and quantify changes in health following therapy (Jones *et al*, 1991).The questionnaire has 50 items with 76 weighted responses. It has good discriminative and evaluative properties and is responsive to therapeutic trials. It was developed and validated in both asthma and COPD. It takes 8-15 minutes to complete and is best scored using a computer. The SGRQ is best thought of as a research or audit tool.

The **SGRQ-C is** a shorter version of the SGRQ, derived from the original version following detailed analysis of data from large studies in COPD. The SGRQ-C has been developed using COPD data only, so is valid for this disease.

In a sample of asthmatic patients, representative of a broad spectrum of asthma severity, Sanjuás and colleagues (2002) studied 116 patients with a mean age (SD) of 42.6 (18.3) year. Patients were assessed twice, at recruitment and after 2 months, to determine the reliability, validity and responsiveness of the AQLQ and the SGRQ. Both questionnaires showed good reliability coefficients (> or = 0.70) which reached the standards for comparison at individual level (> or = 0.90) in the case of activity, impacts and overall SGRQ scores as well as symptoms, activities and overall AQLQ scores. Both AQLQ and SGRQ were able to discriminate among groups of patients based on asthma severity and control and showed, except for the symptoms domain of the SGRQ, large (standardized response means >0.8) and significant changes in the group of patients that improved at follow-up. They concluded that the AQLQ and SGRQ have shown high reliability and validity and, with the exception of the SGRQ symptoms, a high level of responsiveness. In overall terms, not one of these instruments seems to behave better than the other.

#### 1.4.5.4. The Sydney Asthma Quality of Life Questionnaire

The AQLQ-Sydney is a self-administered questionnaire that comprises 20 items with a four-week recall period. The average time needed to complete the questionnaire is five minutes. Lower ratings indicate less impairment (better quality of life). Each item has five response options ranging from “not at all” (scored 0) and “very severely” (scored 4). The total score is calculated as the mean of the 20 item scores, rescaled to a score out of 10 by multiplying the result by 2.5. Four subscale scores can also be calculated as means of subsets of the items, each multiplied by 2.5. Items are grouped into four domains (breathlessness: five items, mood: five items, social: seven items, concerns: three items). For the AQLQ-S, a minimal important difference that should warrant clinical intervention has not been reported in the literature (Marks *et al*, 1992).

#### 1.4.5.5. Living with Asthma Questionnaire

The Asthma Questionnaire is a 68-item quality of life scale designed to be sensitive to quality of life changes in clinical trials. The questionnaire covers 11 domains of life experience, the initial domain and item sets being derived from six qualitative focus groups of asthma patients. Psychometric analysis of responses of 101 asthma patients to the initial 101-item set showed the scale to be one-dimensional despite being multi-domain, and the finding of unidimensionality was replicated during the further three stages of item refinement using 783 patients. The scale compensates for acquiescence bias as well as allowing a 'not applicable' response category. Validity of the scale was demonstrated by confirmation of expected group differences and the retest reliability was 0.948.

In a double-blind, parallel group study involving 120 moderate asthma patients, aged between 18-70 yrs., Rutten-van Mölken and colleagues (1995) assessed the sensitivity to change and the construct validity of four different quality of life instruments in patients with asthma. Patients received either inhaled Salmeterol 50 micrograms twice daily or inhaled Salbutamol 400 micrograms twice daily. In addition to respiratory outcomes, quality of life was measured at a 6 weeks follow-up using: the Asthma Quality of Life Questionnaire (AQLQ); the Living with Asthma Questionnaire (LWAQ); the Sickness Impact Profile (SIP); the Rating Scale (RS); and the Standard Gamble (SG) utilities. Salmeterol led to significant improvements over Salbutamol on virtually all clinical outcomes. Although all the quality of life instruments showed the same trend in favour of Salmeterol, only the AQLQ and RS utilities showed significantly greater improvement on Salmeterol than on Salbutamol. Except for the AQLQ, the correlation between change in lung function and change in quality of life was generally low. Whereas, the AQLQ correlated well with the patient's overall assessment of efficacy ($r = 0.64$), the LWAQ, SIP and utilities failed to show such a correlation. The AQLQ showed the

best correlation with symptom scores. The cross-sectional correlation between the AQLQ and the LWAQ was 0.73, whereas the longitudinal correlation was only 0.29. The SG generally showed poor correlation with other measures, including the RS.

From their findings they concluded that patients given Salmeterol showed a greater improvement in quality of life compared to patients given Salbutamol. Of the disease-specific questionnaires the Asthma Quality of Life Questionnaire was found to be more responsive to change than the Living with Asthma Questionnaire and showed greater validity. Of the generic instruments, the rating scale utilities were most responsive. The Standard Gamble showed poor correlation with other measures (Rutten-van Mölken *et al*, 1995).

Beyond the high respondent burden of the LWAQ than the AQLQ, the later demonstrated greater validity and responsiveness.

In a similar study to compare the responsiveness of health status scores in asthmatic patients during treatment, Oga and colleagues (2002) used three different disease-specific measures: the AQLQ, the LWAQ, and the Airways Questionnaire 20 (AQ20). They followed up 170 patients with newly diagnosed asthma over a 6-month period. A total of 109 patients completed the study. Patients underwent treatment with inhaled corticosteroids in accordance with the guideline. A health status evaluation using the three disease-specific measures, and pulmonary function tests were performed on the initial visit, and at 3 months and 6 months. The effect size and the standardized response mean were used as responsiveness indices. Their results indicated that all health status scores and $FEV_1$ measures improved during the first 3 months ($p < 0.001$) and that the total of the AQLQ scores showed high responsiveness indices ranging from 1.28 to 1.46 between baseline and 3 months, and baseline and 6 months. Spearman correlation coefficients were smaller between the change in $FEV_1$ and the change in the LWAQ. Although the AQ20 also demonstrated high responsiveness, a ceiling effect

was indicated. They also concluded that the AQLQ was the most responsive measure during asthma treatment. The relationship between the change in airflow limitation and the change in the LWAQ was weaker compared to the AQLQ and the AQ20. Although the AQ20 was also responsive and its simplicity is favourable, the ceiling effect should be considered when using it (Oga *et al*, 2002).

#### 1.4.5.6. Assessment of Heath-related Quality of Life Measures

The Australian Institute of Health and Welfare (AIHW, 2004) developed a framework to evaluate various HRQoL measurement instruments with the purpose to identify measures that would be sensitive to differences between populations, subgroups and changes over time; including content that was relevant to HRQoL concerns of people with asthma and, hence, be valid as measures of HRQoL impact of asthma; and also be meaningful and useful in populations with and without asthma. The framework for describing, assessing and making recommendations relating to the suitability of these instruments for population monitoring is described in Table 1.4. This framework included a rating out of six stars (Table 1.5).

**Table 1.4:** Framework for Assessing HRQoL Measurement Instruments (AIWA, 2004)

| | |
|---|---|
| Type of instrument | The type of HRQoL measurement instrument: global, profile or utility measure |
| HRQoL domains | The domains included in instrument: global, physical, psychological and social |
| Content areas | A description of the dimensions included in each instrument |
| Mode of administration | How the instrument was administered (e.g. self-administered, interview, computer assisted telephone survey) |
| Respondent burden | Time effort and other demands placed on those completing the instrument |
| Time recall | The time period over which respondents were asked to recall events |
| Settings used | The setting(s) in which the study using the instrument was conducted |
| Reliability | Internal consistency: the extent to which elements of the questionnaire are measuring the same domain (quantified with Cronbach's α<br>Test–retest repeatability: the extent to which the repeated administration of the instrument under the same conditions results in similar scores (quantified with the interclass correlation coefficient—ICC) |
| Validity | The degree to which an instrument measures what it is supposed to measure |
| *Content validity* | The extent to which the material covered by the instruments encompasses, and is limited to, the intended purpose of the questionnaire. Provides an evaluation of the processes used to derive the content of the instrument. This includes:<br>Source of items: source from which items for the instrument were identified, such as from focus groups (qualitative methods) or previous questionnaires; and<br>Method of selection of items: process used to select items for inclusion in the final instrument (e.g. psychometric methods such as factor analysis). |
| *Construct validity*. | The extent to which the correlation with or difference from other measures, such as markers of disease severity, accords with theoretical expectations |
| *Criterion validity* | Describes comparisons with a gold standard. This method of assessment is not applicable to the evaluation of HRQoL measures. |
| Responsiveness | Describes evidence of the ability of an instrument to detect changes in individuals over time |
| Sensitivity | Describes evidence of the ability of an instrument to detect differences between populations / subgroups / repeated surveys |
| Australian data | Identifies studies implementing the instrument in Australia |
| Other comments | Any further information that informs the overall evaluation of the instrument |
| Usefulness for population monitoring | A star rating system used to rate the usefulness of a measure for population monitoring based on six key questionnaire attributes |

**Table 1.5:** Evaluation Rating System for HRQOL Instruments (AIWA, 2004)

| **Attribute** | ★ | ☆ | **No star** |
|---|---|---|---|
| **Respondent burden (RB)** | <3 minutes to complete, or approximately 1–5 items | 3–9 minutes to complete, or approximately 6–20 items | 10+ minutes to complete, or >20 items |
| **HRQoL domains (D)** | Samples from physical, psychological and social Domains | Global domain sampled Samples | one or two of physical, psychological and social domains |
| **Construct validity (CV)** | Extensive evidence (consistent with several other measures) | Some evidence | No evidence |
| **Test–retest repeatability (T–R)** | ICC>0.7 | ICC 0.4–0.7 | ICC<0.4 |
| **Internal consistency (IC)** | Cronbach's α > 0.7 | Cronbach's α 0.4–0.7 | Cronbach's α <0.4 |
| **Sensitivity (S)** | Extensive evidence (several studies) | Some evidence | No evidence |

*Note:* Where there was a range of values for an attribute for a questionnaire, the least favourable value was used as the basis for the rating.

In their evaluation, the original AQLQ was scored 5stars out of 6, while the Mini-AQLQ and the AQLQ(s) was scored 4 stars (AIHW, 2004). However from the above discussions, selection of the instrument is that of choice and dependent on the task on hand. The task in this project is mainly evaluative and cross-sectional, as a result an instrument that uses generic (AQLQ(s)) rather than patient-specific (AQLQ) activities was more appropriate. The difference in respondent burdens between the use of AQLQ(s) and that of AQLQ instruments are minimal, but the correlation (r) between the two is very high (0.99) (Juniper *et al*, 1999c). The Mini-AQLQ has a low sensitivity but lesser respondent burden and correlates at 0.90 with the AQLQ (Juniper *et al*, 1999c).

In relation to respondent burden, the SGRQ contains more items (76) than the AQLQ-McMaster and the AQLQ-Sydney, and takes approximately 10 minutes to complete. The AQLQ-McMaster contains 32 items and takes 10–15 minutes to complete while the AQLQ-Sydney contains 20 items and takes around five minutes to complete. Therefore, the AQLQ-Sydney has the lowest respondent burden, which is an advantage when including the instrument as a component in a broader population health survey, and is reflected in its higher rating than the other measures. Moreover, the Mini AQLQ-McMaster retains five non-standardised items, which makes it unsuitable for use in cross-sectional surveys.

The SGRQ was designed for use in people with both asthma and chronic obstructive pulmonary disease (COPD) whereas the other questionnaires are designed for use only in adults with asthma. This broader range of the SGRQ comes at the cost of less disease specificity and, hence, potentially less sensitivity and responsiveness (Sanjuas *et al*, 2002).

The SGRQ, AQLQ-McMaster and AQLQ-Sydney have been mainly used in clinical populations of patients with asthma. However, some have been used in population-based samples of patients with asthma (Marks *et al*, 1997; Premaratne *et al*, 1999).

All three questionnaires have been shown to have good test–retest reliability: AQLQ-McMaster (intra-class correlation coefficient, ICC>0.9), SGRQ (ICC>0.9), and AQLQ-Sydney (intra-class correlation coefficient =0.8) (AIWA, 2004).

### 1.5. Project Justification

Asthma is a prevalent disease that constitutes a growing public health problem. It is one of the world's most common chronic diseases that kill about 250,000 people every year (Masoli *et al*, 2004; GINA, 2004). Even though no cure has currently been discovered for asthma, the disease can be managed and effectively treated (Masoli *et al*, 2004). However, beyond the

pharmacologic treatment and the control of environmental and co-morbid conditions, education for a partnership is highly recommended for the management of asthma (GINA, 2006; EPR-3, 2007).

The effects of asthma on quality of life are also significant (AIHW, 2010), and the asthma burden across health care in general has been noted as significant and increasing (Bahadori *et al*, 2009). Within the period 2006 to 2010, new out-patient asthma case reports at public health facilities in Ghana (excluding teaching hospitals) doubled from 0.2% to about 0.4% of out-patient attendance (MoH-GHS Report, 2011).

Even though asthma is incurable, appropriate management can control the disorder and enable people to enjoy a high quality of life (WHO, 2011). Evidence is now abundant that asthma self-management education is effective in improving outcomes of chronic asthma (GINA, 2006; EPR-3, 2007). This implies that patients must actively participate in their own care and consciously use strategies and take actions to minimize exposure to factors that make their asthma harder to control and also be able to adjust treatments to improve their condition. However, patient adherence to asthma medication regimens, tend to be very poor, with the reported rates of non-adherence ranging from 30% to 70% (Rand & Wise, 1994; Bender & Bender, 2005; GINA, 2012), posing a real challenge to patient self-management.

A number of factors have been identified that are associated with non-adherence to asthma therapy (Williams *et al*, 2004; Bender & Bender, 2005; GINA, 2012). Medication-related factors such as difficulties with inhaler devices, complex regimens, side effects, cost of medication, dislike of medication, and distant pharmacies. Other associate factors, unrelated to medications may include but not limited to misunderstanding or lack of instruction, fears about side effects, dissatisfaction with health care professionals (Wells *et al*, 2008). But because poor adherence attenuates optimum clinical benefit (Dunbar-Jacob *et al*, 2000),

patient adherence has been referred to as a primary determinant of the effectiveness of treatment (WHO Report, 2002).

The WHO attributes other important factors to non-adherence that are said to be behavioural in nature and are also dynamic, and therefore amenable to intervention (Sabaté, 2003) and suggests changes in provider, health systems and patient behaviours (WHO, 2003), since non-adherence to medication treatment can have serious consequences in chronically ill patient populations, including poor clinical outcomes, higher re-hospitalization rates, and increased health care costs (Haynes *et al*, 2008; Burman *et al*, 2008; Pinsky, 2009).

In asthma, 'control' is intended as a predictor of management outcomes and therefore it would be expected that during periods of poor asthma control, the health-related quality of life of the patient would be poorer (Vollmer *et al*, 1999), even though the HRQoL is not the same as asthma severity or asthma control (Juniper *et al*, 2004). Self-assessed health status had been suggested to be a more powerful predictor of mortality and morbidity than many objective measures of health (Dominick *et al*, 2002; DeSalvo *et al*, 2006) and the main functions for their use is classified as discrimination, evaluation and prediction (Kirshner & Guyatt, 1985) of health outcomes and conditions.

As a follow-up from various reports recommending pharmacy-based education to asthma patients, that is directed towards the understanding of their medications, the teaching of inhaler skills, as well as home-based intervention skills to increase patient and family capacity to control allergen and irritant exposure (Custovic *et al*, 2000; Morgan *et al*, 2004; Eggleston *et al*, 2005; Klinnert *et al*, 2005; Krieger *et al*, 2005; McConnell *et al*, 2005), this project assessed the impact of pharmaceutical care delivered by pharmacists to asthma patients.

Findings of community pharmacy-based interventions by Cordina *et al* (2001), Saini *et al* (2004) among others have already shown positive results that need to be harnessed. However, findings by Stergachis *et al* (2002) also bring to the fore possible methodological problems in the assessment of the pharmacy impact. Most studies employed case-control methodologies for the assessment of their interventions with varied results. In their report, Stergachis and colleagues (2002) attributed the role of the intervention pharmacist to the negative results of their investigations among other confounding challenges. The opinion of this study is that such confounding challenges could be best minimized through the use of a cohort methodology.

In our health settings most asthma patients tend to receive their medications from the hospital pharmacy as they come in to the out-patient department for their regular reviews. Studies in this area are missing as the few existing studies tend to assess the community pharmacy. This study is therefore relevant by identifying how best pharmacist can impact on the quality of life of asthma patients visiting the various health settings where pharmaceutical services are provided.

### 1.6. Study Hypothesis

The hypothesis of the study is to test any association between changes in HRQoL and the provision of pharmaceutical care in patients with asthma.

The study seeks to identify the type(s) of association (clinical and/or statistical) for the mean difference in HRQoL, after pharmaceutical care intervention.

***Null Hypothesis:*** The mean health-related quality of life (HRQoL) score in patients with asthma, a month after pharmaceutical care intervention is comparable as that of the baseline score.

***Alternative Hypothesis:*** The mean health-related quality of life (HRQOL) score in patients with asthma, a month after pharmaceutical care intervention is not comparable to that of the baseline score.

## 1.7. Study Aims and Objectives

### 1.7.1. Aim of Study

The aim of the study was to investigate the impact of pharmaceutical care delivered by pharmacists on the health-related quality of life of asthma patients.

### 1.7.2. Specific Objectives

1. To assess content and outcomes of counselling and education delivered by pharmaceutical service providers to patients visiting out-patient departments.
2. To assess the prescribing patterns of asthma medications
3. To assess the impact of pharmaceutical care service delivery on asthma control, using the model care plan.
4. To identify relationships between the various domains of the HRQoL and the Peak Expiratory Flow Rates.
5. To model a variation of the health-related quality of life with other patient variables.

# CHAPTER 2

# 2. METHODS

## 2.1. Ethical Clearance

The study was conducted in compliance with the requirements of the Ghana Health Service Ethical Review Committee on Research Involving Human Subjects, and permission (EC-ID no. GHS-EHC: 08/9/11 of 19th October, 2011) (Appendix 1a) granted by this Committee, the Korle-Teaching Hospital, Trust Hospital, Cocao Clinic and the Komfo Anokye Teaching Hospital (Certificate of Registration: reg. no. RD/CR12/052 of 30th March, 2012) (Appendix 1b).

**Phase I - Patient Counseling and Education Assessment**

The first phase of this study was a general descriptive assessment of the counseling and education information content, as well as the knowledge of the participants about the information given by the pharmacy staff. In this section, a questionnaire was developed to capture the general and specific information that participants had as they exited the pharmacy.

## 2.2. Patient Pharmacy-exit Interviews

The main objective of these structured interviews was to generally explore how much of relevant information and knowledge patients visiting the pharmacies on out-patient basis acquired to empower them manage their medications at home. Subsequent to the general information and knowledge of the patients to managing their medication, this study also sought to find out if information provided varied for patients with chronic long-term

conditions and those with short-term acute conditions. It is quite important to understand what information and knowledge patients take back home regarding their health and medications to help them make informed and effective contribution to the management of their conditions. Patients with long-term medical conditions will require more education every step of the way in the prolonged maintenance of their health.

### 2.2.1. Development of Pharmacy-exit Questionnaire

A 26-item interviewer-administered questionnaire (Appendix 2) was developed for pharmacy-exit patient interviews. The questionnaire design was informed by that used in previous studies to review patient self-management (Morgan *et al*, 2004; Cicutto *et al*, 2005; Teach *et al*, 2006) and other publications reviewing patient adherence issues (Sabate, 2003; EPR-3, 2007). The contents of the questionnaire were guided by the components of patient counselling in the Omnibus Budget Reconciliation Act of 1990 (OBRA '90), which mandates the offer to counsel patients about their prescriptions. The specified components for patient who accepts the offer to be counselled, include: Name of medicine; intended use and expected action; route of administration, dosage form, dosage, and administration schedule; common side effects that may be encountered, including their avoidance and the action required if they occur; techniques for self-monitoring of drug therapy; proper storage; potential drug-drug or drug-food interactions or other therapeutic contraindications; prescription refill information; action to be taken in the event of a missed dose (OBRA, 1990).

The thematic areas covered by the questionnaire included:

- Level of patient – dispenser communication
- Patient assessment of the dispensing process
- Patient information and knowledge on current medications and their regimens

- Patient information on precautionary measures while using their current medications

### 2.2.2. Sample Size Estimation for the Pharmacy-exit Interviews

The sample size estimates were based on the WHO (1993) recommended sample size estimates for assessing drug use encounters. The guiding principle of the WHO recommendation is that individual health providers tend to exhibit consistent practices over time, so that a sample drawn at one point in time will provide basically the same results as a sample that covers a longer period and that the goal of a drug use study should be to estimate percentage indicators that summarize values for the sample as a whole with a 95% confidence interval of plus or minus 7.5%. It further noted that a study of individual facilities should measure facility-specific percentage indicators with a 95% confidence interval of plus or minus 10% (WHO, 1993).

The suggestion is that when it is important to compare individual facilities or prescribers, the size of samples drawn within each facility or per prescriber must be higher than 30 in order to get more reliable within-facility estimates of prescribing patterns. At least 100 cases per health facility or per prescriber would be recommended (WHO, 1993). A sample of 100 prescription encounters was therefore estimated for each pharmacy.

### 2.2.3. Inclusion and Exclusion Criteria for the Pharmacy-exit Interviews

All patients visiting the out-patient pharmacy departments were recruited for this survey, however, excluded from the survey were those collecting medicines for their relatives on the wards and those who were visibly sick and would want to be excused from participation.

### 2.2.4. Data Collection on Patient Counseling and Education

Data collection for patient counseling and education assessment was carried out from 1st November, 2011 to 2nd January, 2012. Data for 230 prescription encounters were collected from two pharmacies at the Korle-bu Teaching hospital and for 158 encounters from the Cocoa clinic.

Patients were recruited as they exited the pharmacy with their medications. Patients who agreed to participate in the study were provided the information about the study and signed the Patient Consent Form 1 (Appendix 3) for the study. Participants were taken through the 26 items interviewer- administered questionnaire used for the data collection and provided information on their encounters with the pharmacy staff. Data collection was organized on a 2 days per week basis for a period of 3 months.

### 2.2.5. Data Analysis for the Pharmacy-exit Interviews

Data collected was entered onto an Excel spreadsheet in Microsoft professional Plus 2010 and exported to SPSS v.16 for analysis to generate various tables and charts to demonstrate the various sub-themes in this section.

## Phase II- Assessment of Prescribing Patterns of Asthma Medications

Phase II of this study was a review of the prescribing patterns of asthma medications in the country. In this section, a questionnaire was developed to capture the prescriptions issued to participants with asthma as they visited the various health facilities.

## 2.3. Prescribing Patterns of Asthma Medications

The main objective of this assessment was to find out how treatments for asthma were being prescribed. This aspect of the study sought to identify the types of medications being used for the management of asthma, how these medicines were prescribed in relation to national international guidelines on the management of asthma.

It is quite important to understand how asthma is managed when inhalation technique among patients with asthma was generally inadequate. Management of asthma required adjustments of therapy upwards or downwards to keep the patient in good control.

### 2.3.1. Development of Prescribing Pattern Data Collection Tool

A 9-item tool (Appendix 7) was developed to pick data on prescribing patterns on asthma. The contents of the questionnaire were guided by the components of patient counselling in the Omnibus Budget Reconciliation Act of 1990 (OBRA '90), which mandates the offer to counsel patients about their prescriptions and also by the recommendations from the Pharmaceutical Care approach of assessing potential and actual drug therapy problems (AphA, 1992).

The thematic areas covered by the tool included:

- Background information of participants involved in asthma prescribing pattern assessment
- Types of medications and the various regimens used in the management of study participants
- Conformity of pharmacologic therapy of asthma management to treatment guidelines and protocols

### 2.3.2. Inclusion and Exclusion Criteria for Prescribing Pattern Assessment

Though no sample size estimates were calculated for this section of the study, data was collected over a 2-months period to assess how patients with asthma were managed at their previous review visit. Prescribing data on all patients with asthma visiting the health facility were included in the study.

Prescribing data on patients not diagnosed with asthma were excluded from this study.

### 2.3.3. Prescribing Pattern Data Collection

Data collection on prescribing patterns for patient with asthma was carried out from June, 2012 to August, 2012. Data on 409 prescription encounters were collected from 4 hospitals across the country.

| **Hospital Facility** | **Tamale (A)** | **Trust (B)** | **Komfo Anokye (C)** | **Kole Bu (D)** |
|---|---|---|---|---|
| Number of Prescriptions | 52 | 71 | 151 | 135 |

Information was collected on the participants previous visit prescription. This was to ensure that information was collected on participants who did not patronize the facility's pharmacy. Patients went away with their folders and therefore the records section had little or no data on these patients. The pharmacy did not have information on the medicines that were not available at the time of patient-visit and information on prescribing patterns from the pharmacy was incomplete. Prescribing information was collected as patients waited to see their physicians.

#### 2.3.4. Data Management and Analysis for Prescribing Pattern Assessment

Data collected was entered onto an Excel spreadsheet in Microsoft Professional Plus 2010 for analysis to generate various tables and charts to demonstrate the sub-themes under this section.

**Phase III – Assessment of Pharmaceutical Care Delivery on Asthma Control**

Phase III of this study was subdivided into 3 parts:

Part I was a cross-sectional description of patient baseline characteristics.

Part II was the provision of pharmaceutical care intervention to asthma patients at baseline

Part III was a post-pharmaceutical care intervention assessment of patient baseline clinical characteristics.

### 2.4. Study Materials for Pharmaceutical Care Assessment

The Asthma Quality of Life Questionnaire (Appendix 4) was used for the assessment of HRQoL in study participants. The Peak Expiratory Flow Meter was used to assess participants' lung function whilst the Model Pharmaceutical Care Plan (Appendix 5) and the Inhalers served as intervention tools to impact asthma control.

#### 2.4.1. Standardized Asthma Quality of Life Questionnaire

The Asthma Quality of Life Questionnaire (AQLQ(S)) (Appendix 4) was adopted to measure the functional problems (physical, emotional, social and occupational) that are most troublesome to adults (17-70 years) with asthma. The AQLQ(S) was a disease-specific instrument that had been validated in clinical trials (Juniper *et al*, 1999a). The AQLQ(S) contains 32 questions (items) comprising four domains: Activity Limitations, Asthma

Symptoms, Emotional Function and Environmental Exposure. Each item was scored on a 7-point Likert scale where 1 indicated severe impairment and 7 indicated no impairment. The overall score for HRQoL was the mean score of the 32 items.

A change in mean overall or domain score of 0.5 had been shown to represent the smallest change of importance to the patient (the "minimal important difference"), and a change in score of 1.0 represents a moderate change (Juniper *et al*, 1994). However, a maximum overall AQLQ(S) score of 7 represented no impairment in QOL due to asthma, and scores approaching 7 imply a minimal impact of asthma on QOL.

It has been demonstrated that this questionnaire was reproducible at a time when patients were stable and without any exacerbation of their asthma (interclass correlation coefficient of 0.92) and had also proven responsive in before-after studies (Juniper *et al*, 1993; Rowi, 1993).

The construct validity for the questionnaire has also been supported by significant relationships with both conventional measures of asthma severity and generic quality of life instruments (Juniper *et al*, 1993).

### 2.4.2. Peak Expiratory Flow Rate Meter

The AIRZONE® flow meter by Clement Clarke International of Essex, UK is commercially available for the assessment of lung function. The peak flow test measures how hard and fast one can breathe out. The AIRZONE® flow meter, as demonstrated in figure 2.1, is a plastic tube with a mouthpiece through which one blows into the meter. The meter has a calibrated scale on one side of the tube with a marker that indicates the reading of individual patients

lung function. The flow meter had a reading range from 60 - 800 L/min and the marker was set at zero before used.

**Figure 2.1:** AIRZONE® flow meter by Clement Clarke International, Essex, UK

### 2.4.3. Model Pharmaceutical Care Assessment and Intervention Plan

The Model Pharmaceutical Care Assessment and Intervention Plan instrument (Appendix 5) was developed by the investigator, piloted and submitted as part of the documents for ethical clearance.

Development of the "Model" followed the principal elements of pharmaceutical care that defined "the care" as *medication-related* and *directly provided* to the patient with *definite outcomes*, that are intended to improve the patient's *quality of life*; and for which the provider accepts personal *responsibility* for the outcomes. (ASHP Statement, 1993)

The Model captured patient background information as well as other patient specific data review in 5 activity areas: I - medication use review, II - inhaler technique review, III - adverse medication events (AME) review, IV - peak expiratory flow rates review and V - environmental trigger factors. Activities I and III (medication use review and AME) explored actual drug-related problems, whilst activities II, IV and V (inhaler technique and environmental exposures) explored potential drug-related problems.

The care-provider administered Model was a structured questionnaire developed to collect patient background information such as age, year diagnosed with asthma, years on various inhalers and history of emergency room visits. The Model gathers from each patient: name and types of current medications; duration of use for each medication and the level of compliance; as well as the perceived adverse events associated with their various medicines.

Inhaler technique is assessed with a 7-point score marks that reflected the performance on the steps for the use of inhalers. Each correct step is 1-point score. The 7-point score marks were the extension of the manufacturers inhalation steps found in the product leaflets. The extension became necessary to ensure that each activity is captured as a point and that 2 or more activities are not captured as one point. Combining activities partially fulfilled into a single point created challenges during the pilot phase.

The organization and development of the instrument was based on principle guiding the provision of pharmaceutical care as envisaged in ASHP statement (ASHP, 1993), which required the gathering and collation of both subjective and objective patient data in the assessment of actual and potential problems. In addition to these were the various steps and directions found in product literature on inhalation technique and the use of peak expiratory flow-meter.

This structured questionnaire was important for this study since the components and organization allowed for a systematic approach to identification and resolution of patient drug-related problems that subsequently affects health-related quality of life.

### 2.4.4. Types of Inhalers Devices for Inhaler-use Technique Assessment

Patients used various inhalers for the management of their asthma. An inhaler or puffer is a medical device used for delivering medication into the body via the lungs. It is mainly used in the treatment of asthma and Chronic Obstructive Pulmonary Disease (COPD). To reduce deposition in the mouth and throat, and to further reduce the need for precise synchronization of inhalation with actuation of the device, metered dose inhalers (MDIs) are sometimes used with a complementary spacer or holding chamber device.

The inhaler devices were used in this study as an object to assess and measure participant inhalation technique. The appropriate inhalation technique enables adequate quantities of inhaler contents to be delivered into the lungs to provide the necessary therapeutic responses.

#### 2.4.4.1. Metered-Dose Inhalers Used for Inhaler Technique Assessment

The most common type of inhaler is the pressurized metered-dose inhaler. Figure 2.2 illustrated an MDI and the mechanism by which it works. Every asthma patient is recommended to use Salbutamol inhaler to manage acute attacks of the condition. In this study, the inhaler-use technique was assessed to ascertain the level of appropriate use. In MDIs, medication is most commonly stored in solution in a pressurized canister that contains a propellant, although it may also be a suspension. The MDI canister is attached to a plastic, hand-operated actuator. The Ventolin® inhaler (CFC-free) comprises a suspension of Salbutamol sulphate in the non-CFC propellant Hydrofluoroalkane (HFA 134a). The suspension is contained in an aluminum alloy can, internally coated with fluoropolymer and sealed with a metering valve. Each canister is fitted with a plastic actuator incorporating an atomizing nozzle and fitted with a dust cap.

The inhaler delivers 100 mcg of Salbutamol (as sulphate) per actuation into the mouthpiece of a specially designed actuator. Each canister contains at least 200 actuations.

The correct procedure for using an MDI is to first fully exhale, place the mouth-piece of the device into the mouth, and having just started to inhale at a moderate rate, depress the canister to release the medicine. The aerosolized medication is drawn into the lungs by continuing to inhale deeply before holding the breath for 10 seconds to allow the aerosol to settle onto the walls of the bronchial and other airways of the lung.

For the relief of acute bronchospasm, in both children and adults, 100 to 200 mcg of Salbutamol may be used if required. In chronic asthma therapy in children and adults, up to 200 mcg of Salbutamol is used four times daily.

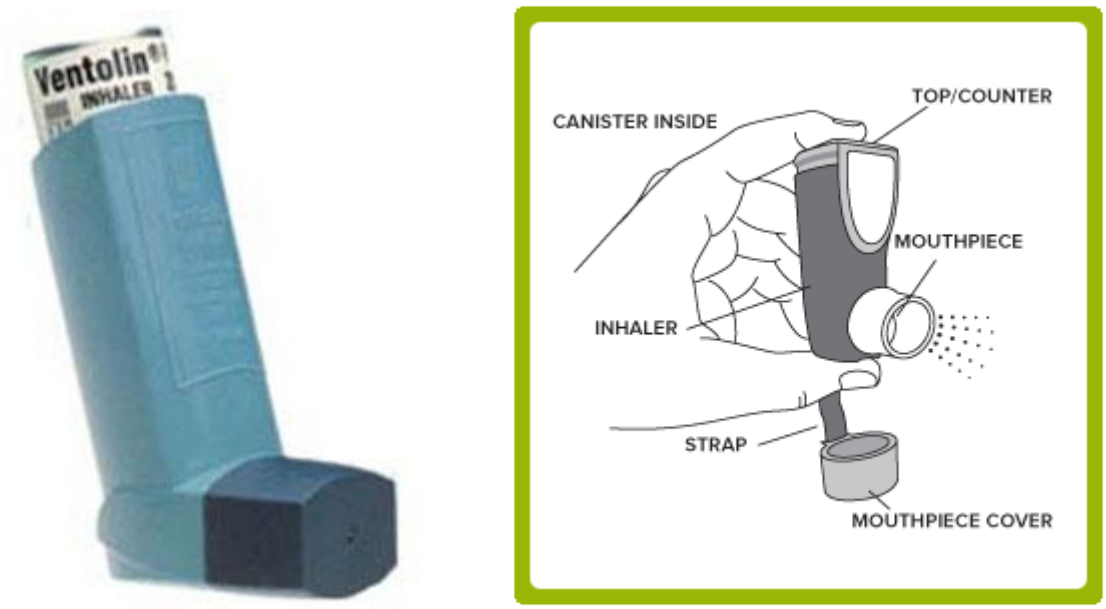


**Figure 2.2:** The Metered-Dose Inhaler Device

#### 2.4.4.2. Dry Powder Inhalers Used for Inhalation Technique Assessment

Dry powder inhalers (DPI) release a metered or device-measured dose of powdered medication that is inhaled through a DPI device. Unlike the MDIs, the DPIs contain no propellants, but the powder is stored in a plastic container of various shapes. By a twist action or a lever mechanism, a fixed dose of the powdered medication is available for inhalation.

After full exhalation, the mouth-piece of the device is placed into the mouth and forcefully and deeply, the powder is inhaled into the lungs.

Figure 2.3 demonstrates two types of DPIs, Seretide Accuhaler and Symbicort which delivers powdered combinations of a corticosteroid and a long-acting beta-agonist that were used by most participants in this study.

Seretide® is a product of GlaxoSmithKline that uses the lever system to issue out fixed-doses of Salmeterol xinafoate 50 mcg with Fluticasone propionate either as 100 mcg, 250 mcg or 500 mcg or for inhalation. The strength of the dose of the Accuhaler is based on the Fluticasone (100 mcg, 250mcg and 500mcg), since the various Fluticasone doses are in combination with a fixed dose of 50 mcg of Salmeterol.

Symbicort® is a product of AstraZeneca that uses a twist system to issue out a fixed-dose of 80 mcg or 160 mcg of Budesonide and 4.5 mcg of Formoterol fumarate dehydrate.


**Figure 2.3:** Dry Powder Inhaler Devices *(courtesy: GlaxoSmithKline & AstraZeneca)*

### 2.4.5. Sample Size Estimation for Pharmaceutical Care Assessments

Assuming a mean HRQoL difference size of 0.5 (the minimum important difference of clinical significance) (Juniper *et al*, 1994) and a standard deviation of HRQOL score of 0.8 from previous studies in the literature, the calculated standardized effect size was estimated to be approximately 0.6 (0.5/0.8). To estimate the sample size to test the hypothesis, a power (β)

of 0.9 and the level (two-sided) of statistical significance (α) of 0.05 were set. Using these settings, the estimated sample size required per each group, when using the t-test to compare means of continuous variables to determine the minimum important difference of 0.5 was 60 patients.

### 2.4.6. Study Sites for Pharmaceutical Care Assessments

Four clinical sites were used in the study. Two were teaching hospitals that managed referral cases from various health institutions and run specialist asthma clinics once a week. The Trust hospital, though not a teaching hospital, also runs a specialist clinic once a week. The fourth hospital was the Cocoa Clinic that runs a generalist out-patient and in-patient clinics.

Komfo Anokye teaching hospital is located in the middle belt, specifically in the Ashanti region and serves as a referral center for health facilities around the middle belt. The hospital is managed by consultants and specialists who run various clinics.

The Korle-bu teaching hospital, which is located in Accra, performs similar functions like the Komfo Anokye teaching hospital.

The Trust hospital and the Cocoa clinic are both located at different parts of Accra and serve patients within and beyond their geographical locations.

### 2.4.7. Inclusion and Exclusion Criteria for Pharmaceutical Care Assessments

Patients aged 17 – 70 years who have been medically diagnosed with asthma and regularly attends out-patient clinic at the selected sites were included in this survey. Included in the survey were patients whose prescriptions were not changed at the first encounter in the survey. Participation was restricted to those who can read and write in English and had no other active co-morbidities.

#### 2.4.8. Study Subjects

Ninety two (92) adults with symptomatic asthma, without other active co-morbidities, who visited the out-patient clinic, participated in the study. Fifteen of these patients were lost to follow-up. Every effort to locate them for follow-up did not work as some of them refused to pick their phones or did not show up for their appointments. The project had to follow some participants to their homes, since they were not able to make time for the revisits.

### 2.5. Characterization of Asthma Patients Visiting Specialist Out-patients Clinics

This section profiled in detail the general baseline characteristics of asthma patients who visited the specialist out-patient clinics for scheduled review. This was important for the assessment of impact of the planned intervention to draw comparison between the pre- and post- intervention status.

#### 2.5.1. Baseline Characterization of Asthma Patients

The interviewer administered questionnaire termed ‘Model Pharmaceutical Care Assessment and Intervention Plan instrument’ (Appendix 5) was developed to capture asthma specific patient baseline information prior to the planning and delivery of pharmaceutical care intervention. In addition to this questionnaire, the AQLQ(s) was used to capture the health-related quality of life status of participants. The baseline assessments were important to this study because it helped to describe the outcomes of the current method of pharmaceutical care delivery to patients with asthma and also provided the basis for comparison of the outcomes from the use of the model care plan.

### 2.5.2. Data Collection for Asthma Patient Characterization

Data for baseline asthma patient characterization were collected from December, 7th 2012 to August, 20th 2013. Total number of participants recruited was 92 from the 4 health facilities.

| **Facility** | **Cocoa Clinic (A)** | **Trust Hospital (B)** | **Komfo Anokye Teaching Hospital (C)** | **Korle-bu Teaching Hospital (D)** |
|---|---|---|---|---|
| Participants | 7 | 10 | 18 | 57 |

Facilities A and B had very few participants that met the inclusion criteria. Many patients encountered at the asthma clinic in facility B were mostly children below the age of 17 years. The purpose of the study was explained to patients attending the out-patient specialist asthma clinics. Patients were informed that they are free not to take part in the study and that they would still receive the services of the hospital staff as required. Patients were informed that their data remained confidential and that they may have to be re-assessed on their next scheduled appointment. Patients who accepted to participate in the study were handed out the Patient Consent Form 2 (Appendix 6) to read further about the study and affirm their participation in the study. Patients who agreed to participate in the study were then referred to the interview rooms for assessment and data collection. Data variables collected to profile asthma patients visiting the OPD specialist clinics were grouped into five thematic areas:

Health-related Quality of Life Measurements

Medication-use Review

Measurement of Peak Expiratory Flow Rates

Assessment of Inhaler-use Technique

Assessment of Environmental Trigger-factors

### 2.5.3. Assessment of the Patients' Health-related Quality of Life

Participants were introduced to the standardized Asthma Quality of Life Questionnaire (Appendix 4) and asked to recall how they have been in general over the past 2 weeks and indicate same on the questionnaire by encircling the number in a range of 1-7 that represented how they have been. Participants were advised and encouraged to answer the questions based on their understanding of the question and to answer all questions.

The possible answer in the range were explained to participants to enable them appreciate what the various levels within the range (see below) represent.

Totally limited

Extremely limited

Very limited

Moderately limited

Some limitation

A little limitation

No limitation

Participants were to choose "totally limited", if their asthma condition had made them totally unable to perform the activity in question. If their asthma condition has not affected their ability to perform the said activity, then it is "No limitation". Where there is some level of limitation, the participants were to choose within the range, the level they perceive to be the extent of limitation from their asthma condition.

### 2.5.4. Medication-use Review for the Patients

Using the Model Pharmaceutical Care Assessment and Intervention Plan instrument (Appendix 5),participant medication-use reviews were undertaken to ascertain which medications participants were using (both prescribed and self-medicated), as well as their

knowledge about the medications and their regimens. The review also identified the adherence status to the various medications and the problems and side-effects that participants perceived may be associated with the use of their medications.

Participants were asked to identify or show to the study team their current medications and also to mention names of other medications which they had at home for their asthma. Participants were further asked to explain how they used (doses and dosage regimens) their current medications and if that is the same way they had been instructed (cross-checked from current prescription) to do and whether they experienced or perceived side-effects from any of their medicines. Participants narrated their drug-use experience and all their challenges from which it was agreed with them regarding their adherence to therapy.

### 2.5.5. Peak Expiratory Flow Rate Measurements

Peak expiratory flow rates were measured for each participant for an objective assessment of asthma control.

Participants were handed out the “Airzone” flow meter and a new unused mouth piece attachment. How to use the flow meter and the assessment process was then explained to them. In an upright position, either sitting or standing, participants were instructed to hold the peak expiratory flow meter in a level horizontal position. After returning the maker to the start point and fingers out of the way from blocking the maker on the meter, participants were instructed to take a deep breathe in, and to put their lips tightly around the mouthpiece attachment mounted on the flow meter and blow as hard and fast as they could. The meterwas maintained in the initial horizontal level position as the readings indicated by the maker on the meter were noted and entered on the model pharmaceutical care instrument.

The entire process was repeated two more times to capture the three best readings for each participant. On each occasion, further coaching was provided where needed, to ensure

participants performed the technique better than previously. Participants were allowed to take their time and rest awhile between assessments. Each used mouthpiece attachment was donated to the user.

### 2.5.6. Patient Inhaler-use Technique Assessment

The study reviewed and corrected problems with inhaler-use technique for all participants individually. Practical inhaler technique was assessed and scored for each participant on a 7-step score sheet that allocated 1 point for each correct step.

Before the assessment, each participant was informed about what the health condition usually referred to as "Asthma" is and how the use of inhaled medicines helps to manage and maintain control of the condition. Participants were informed about the links between good inhaler-use techniques, adequate medicine intake and asthma control. They were also informed about the limits on the doses from their inhalers that can be used to avoid the occurrence of adverse effects.

Participants were tasked to demonstrate how they used their inhalers, while the performance of each step was noted and ticked as correct or wrong on the Model Pharmaceutical Care Assessment and Intervention Plan instrument sheet (Appendix 5). Dummy empty inhalers were used for the demonstration of the technique by participants. Participants were allowed if they had, to use their own inhalers to demonstrate the inhalation technique. Where participant has not yet used the inhaler for the morning and he/she is willing to use their personal inhalers to demonstrate, permission was granted to do so.

The sum of the correct steps for each inhaler provided the total inhaler-use technique score for that inhaler (dry powder inhalers or metered-dose inhaler) in particular. Participants were informed about their scoring for the various steps and encouraged with coaching master the correct technique. This was done repeatedly till participants got all the steps for the inhalers correct.

### 2.5.7. Assessment of Environmental Trigger Factors in Patients

In a discussion with participants to identify environmental trigger factors that worsen their condition, participants were asked to explain environmental encounters that tend to worsen their asthma condition. Information generated through these discussions was followed up with participants to identify environmental trigger factors that affect each participant. Each participant explained how they encountered the various trigger factors and the impact of such encounters on their asthma condition, and what they have been doing to prevent the impact of these trigger factors on their condition.

## 2.6. Provision of Pharmaceutical Care Intervention

In part II of this study, the individual baseline profile of participants' were reviewed to identify care-needs for intervention that was tailored to each individual participant. Issues relating to medication-use, inhaler-use technique and management of environment trigger factors were addressed with the participants. Participants were then re-assessed four weeks after the care intervention to identify changes that may have occurred in relation to their asthma control.

### 2.6.1. Delivery of Pharmaceutical Care Intervention

To identify care-needs to be addressed with each participant, the demographics, medication profile, symptoms, inhaler-use technique, environmental trigger-factors and perceived side effects captured from baseline assessment of the participant were reviewed. Participant age and sex were considered while reviewing the extent of adherence to medications to explore reasons of poor adherence. Inhaler medication affordability, perceived side effects and inhaler carriage were also reviewed in non-adherent participants.

Participants with inadequate inhaler-use technique were coached continuously to master the technique till they were able to score all the steps correctly. Emphasis was placed on the incorrect steps and participants were provided explanation as to why each step was important and the need to ensure that adequate amounts of the inhaler medicines got into their lung spaces. Participants inhaler-use techniques were assessed and scored based on the following technique steps:

**For dry powder inhalers**

Step 1 - Remove the cap or open mouthpiece

Step 2 – Hold in upright position with mouthpiece upwards

Step 3 – (***for turbohaler***) – Rotate grip anticlockwise, then then back until a click is heard

(***for diskhaler***) – Pull lever to release medicine

Step 4 – Breathe out slowly and completely (not into the mouthpiece)

Step 5 – Place the mouthpiece between the front teeth and seal the lips around it

Step 6 - Breathe in through the mouth quickly (forcefully) and deeply over two to three seconds

Step 7 – Remove the inhaler from the mouth. Holds breathe as long as possible 4-10 seconds). Breathe out slowly.

**For metered-dose inhalers**

Step 1 - Remove the cap or open mouthpiece

Step 2 – Hold the inhaler upright with thumb on base and index finger on top of canister

Step 3 – Shake the inhaler up and down vigorously

Step 4 – Breathe out slowly and completely

Step 5 – Hold the mouthpiece firmly between lips

Step 6 - Breathe in through the mouth slowly and deeply, whilst the inhaler is pressed to release medication

Step 7 – Remove the inhaler from the mouth. Holds breathe as long as possible 4-10 seconds). Breathe out slowly.

## 2.7. Post-intervention Characterization of Asthma Patients

Post-intervention characterization of asthma patients involved a repeated collection of both subjective and objective patient data. On the same questionnaires used at baseline, the post-intervention quality of life and peak expiratory flow rates were captured.

### 2.7.1. Post-intervention Assessment of Health-related Quality of Life

Post-intervention assessment of participants' health-related quality of life with the Asthma Quality of Life Questionnaire with Standardized Activities (AQLQ(s)) {Appendix 4} was organized on the scheduled visit to the clinics. Participants were handed over the self-administered questionnaires to answer the same questions they answered during the previous encounter. Participants were provided with pens to encircle the answers that best described how they had been over the current past 2 weeks. Participants were advised to consider how they were feeling the first time they filled the form and compare that to how they feel currently to decide whether for each question the situation had improved, remained the same or worsened and let that reflect in their answers to all the questions on the AQLQ(s). Where participants felt there had not been any change in the way they felt during the 2 weeks before the encounter, they were to encircle the same number.

### 2.7.2. Post-intervention Measurement of Peak Expiratory Flow Rates

Post-intervention measurements of peak expiratory flow rates (PEFR) were organized for participants immediately after the quality of life assessments. In a standing or up-right sitting position, participants were made to repeat their PEFR by blowing into the peak flow meter device and the best two readings were picked onto the their data forms.

## 2.8. Data Management and Analysis

Data collected was entered onto an Excel spreadsheet in Microsoft professional Plus 2010 and exported to SPSS v.16 for analysis. Data was analyzed to generate various tables and charts to demonstrate similar themes, frequencies, trends and number counts.

### 2.8.1. Data Management

All the data from the study were captured on the appropriate instruments. The Patient Consent Form, the standardized Asthma Quality of Life Questionnaire and the Model Pharmaceutical Care Assessment and Intervention Plans were given same code for each participant before data entry. All data instruments were then checked for completeness of entries. There were immediate follow-ups with patients for any omissions of data. Data collected were then entered onto an Excel spreadsheet in Microsoft professional Plus 2010 on daily basis to double-check their completeness and the need for an early follow-up in case of undetected omissions.

The collated and clean data from the Excel spreadsheets were imported onto SPSS v.16 for analysis.

### 2.8.2. Data Analysis

Data from the study were subjected to both descriptive and statistical analysis. Data were analyzed to generate various tables and charts to demonstrate similar themes, frequencies, trends and number counts under the following themes:

- Patient Counseling and Education at Out-patient Pharmacy in a Teaching Hospital
- Baseline Characteristics of Asthma Out-patient Clinic Participants
- Comparison of Asthmatic Patients' Characteristics Post Pharmaceutical Care Intervention
- Modeling a Health-related Quality of Life Variation

Data were analyzed to test the study hypothesis. Using a Student paired t-test; the mean differences of the baseline and post pharmaceutical care intervention HRQoL were analyzed. Correlation analyses were performed for the various domains of the HRQoL and also with the peak expiratory flow rates (PEFR).

Regression analyses were also performed on variables with strong correlations to the general HRQoL to generate a variation of HRQoL.

Additional analysis was performed to determine the relative risk (relative chance of attainment) for the pharmaceutical care intervention and to determine patient benefit ratio from the intervention.

# CHAPTER 3

# 3. RESULTS

## 3.1. **Patient Counselling and Education at Out-patient Pharmacy**

Patient pharmacy-exit interview data was collated and organized into the following sub-themes:

### 3.1.1. Background Information on Pharmacy-exit Interview Participants

Pharmacy-exit interview participants were grouped into those with acute (158 encounters) and those with chronic long-term (230 encounters) health conditions (Table 3.1). The percentage of participants was approximately 44% males to 56% females in both the acute and chronic condition groups respectively as in table 3.1.

**Table 3.1:** Characteristics of Pharmacy-exit Interview Participants

| **Health Condition of Participants** | | **Acute Condition (%)** | **Chronic Condition (%)** |
|---|---|---|---|
| **Number of Participants** | | 158 (41) | 230 (59) |
| **Sex of Participants** | Male | 69 (44) | 102 (44) |
| | Female | 89 (56) | 128 (56) |
| **Pregnant Participants** | | 13 (8) | 9 (4) |

More than 50% of participants in both the acute health condition and the chronic health condition groups had at least secondary education (Table 3.2). The mean age of participants was 54 (±16).

**Table 3.2:** Educational Background of Pharmacy-exit Interview Participants

| **Educational Background of Participants** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Participants with Acute Health (%) (n=158)** | | | | **Participants with Chronic Health (%) (n=230)** | | | |
| None | Primary | Secondary | Tertiary | None | Primary | Secondary | Tertiary |
| 8 (5) | 10 (6) | 83 (53) | 57 (36) | 19 (8) | 22 (10) | 109 (47) | 80 35) |

3.1.2. Participant-Dispenser Communications

Many participants could communicate in various local dialects apart from the English language. From table 3.3, about 48% of acute and 55% of chronic health participants were counselled and educated using the English language, while 48.1% and 38.3% of acute and chronic health condition participants were counselled and educated using the Twi language. About 98% of acute and 97% of chronic health condition participants said they understood the dispensing communication.

**Table 3.3:** Patient and Dispenser Communication Languages

| *Languages* | **Participants with Acute Health Condition *(n=158)*** | | **Participants with Chronic Health Condition *(n=230)*** | |
|---|---|---|---|---|
| | *Language Understood by Participants (%)* | *Language Used in Counselling (%)* | *Language Understood by Participants (%)* | *Language Used in Counselling (%)* |
| English | 121 (76.6) | 75 (47.5) | 182 (79.1) | 127 (55.2) |
| Ga | 69 (43.7) | 4 (2.5) | 107 (46.5) | 15 (6.5) |
| Twi | 132 (83.5) | 76 (48.1) | 182 (79.1) | 88 (38.3) |
| Hausa | 13 (8.2) | - | 18 (7.8) | - |
| Ewe | 18 (11.4) | - | 47 (20.4) | - |
| French | 3 (1.9) | 3 (1.9) | - | - |
| Understanding of dispensing communication | 155 (98.1) | | 80 7.0) | |

3.1.3. Participant Satisfaction and Rating of Pharmacy Services

Most participants in both the acute (93.7%) and chronic (97%) health condition groups claimed they were satisfied with services at the dispensary, but rated the services mostly as "okay" to "excellent" as in table 3.4.

**Table 3.4:** Participant Expressed Satisfaction with Dispensing Activities at the Pharmacy

| **Participant Rating[1] of Services** | **Participants with Acute Health Condition (%) (n=128)** | **Participants with Chronic Health Condition (%) (n=230)** |
|---|---|---|
| "Bad" | - | 5 (2.2) |
| "Not Acceptable" | 6 (3.8) | - |
| "Okay" | 104 (65.8) | 162 (70.4) |
| "Just Right" | 3 (1.9) | 1 (0.4) |
| "Alright" | 5 (3.2) | 7 (3) |
| "Good" | 13 (8.2) | 21 (9.1) |
| "Great" | 19 (12) | 23 (10) |
| "Excellent" | 8 (5.1) | 11 (4.8) |
| Participant Expressed Satisfaction | | |
| Participant Satisfaction with Services | 148 (93.7) | 223 (97) |

*Rating themes were based on pilot-test participants' expressions[1]*

### 3.1.4. Participants Information about their Health and Home Medications

Most participants in the chronic health condition group (89.6%) and about 58% of participants in the acute health condition group had knowledge of their health conditions (Table 3.5). All the 206 participants in the chronic health condition group who had knowledge of their health condition had the education from their physician. Only one participant from the acute health condition group had his/her education from a nurse.

**Table 3.5:** Participant Knowledge about their Health Condition

| **Health Condition** | **Knowledge of the Health Condition** | **Participant Informant** | | |
|---|---|---|---|---|
| | | *Physician* | *Nurse* | *Pharmacist* |
| Acute *(n=158)* | 92 (58.2) | 91 (57.6) | 1 (0.6) | - |
| Chronic *(n=230)* | 206 (89.6) | 206 (89.6) | - | - |

From table 3.6, about 34% of participants with acute health condition had some home medications, but only 18% of participants with home medicines in this group did not remember the names of their home medicines.

A slightly higher proportion (44%) of chronic health condition participants had some home medications; however only 10% of this group did not remember the names of their medicines.

**Table 3.6:** Availability of Home Medicines

| **Participants** | **Participants with Acute Health Condition (%) (n=158)** | **Participants with Chronic Health Condition (%) (n=230)** |
|---|---|---|
| Participants with Home Medicines | 54 (34) | 101 (44) |
| Participants without Home Medicines | 104 (66) | 129 (56) |

Of the participants with home medicines, 82% and 92% in the acute and chronic disease group respectively knew the names of their home medicines (Table 3.7).

**Table 3.7:** Participants Knowledge of Names of Home Medicines

| **Participants** | **Participants with Acute Health Condition (%) (n=54)** | **Participants with Chronic Health Condition (%) (n=101)** |
|---|---|---|
| Participant knew Name of Home Medicine | 44 (82) | 91 (90) |
| Participant does not know Name of Home Medicine | 10 (18) | 10 (10) |

### 3.1.5. Participants Knowledge about Pharmacy-exit Medications

Table 3.8 presents data on comparison of medicine-label information availability and participant knowledge on these information pieces. About 61% and 77% of acute and chronic health condition participants respectively knew the names of their exit medicines. About 10% and 22% of medicine labels in the Acute and Chronic health condition groups respectively contained information on how to store the medicine, and approximately 5% of participants in the Acute health condition group and 9% in the Chronic health condition group knew how to store their medicines.

**Table 3.8:** Label Information Content and Participant Knowledge about their Medications

| **Medication Management Information Items** | **Labels with Medicine Management Information (%)** | | **Participant with Knowledge on Medicine Management Information (%)** | |
|---|---|---|---|---|
| | ***Acute Health Condition (n=158)*** | ***Chronic Health Condition (n=230)*** | ***Acute Health Condition (n=158)*** | ***Chronic Health Condition (n=230)*** |
| Dosage Form | 158 (100) | 230 (100) | 157 (99.4) | 230 (100) |
| Name of Medicine | 156 (98.7) | 229 (99.6) | 97 (61.4) | 177 (77.0) |
| Strength of Medicine | 140 (88.6) | 222 (96.5) | 82 (51.9) | 172 (74.8) |
| Dose per Administration | 157 (99.4) | 227 (98.7) | 146 (92.4) | 220 (95.7) |
| Frequency of Administration | 156 (98.7) | 226 (98.3) | 148 (93.7) | 223 (97.0) |
| Duration of Administration | 142 (89.9) | 210 (91.3) | 117 (74.1) | 187 (81.3) |
| What to avoid whilst using Medication | 3 (1.9) | 3 (1.3) | 4 (2.5) | 9 (3.9) |
| Possible Side-effects | 5 (3.2) | 6 (2.6) | 2 (1.3) | 11 (4.8) |
| How to Store Medicine | 16 (10.1) | 58 (25.2) | 8 (5.1) | 20 (8.7) |

Figure 3.1 presents the various precautionary information types provided by dispensary staff to participants. Less than 20% of participants from the 2 groups received any type of precautionary information. About15% of participants in the chronic health condition group were informed about what to do in case they felt bad or reacted to any of their medications and about 10% of acute health condition group participants had similar information.

For the management of missed doses, about 2% and 12% of acute and chronic health condition group participants respectively had any education on what to do.

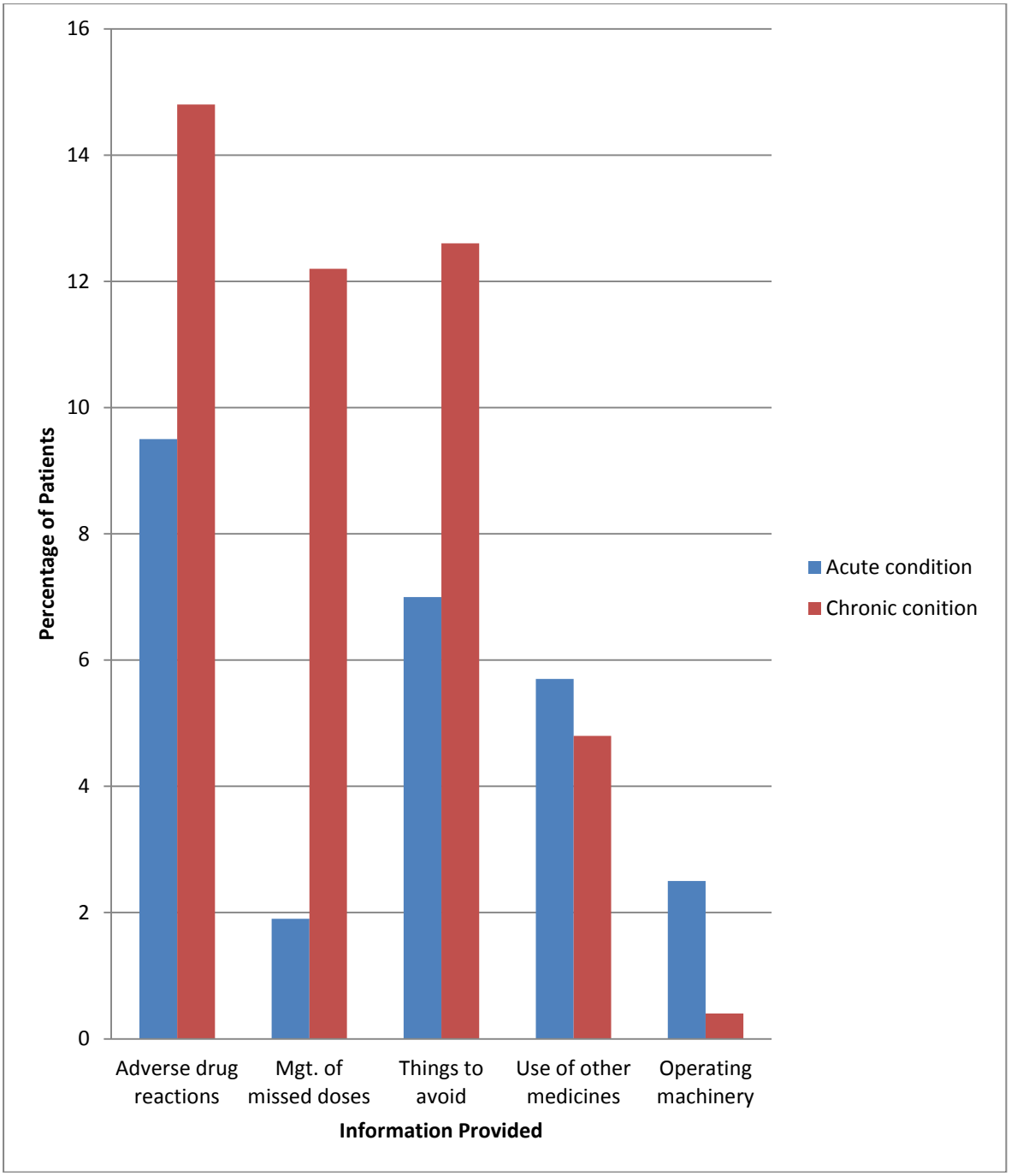


**Figure 3.1:** Precautionary Information Provided by Pharmacy to Participants

When asked about additional things the pharmacy could do for them, most participants expressed satisfaction with the services, but a few participants (10.9%) in the chronic health condition group wished for further education on side effects, while 9.6% of participants from the group wished for "improved relationship between pharmacy staff and patients" (Table 3.9). Some participants (4.4%) from the acute health condition group were interested in information on "how the medicine works" and for other participants (2.5%) in the same group, "directions on where to get the unavailable medicines" (Table 3.9).

**Table 3.9:** Additional Information Expectations of Participants from Pharmacy

| **Additional Expectation** | **Participants with Acute Health Condition (%)** ***(n=158)*** | **Participants with Health Chronic Condition (%)** ***(n=230)*** |
|---|---|---|
| Satisfied with pharmacy services | 132 (83.5) | 171 (74.3) |
| How to administer medications | - | 1 (0.4) |
| Education on side effects | 4 (2.5) | 25 (10.9) |
| Information on what to avoid | - | 3 |
| Information on how medicine works | 7 (4.4) | 5 (2.2) |
| Where to get unfilled prescriptions | 4 (2.5) | 2 (0.9) |
| Improved relationship between pharmacy staff and patients | 11 (7.0) | 22 (9.6) |
| Information on dosage regimens | - | 1 (0.4) |

## 3.2. Prescribing Patterns of Asthma Medications

Background and prescribing information for patients diagnosed with asthma was collated and organized into the following sub-themes:

### 3.2.1. Background Characteristics of Participants

The age range of participants in the asthma prescribing pattern assessment was 5 to 92 years (Table 3.10). The percentage of participants was approximately 32% males to 68% females as in table 3.10.

**Table 3.10:** Background Information on Prescribing Pattern Participants

| | |
|---|---|
| **Number of Male Participants (%)** | 129 (32) |
| **Number of Female Participants (%)** | 280 (68) |
| **Mean Age (SD)** | 41± 21 years |
| **Age Range** | 5 - 92 years |

### 3.2.2. Therapeutic Management of Study Participants

The most commonly prescribed medication was the metered-dose Salbutamol inaler (192 participants) followed by the dry-powder Fluticasone / Salmeterol 250/50 mcg inhaler (98 participants) as in table 3.11.

**Table 3.11:** Step of Therapy and Regimen of Asthma Medications Prescribed for Participants

| Medications | Type of Medication | Strength of Medication Type | Number of Participants | Step of Therapy for use of Medication |
|---|---|---|---|---|
| **Salbutamol** | MDI | 100 mcg | 192 | All steps |
| | Nebule | 2.5 mg | 1 | Emergency |
| | | 5 mg | 7 | Emergency |
| **Budesonide** | DPI | 200mcg | 4 | Step II |
| **Fluticasone/Salmeterol** | DPI | 100/50 mcg | 9 | Step III |
| | | 250/50 mcg | 98 | Step III |
| **Budesonide/Formoterol** | DPI | 80/4.5 mcg | 11 | Step III |
| | | 160/4.5 mcg | 54 | Step III |
| **Prednisolone** | Tablet | 5 mg | 34 | Emergency |

*Note* Steps refer to recommendations in Standard Treatment Guidelines, MoH, Ghana.*

### 3.2.3. Conformity of Pharmacologic Treatment to Guidelines

About half (46%) of the total prescription with dry-powder Fluticasone/Salmeterol 250/50 mcg inhalers (98), did not conform with the recommended regimens in the National Standard Treatment Guidelines{STG} (Table 3.12).

**Table 3.12:** Prescribing Pattern of asthma Medications to Participants

| Medication | Recommended Regimen | Number of Participants on Recommended Regimen | Number of Participants Regimens not recommended |
|---|---|---|---|
| **Salbutamol 100 mcg** | 2 puffs PRN | 200 | - |
| **Fluticasone/Salmeterol** (DPI) 100/50 mcg | 1 puff 12 hourly | 8 | - |
| **Fluticasone/Salmeterol** (DPI) 250/50 mcg | 1 puff 12 hourly | 52 | 45 |
| **Budesonide/Formoterol** (DPI) 80/4.5 mcg | 1-2 puffs 12 hourly | 11 | - |
| **Budesonide/Formoterol** (DPI) 160/4.5 mcg | 1-2 puffs 12 hourly | 45 | - |
| **Prednisolone 5 mg** | | 34 | - |

*Note* 14 were without stated regimens*

## 3.3. Baseline Characteristics of Asthma Out-Patient Clinic Participants

Study results for this section have been organized in the following thematic areas:

### 3.3.1. General Background Characteristics at Baseline

Study participants were predominantly female (61%) and had a mean age of 46 (±15) years. The mean peak expiratory flow rate was 284(±103) for the 77 participants in this section of the study.

**Table 3.13:** Background Characteristics of Asthma Clinic Participants at Baseline

| **Participants Characteristics (n=77)** | | |
|---|---|---|
| **Mean age (SD) of participants** | | 46 (15) |
| **Sex (n)** | *Male* | 30 (39%) |
| | *Female* | 47 (61%) |
| **Mean Peak expiratory flow rate (SD)** | | 266.27(85.28) L/min. |

### 3.3.2. Participants' Inhaler Medication Profile

Majority of participants used Symbicort® (54%) and Seretide® (31%) inhalers in various combinations (Table 3.14). Almost all participants (96%) used Salbutamol inhalers; however, 3% (n=2) of participants used Seretide inhaler only and 1% (n=1) of participants used Symbicort inhaler only.

**Table 3.14:** Participant Asthma Medication Profile

| **Inhaled Medication(s)** | **No. of Participants (%)** | **Patients on Prednisolone And Inhaler Medication(s)** |
|---|---|---|
| *Salbutamol inhaler Only* | 5 (7) | - |
| *Salbutamol+beclomethasone* | 1 (1) | - |
| *Salbutamol+pulmicort inhalers* | 8 (10) | 1 |
| *Salbutamol+symbicort inhaler* | 37 (48) | 2 |
| *Salbutamol +seretide inhaler* | 20 (26) | 3 |
| *Symbicort® only* | 2 (3) | - |
| *Seretide® only* | 1 (1) | - |
| *Salbutamol +seretide+ipratropium* | 1 (1) | 1 |
| *Salbutamol +seretide + symbicort* | 2 (3) | - |

Table 3.15 presents the number of years participants had used various inhaler types. While 42% of participants had used "Reliever" inhalers for 10 years or more, only 4% of participants had used "Preventer" inhaler for that long. However, at least 55% of participants have used a "Preventer" for a minimum of one year. Some 6 participants on "Reliever" inhalers and 7 other participants on "Preventer" inhalers could not recollect for how long they had used these medicines.

**Table 3.15:** Participant Inhaler Medication Usage

| **Years of Inhaler Usage** | **Participant Inhaler Type (n= 77)** | |
|---|---|---|
| | **Reliever (%)** | **Preventer (%)** |
| *≥10 years* | 31 (42.3) | 3 (3.9) |
| *6 –9 years* | 8 (10.4) | 7 (9.1) |
| *1-5 years* | 27 (35.1) | 42 (54.5) |
| *≤ 1 year* | 5 (6.5) | 18 (23.4) |
| *Cannot recollect* | 6 (7.8) | 7 (9.1) |

3.3.3. Participants' Inhaler-use Technique

Baseline inhaler-use technique captured on table 4.16 indicated that only 12% and 17% of participants on dry powder inhalers (DPI) and metered dose inhalers (MDI) respectively scored 7 for adequacy of inhaler-use technique. The mean inhaler-use technique scores were 4.66 (1.3) for the use of DPIs and 5.03(1.43) for the use MDIs.

**Table 3.16:** Participant Inhaler-use Technique Score

| | **Inhaler-use Technique Score (7-point scale)** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Inhaler Type** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | ***Percentage (%) with Adequate Technique*** | ***Mean Score (SD)*** |
| **DPI* (n=66)** | 0 | 2 | 10 | 23 | 16 | 9 | 8 | 12.12 | 4.66(1.3) |
| **MDI* (n=63)** | 1 | 3 | 3 | 13 | 19 | 13 | 12 | 17.46 | 5.03(1.43) |

**PDI- dry powder inhaler *MDI – metered dose inhaler*

### 3.3.4. Environmental Trigger-factors Affecting Participants

Dust, perfume/scent and smoke were the commonly mentioned environmental trigger-factors that worsened the asthma condition of participants (table 4.17). Other trigger-factors like room air-conditioning, fresh grass cutting, and alcohol and beer intake affected about 5% of participants. From table 3.14, about 78%, 78% and 70% of all participants were affected by dust, perfume, scent and smoke respectively.

**Table 3.17:** Number of Participants Affected by Environmental Trigger-factors

| **Trigger-factor type** | **Participants Affected (n=77)** | **Frequency (%)** |
|---|---|---|
| Dust | 60 | 77.92 |
| Perfume /Scent | 60 | 77.92 |
| Smoke | 54 | 70.13 |
| Food / Spices | 21 | 27.27 |
| Weather Changes | 19 | 24.68 |
| Stress / Tiredness/Emotions | 14 | 18.18 |
| Cold Drinks | 11 | 14.29 |
| Others (beer, fresh grass-cutting, alcohol & air-conditioner) | 4 | 5.19 |

Majority of participants (44%) were affected by a combination of dust, smoke and perfume, but about 4% could not identify any environmental factors that worsened their asthma condition (Table. 3.18).

**Table 3.18:** Permutations of Environmental Trigger-factors Affecting Participants **(n=77)**

| **Trigger-factors** | **Dust** | **Smoke** | **Perfume** | **Dust/ Perfume** | **Dust /Smoke** | **Smoke/ Perfume** | **Dust/Smoke/ Perfume** | **Nothing** |
|---|---|---|---|---|---|---|---|---|
| Weather | 0 | 0 | 0 | 2 | 3 | 2 | 4 | 0 |
| Stress | 3 | 0 | 0 | 0 | 0 | 1 | 3 | 1 |
| Cold Drinks | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 |
| Weather/Stress | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| Weather/Cold Drinks | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |
| Stress /Cold Drinks | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Weather/ Stress /Cold drinks | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Food | 0 | 0 | 0 | 2 | 1 | 1 | 7 | 0 |
| Food/Cold drinks | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| Food/Stress | 0 | 0 | 0 | 0 | 1 | 0 | 4 | 0 |
| Weather/ Food/Cold drinks | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| Weather/Food | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| Others | 0 | 0 | 0 | | 2 | 0 | 2 | 0 |
| Nothing | 2 | 0 | 3 | 4 | 2 | 5 | 10 | 1 |
| **Total (%)** | **6(8)** | **0** | **4(5)** | **11(14)** | **9(12)** | **11(14)** | **34(44)** | **2(3)** |

### 3.3.5. Baseline Health-Related Quality of Life of Participants

From table 3.19, the health-related quality of life of participants in the study averaged 4.16 ($\pm$1.13). Within the various domains, Activity Limitation had the highest score of 4.37($\pm$1.14) while the Environmental domain had the least score 3.29($\pm$1.56).

**Table 3.19:** Baseline Health-related Quality of Life of Participants

| **Variable** | **Score Rate** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **Mean (SD)** |
|---|---|---|---|---|---|---|---|---|---|
| **Health-related Quality of Life** | | 1 | 3 | 19 | 23 | 22 | 8 | 1 | 4.16 (1.13) |
| **Emotional Function domain** | | 2 | 13 | 18 | 20 | 12 | 8 | 4 | 3.91 (1.45) |
| **Environmental Stimuli domain** | | 8 | 18 | 18 | 13 | 8 | 11 | 1 | 3.29 (1.56) |
| **Symptoms domain** | | 1 | 4 | 22 | 26 | 15 | 9 | 0 | 3.99 (1.09) |
| **Activity Limitation domain** | | 1 | 4 | 14 | 21 | 24 | 12 | 1 | 4.371.14) |

## 3.4. Post-Pharmaceutical Care Comparison of Participant Characteristics

Post-pharmaceutical care intervention data has been arranged in the following order:

### 3.4.1. Post-pharmaceutical Care Comparison of HRQoL with Composite Domains

There were major changes in the number of participants who scored 3, 4, 6 and 7 in pre-intervention health-related quality of life and marginal changes in the numbers who scored 1, 2 and 5 points (Fig. 3.2).Whilst the number of participants who scored 2, 3 and 4 at baseline dropped, those who scored 5, 6 and 7 points at the post- intervention stage increased. The number of participants at HRQoL score point 1 did not change after intervention.

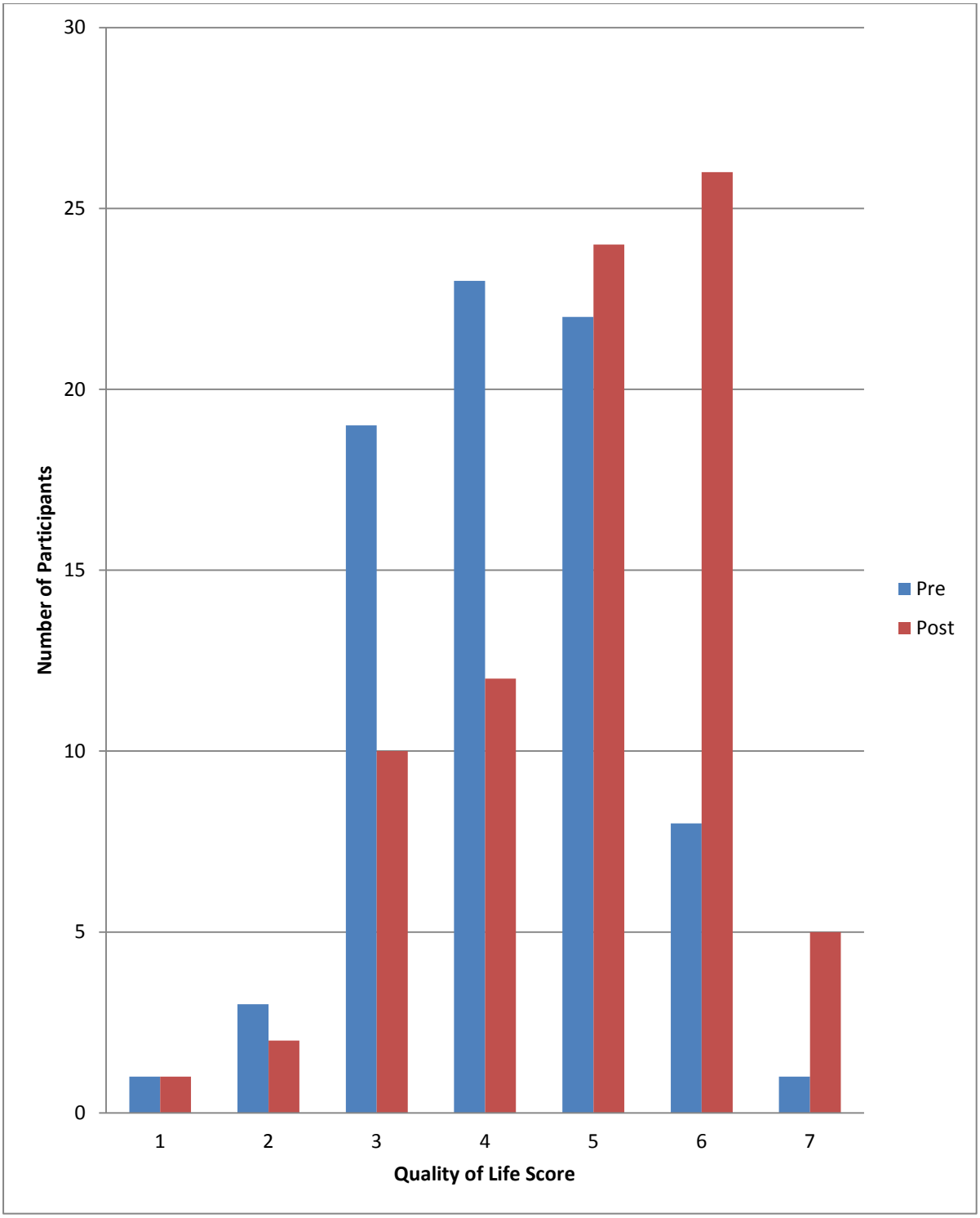


**Figure 3.2:** Health-related Quality of Life Scores of Study Participants

There were major changes in the number of participants in almost all emotional function domain scores points except for score point 1 (Fig 3.3).The number of participants in post-intervention emotional function domain score points 1, 5, 6 and 7 increased, whilst pre-intervention numbers at score points 2, 3, and 4 decreased.

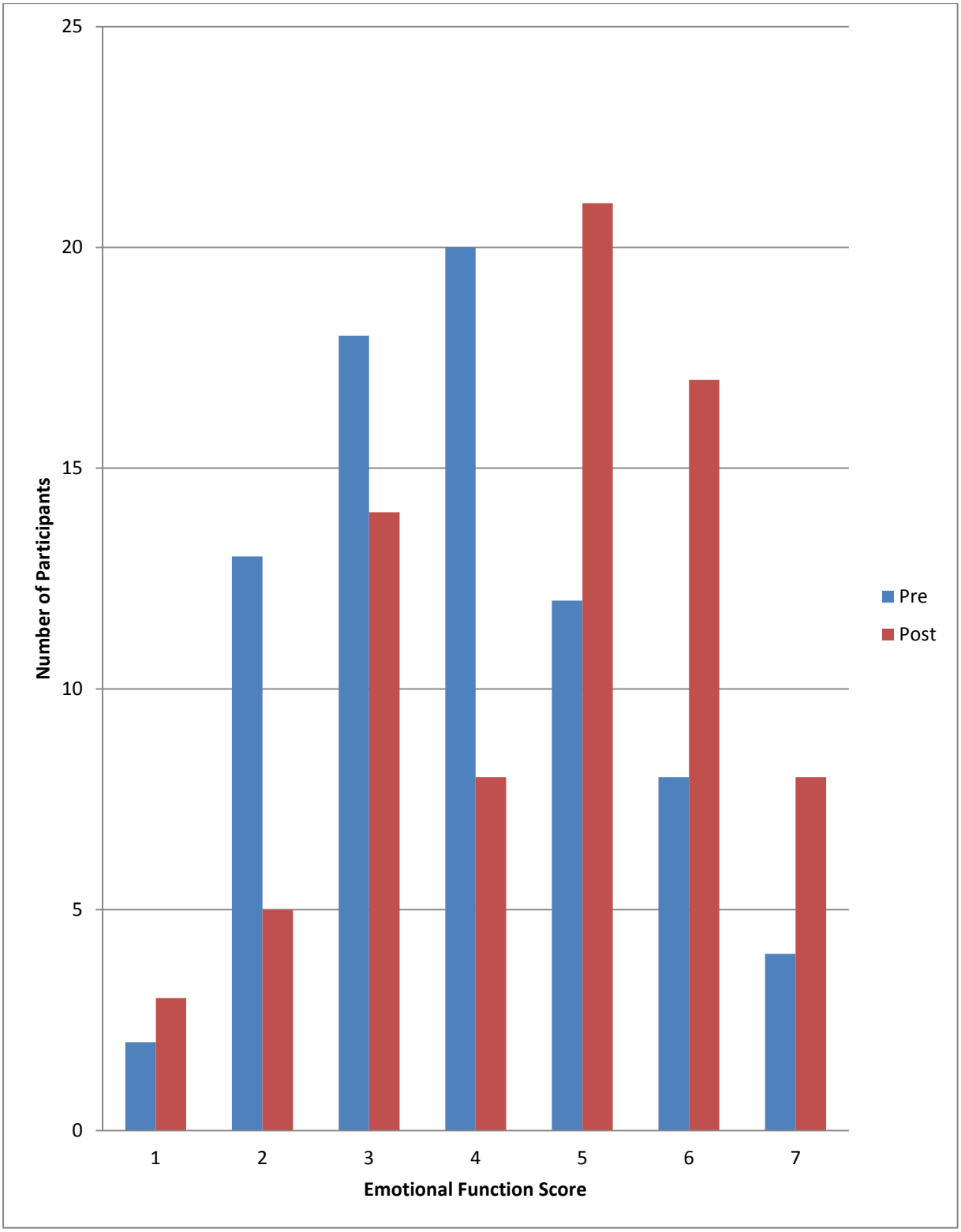


**Figure 3.3:** Emotional Function Scores of Study Participants

The number of participants at environmental stimuli domain score points 1, 2, 3, and 4 dropped after the intervention stage, but increased at points 5, 6 and 7 (Fig. 4.4).The number of participants at the environmental stimuli domain score point 1 reduced by half at post-intervention stage.

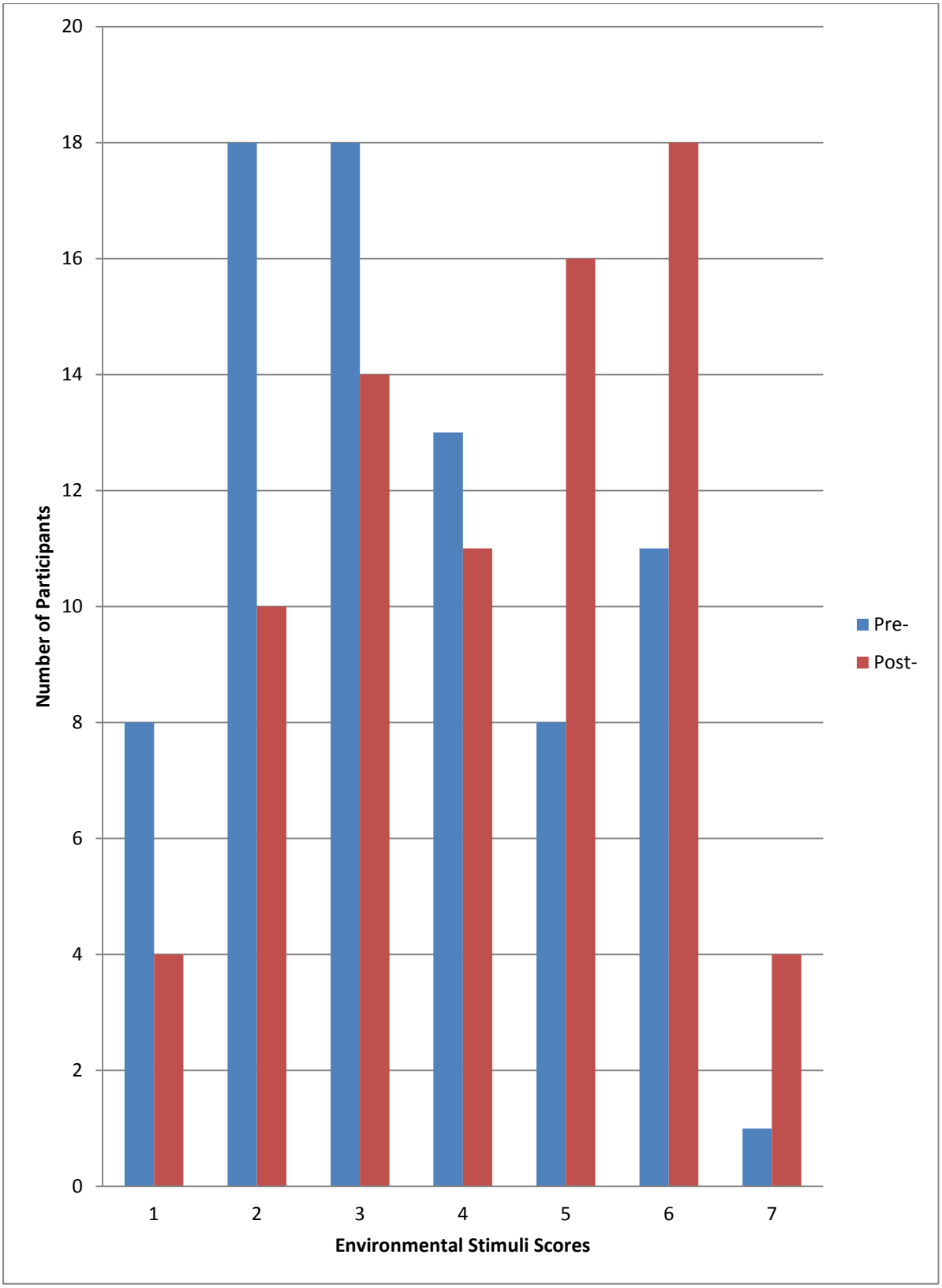


**Figure 3.4:** Environmental Stimuli Scores of Study Participants

The number of participants in baseline activity limitation domain dropped at score points 2, 3, 4 and 5, whilst those at domain score points 6 and 7 increased at the post-intervention stages. There was however no change in number of participants at domain score-point 1 (Fig. 3.5).

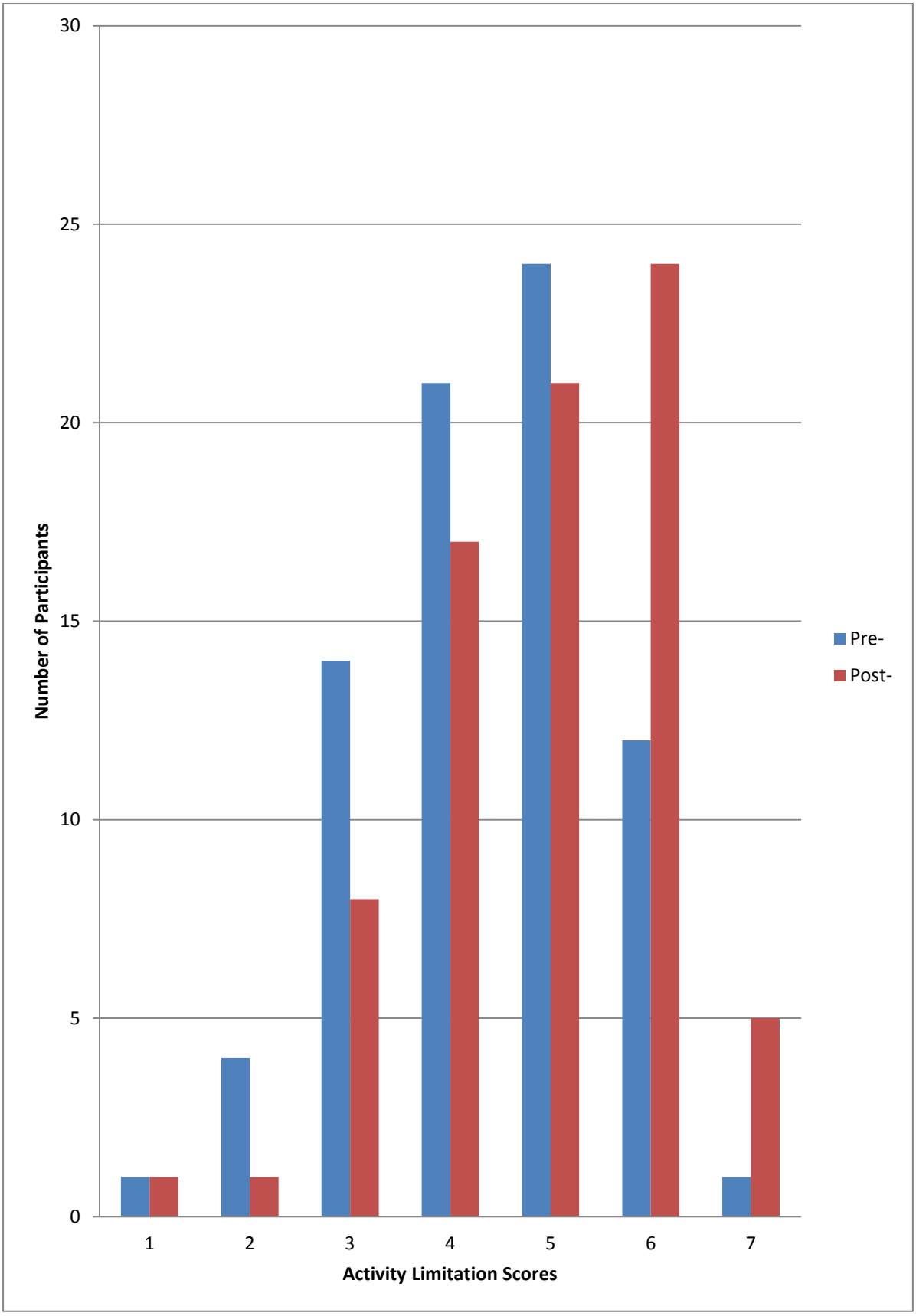


**Figure 3.5:** Activity Limitation Scores of Study Participants

There were no participants at symptoms domain score point 7 before the intervention and also at score point 1 after the intervention (Fig. 3.6).The number of participants dropped at domain score points 1, 2, 3 and 4, and increased at points 5, 6 and 7.

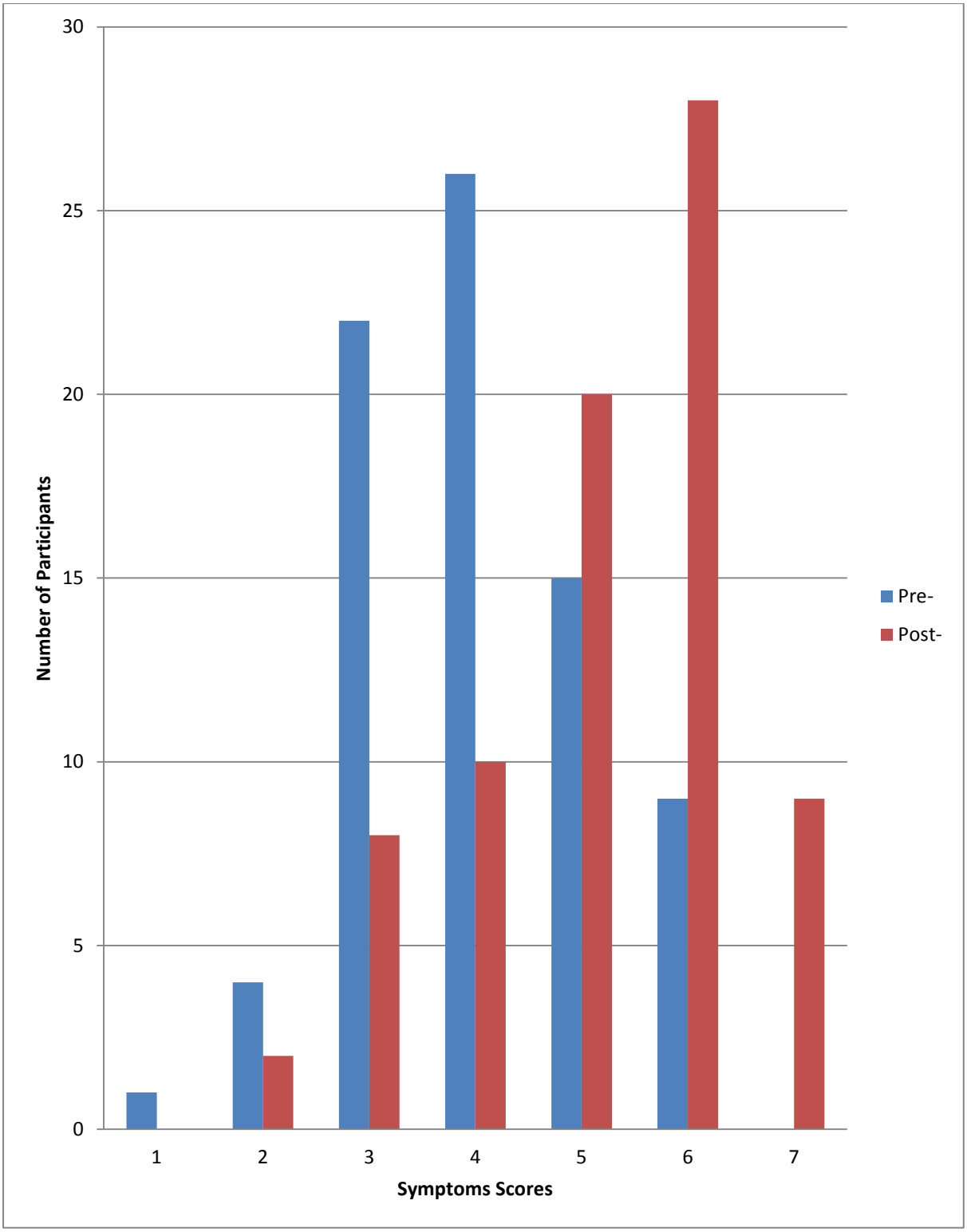


**Figure 3.6:** Symptoms Scores of Study Participants

### 3.4.2. Changes in HRQoL Characteristics of Participants Post-intervention

The quantum of change in HRQoL is displayed in table 3.20. About 56% of participants had a positive change in HRQoL, while 9% had a negative change after the pharmaceutical care intervention. However, about 35% of participants had changes that are not clinically significant.

**Table 3.20:** Quantum Changes in Quality of Life Post-Pharmaceutical Care

| **Change** | **Health Related Quality of Life (n=77)** | | | | | | |
|---|---|---|---|---|---|---|---|
| **Quantum** | **-3** | **-2** | **-1** | **0** | **1** | **2** | **3** |
| **Range** | -3.49-(-2.50) | -2.49- (-1.50) | -1.49- (-0.50) | -0.49-0.49 | 0.50-1.49 | 1.50-2.49 | 2.50-3.49 |
| **Number of Participants (%)** | 0 (0.00) | 1 (1.30) | 6 (7.79) | 27 (35.06) | 29 (37.66) | 12 (15.58) | 2 (2.60) |
| **Change rate (%)** | | 7 (9.09) Negative Change | | 27(35.06) No Change | | 43(55.84) Positive Change | |

From table 3.21, the paired mean difference values for the HRQoL and all the domains were above 0.5, the mean important difference. The paired mean difference for the HRQoL at 95% CI was 0.697 ($\pm$ 0.89) and a T = 6.845 (2-tailed $p < 0.05$). The paired mean difference at 95% CI was highest for the Symptoms domain 1.134 ($\pm$0.985) and lowest for the Activity Limitation domain 0.548 ($\pm$0.92).

**Table 3.21:** Paired Mean Difference Statistics of Health Related Quality of Life

| **Health-Related Quality of Life Domain** | | **Mean (SD)** | **Paired Differences** | | | **T** | **Df** | **Sig. (2-tailed)** |
|---|---|---|---|---|---|---|---|---|
| | | | **Mean (SD)** | ***95% CI of the Difference*** | | | | |
| | | | | **Lower** | **Upper** | | | |
| **HRQoL** | *Pre-* | 4.15 (1.132) | 0.697 (0.891) | 0.49 | 0.90 | 6.845 | 76 | 0.000 |
| | *Post-* | 4.85 (1.271) | | | | | | |
| **Activity Limitation** | *Pre-* | 4.37 (1.143) | 0.548 (0.921) | 0.34 | 0.76 | 5.256 | 76 | 0.000 |
| | *Post-* | 4.92 (1.224) | | | | | | |
| **Symptoms** | *Pre-* | 3.998 (1.086) | 1.134 (0.985) | 0.911 | 1.358 | 10.104 | 76 | 0.000 |
| | *Post-* | 5.132 (1.304) | | | | | | |
| **Emotional Function** | *Pre-* | 3.907 (1.453) | 0.714 (0.938) | 0.501 | 0.927 | 6.684 | 76 | 0.000 |
| | *Post-* | 4.621 (1.583) | | | | | | |
| **Environmental Stimuli** | *Pre-* | 3.289 (1.562) | 0.776 (1.099) | 0.526 | 1.025 | 6.195 | 76 | 0.00 |
| | *Post-* | 4.065 (1.685) | | | | | | |

From table 3.22, the paired mean difference between baseline and post-pharmaceutical care intervention peak expiratory flow rate was 17.533 L/min. (95% CI: 2.876-32.190) ($p<0.05$).

**Table: 3.22.** Paired Mean Difference Statistics of Peak Expiratory Flow Rate

| | **Mean (SD) L/min.** | | **Paired Differences** | | | **T** | **Df** | **Sig. (2-tailed)** |
|---|---|---|---|---|---|---|---|---|
| | | | **Mean (SD) L/min.** | ***95% CI of the Difference*** **Lower** | **Upper** | | | |
| **Peak Flow Rate** | *Pre-* | 266.467 (85.857) | 17.533 (63.705) | 2.876 | 32.190 | 2.384 | 74 | 0.020 |
| | *Post-* | 284.000 (103.294) | | | | | | |

3.4.3. Pharmaceutical Care Intervention on Asthma Patients Affected by Various Environmental Trigger-factors

Table 3.23 is a two-by-two table involving participants who are affected or otherwise by the common environmental trigger-factors and the extent of change in their HRQoL after the intervention. From the table 3.23, 60 out of the 77 participants were affected by dust amongst others, whilst the other 17 participants were not affected by dust. Of the 60 participants affected by dust, 39 had a change in HRQoL of 0.5 or more. Also 6 out of the 17 participants who were not affected by dust had similar changes in HRQoL ($p \geq 0.5$).

**Table 3.23:** Changes in HRQoL of Participants Affected by various Trigger-factors

| **Participants Affected by Trigger-factors (n=77)** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Changes in** | **Dust** | | **Smoke** | | **Perfume** | | **Dust/smoke/perfume** | |
| **HRQoL** | *Yes* | *No* | *Yes* | *No* | *Yes* | *No* | *Yes* | *No* |
| (HRQoL≥0.5) | 39 | 6 | 34 | 12 | 36 | 10 | 21 | 20 |
| (HRQoL<0.5) | 21 | 11 | 19 | 12 | 23 | 8 | 10 | 26 |
| **Total** | 60 | 17 | 53 | 24 | 59 | 18 | 31 | 46 |

The relative chance of attaining a change in HRQoL of not less 0.5 points from participants who were affected by at least dust/smoke/scent combination was 1.56 (95% CI; 1.03-2.35) (Table 3.24). The Z-stat was 2.12 ($p<0.05$) and a number of 4 (2-34) participants were needed to achieve a change in HRQoL of at least 0.5 in a participant.

**Table 3.24:** Relative Chance of HRQoL Changes in Participants Affected by Common Trigger Factors

| **Items** | **Environmental Trigger Factors and HRQoL of Participants** | | | |
|---|---|---|---|---|
| | ***Dust*** | ***Smoke*** | ***Scent*** | ***Dust/Smoke/Scent*** |
| Relative Chance | 1.84 | 1.28 | 1.10 | 1.56 |
| 95% CI | 0.94-3.60 | 0.82-2.01 | 0.69-1.74 | 1.03-2.35 |
| Z-stat | 1.79 | 1.09 | 0.40 | 2.12 |
| P | 0.074 | 0.28 | 0.69 | 0.034 |
| Chance Difference | 0.297 | 0.14 | 0.05 | 0.25 |
| | (0.04-0.55) | (-0.09-0.37) | (-0.20-0.31) | (0.03-0.47) |
| Number Needed to Intervene* | 3 (2-25) | 7(3+) | 19(3+) | 4(2-34) |

*Number needed to intervene to achieve one clinically significant HRQoL change

## 3.5. Modelling a Variation of the Health Related Quality of Life

Data on modelling a variation between the domain and the HRQoL has been organized in the following order:

### 3.5.1. Relationship between the Various Domains and the Composite HRQoL

In table 3.25, data on the relationship between the general HRQoL and its' domains are displayed. The weakest relationship ($r = 0.674$; $p<0.05$) existed between the variables of the

Symptoms domain of the baseline and the post- pharmaceutical care intervention. However, the relationship ($r = 0.942$; $p<0.05$) between the differences of the general HRQoL and those of the Symptoms domain was the strongest.

**Table 3.25:** Relationship between various Domains of Health-related Quality of Life

| **Variables** | **Correlation** | **Sig. (2-tailed) at 0.01** | **N** |
|---|---|---|---|
| Pre/post HRQoL | 0.729 | 0.000 | 77/77 |
| Pre/post AL | 0.703 | 0.000 | 77/77 |
| Pre/post S | 0.674 | 0.000 | 77/77 |
| Pre/post EF | 0.813 | 0.000 | 77/77 |
| Pre/post ES | 0.773 | 0.000 | 77/77 |
| Diff. HRQoL/Diff. AL | 0.914 | 0.000 | 76/76 |
| Diff. HRQoL/Diff. S | 0.943 | 0.000 | 76/76 |
| Diff. HRQoL/Diff. EF | 0.859 | 0.000 | 76/76 |
| Diff. HRQoL/Diff. ES | 0.813 | 0.000 | 76/76 |

*AL – Activity limitation: S – Symptoms: EF – Emotional function: ES – Environmental stimuli*

A plot of HRQoL and domain variables of the study participants are illustrated on charts 3.1-3.9. Charts 3.1 to 3.5 show baseline HRQoL variation with the post-intervention domain variables, whilst charts 3.6 to 3.9 show variation of the differences in HRQoL and those of the various domains.

The relationship of variability between pre- and post-intervention HRQoL was positive and linear (Chart 3.1).The points were moderately scattered from the best fit line and 53% of the post HRQoL values was explained by the pre-HRQoL values.

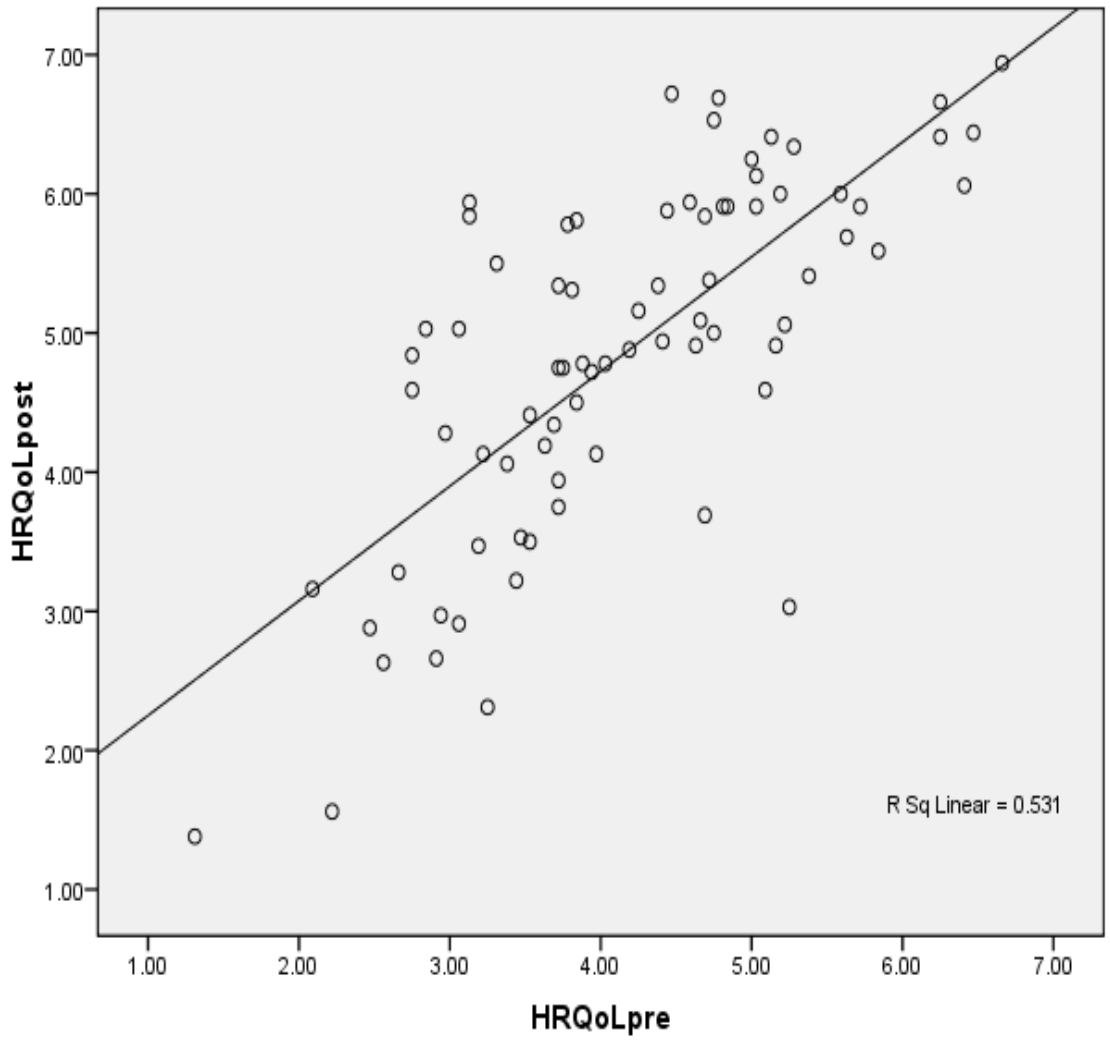


**Chart 3.1:** Scattered Plot of Post- vs. Pre-PharmCare Health –Related Quality of Life

The relationship of variability between pre- and post-intervention AL was positive and linear (Chart 3.2). The points were moderately scattered from the best-fit line and 49% of the variability in the post-activity limitation domain values was explained by the pre-activity limitation values.

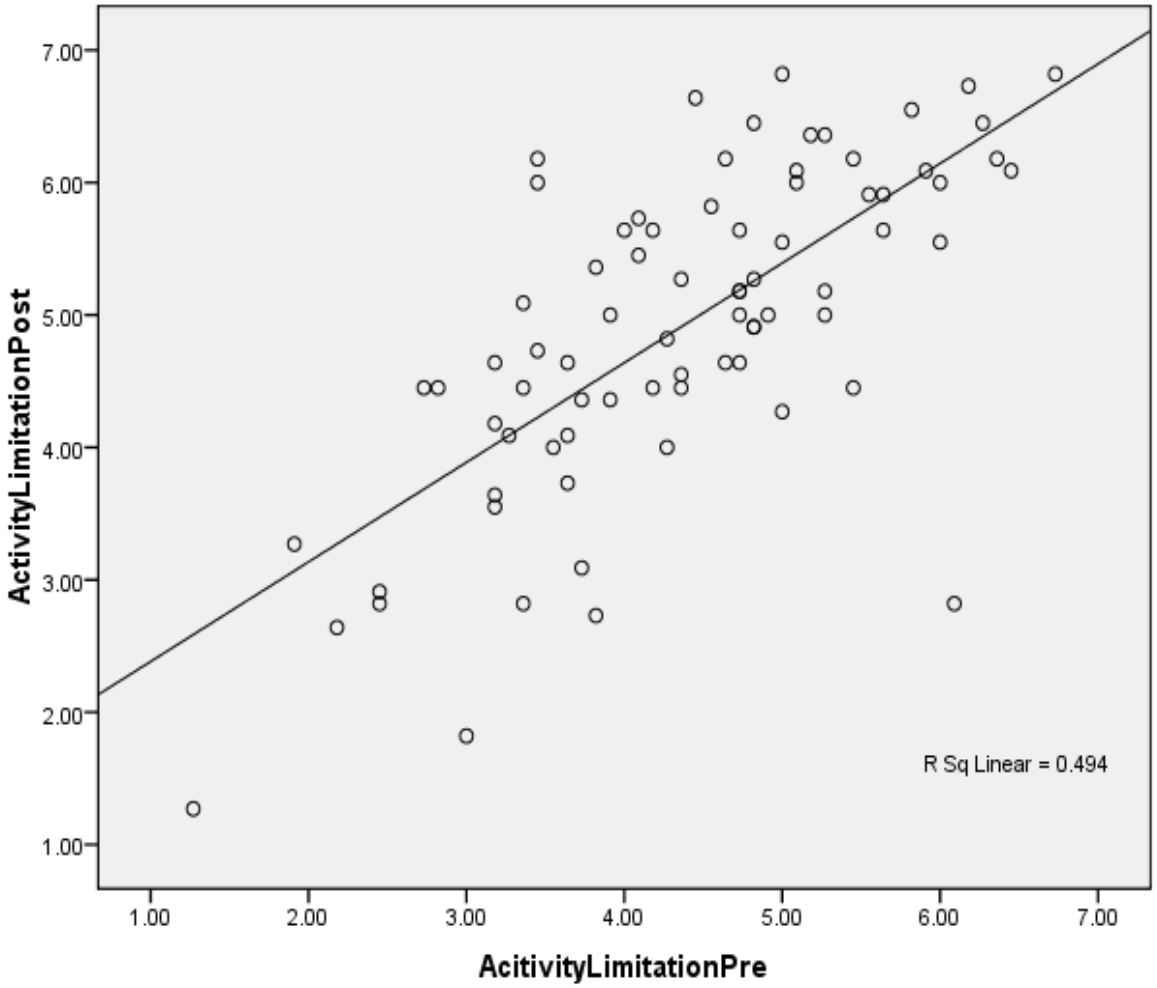


**Chart 3.2:** Scatter Plot of Post- vs. Pre-PharmCare Activity Limitation

The relationship of variability between pre- and post-intervention HRQoL was positive and linear (Chart 3.3). The points in this chart were moderately scattered from the best-fit line but more scattered away from the best-fit line than those in chart 3.2 and only 42% of the variability in the post-symptoms domain values was explained by the pre-symptoms values.

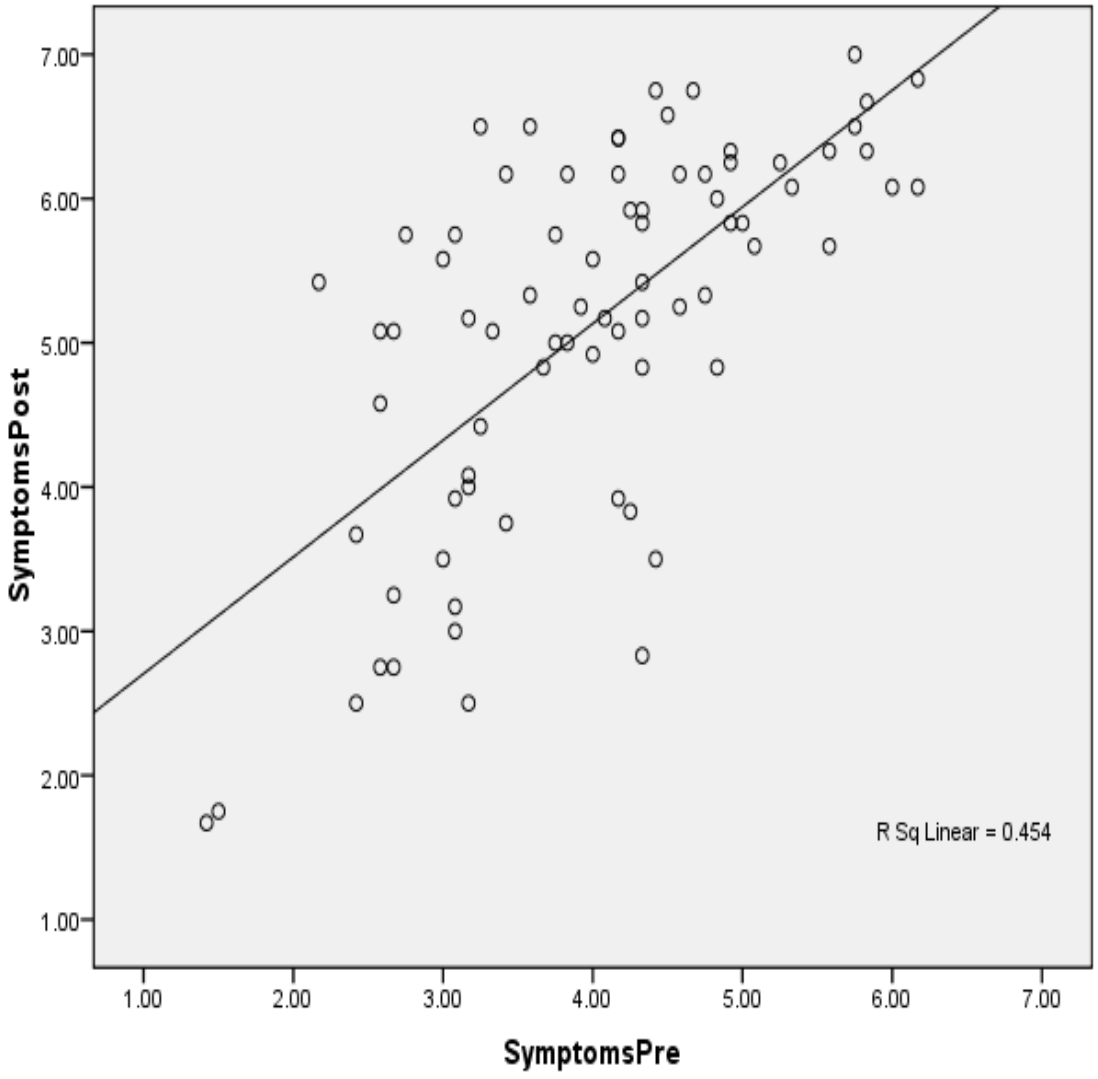


**Chart 3.3:** Scatter Plot of Post- vs. Pre-PharmCare Symptoms

The relationship of variability between pre- and post-intervention EF was positive and linear and 66% of the variability in the post-emotional function domain values was explained by the pre-emotional function values (Chart 3.4). The points in this chart are strongly scattered around the best-fit line than those in the pre/post symptoms and activity limitations domains.

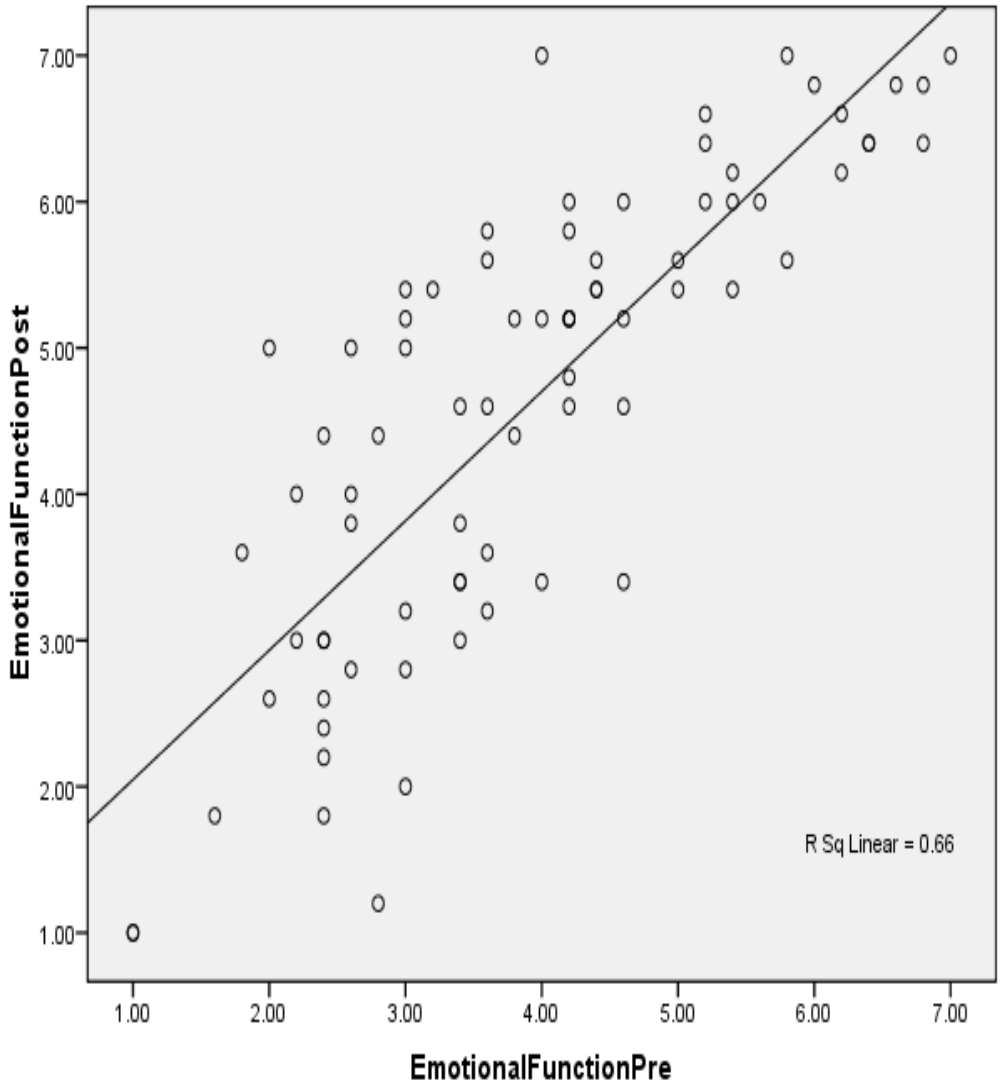


**Chart 3.4:** Scatter Plot of Post- vs. Pre-PharmCare Emotional Function

The relationship of variability between pre- and post-intervention ES was positive and linear and approximately 60% of the variability in Post-environmental stimuli domain values was explained in the post-environmental stimuli values (Chart 3.5). The points in this chart are strongly scattered around the best-fit line for this relationship, but not as strong as the relationship in the pre- and post-EF domain.

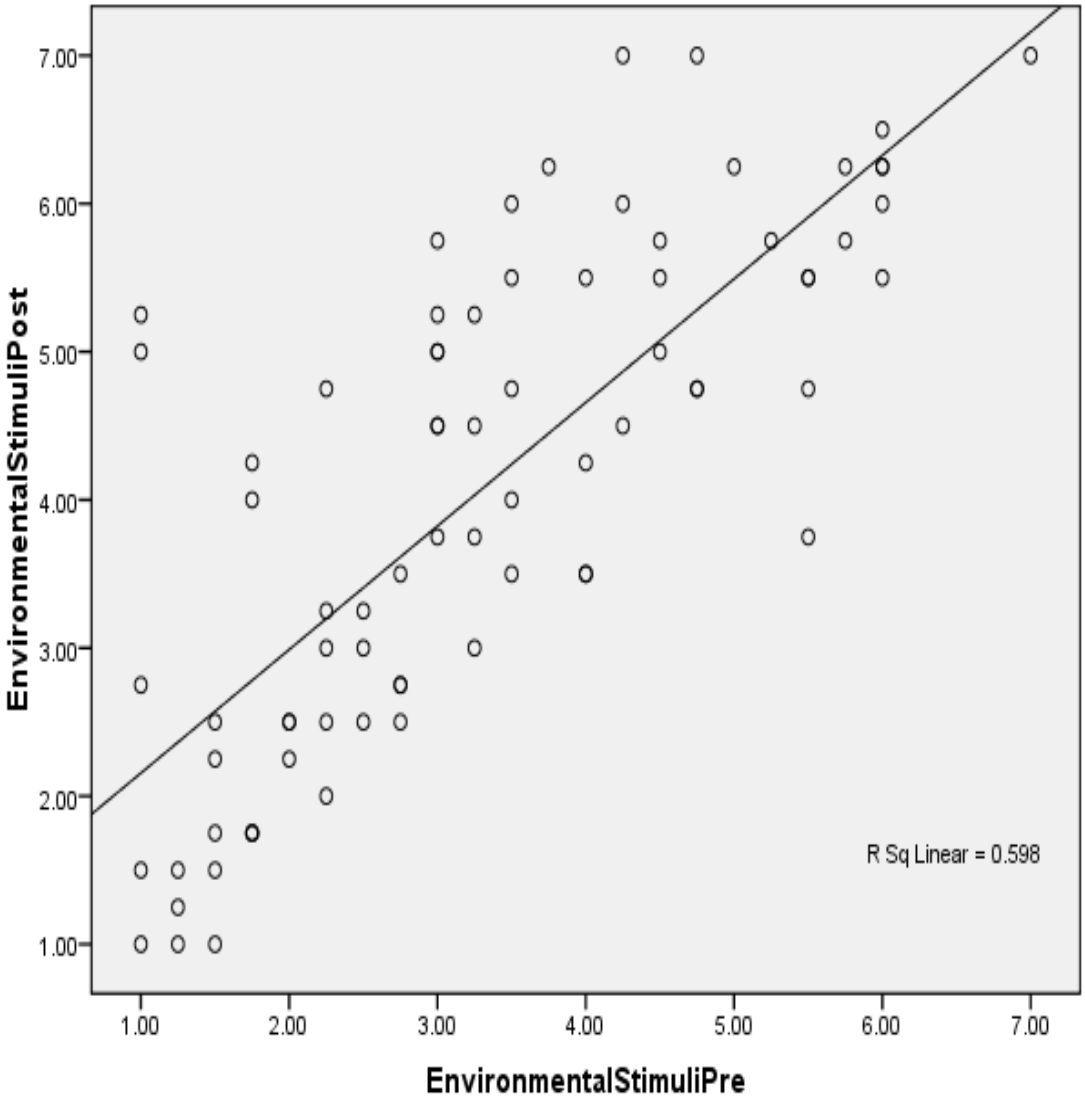


**Chart 3.5:** Scatter Plot of Post-/ vs. Pre-PharmCare Environmental Stimuli

The relationship of variability between the differences in the HRQoL and those of the AL domain was positive and linear and as much as 84% of the variability of the differences in the HRQoL values was explained by the differences in activity limitation domain values (Chart 3.6). The points in this relationship were strongly scattered around the best-fit line than those in the relationship between the differences in the HRQoL with emotional function domain and also with the environmental stimuli domain.

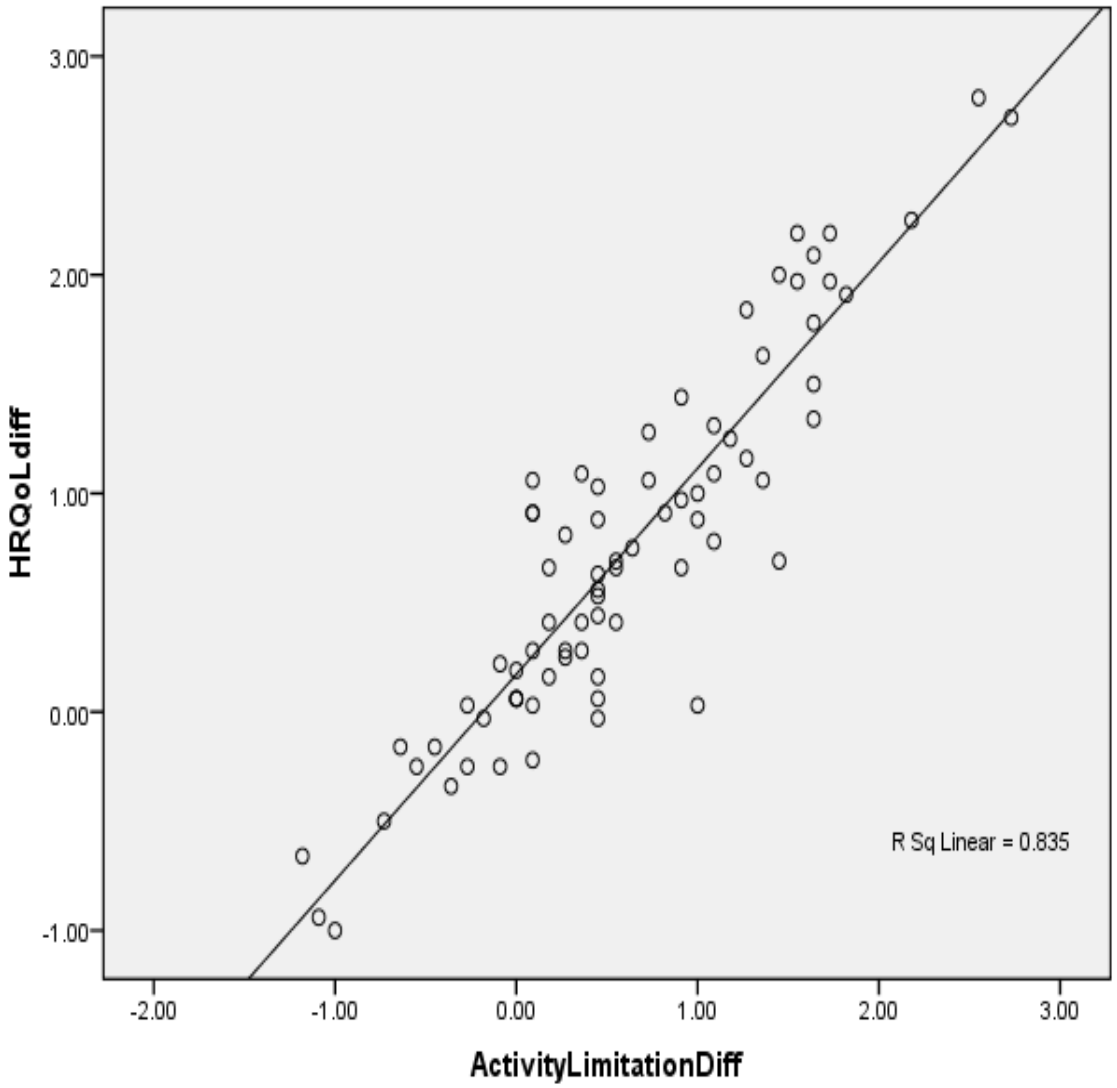


**Chart 3.6:** Scatter Plot of Differences of Health-related Quality of Life vs. Differences in Activity Limitation Domain

The relationship of variability between differences in the HRQoL and those of the EF was positive and linear. About 74% of the variability in the differences in HRQoL values was explained by the emotional function domain values (Chart 3.7). The points in this relationship were strongly scattered around the best-fit line more than those found in the relationship between the differences in HRQoL and the environmental stimuli domain.

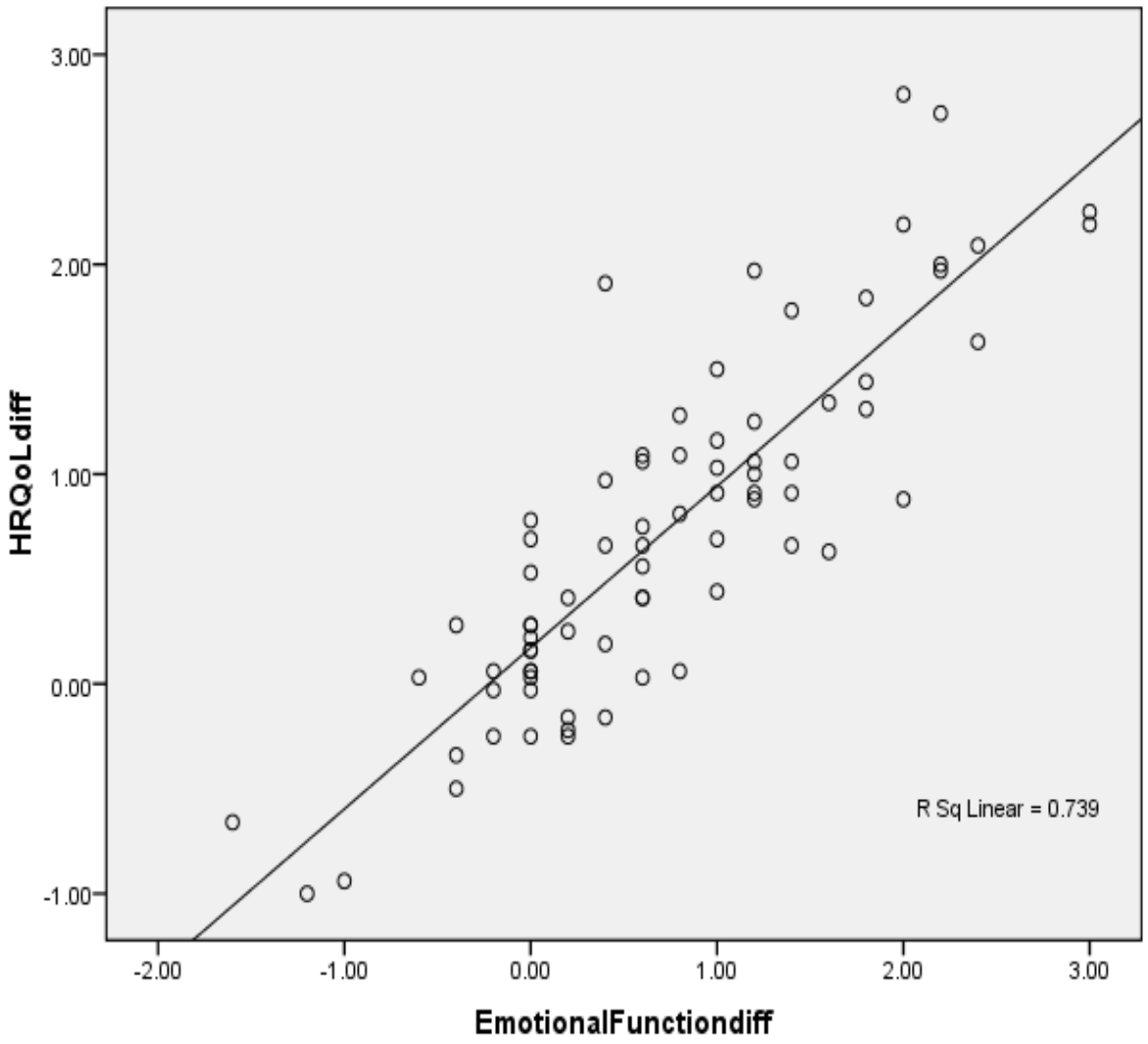


**Chart 3.7:** Scatter Plot of Differences in Health-related Quality of Life vs. Differences in Emotional Function Domain

The relationship of variability between the differences in the HRQoL and those of the ES domain was positive and linear. About 66% of the variability in the differences in HRQoL values was explained by the differences in the environmental stimuli domain values (Chart 3.8). The points in this relationship were strongly scattered around the best-fit line but not as strongly as in the differences of the HRQoL and the activity limitation domain.

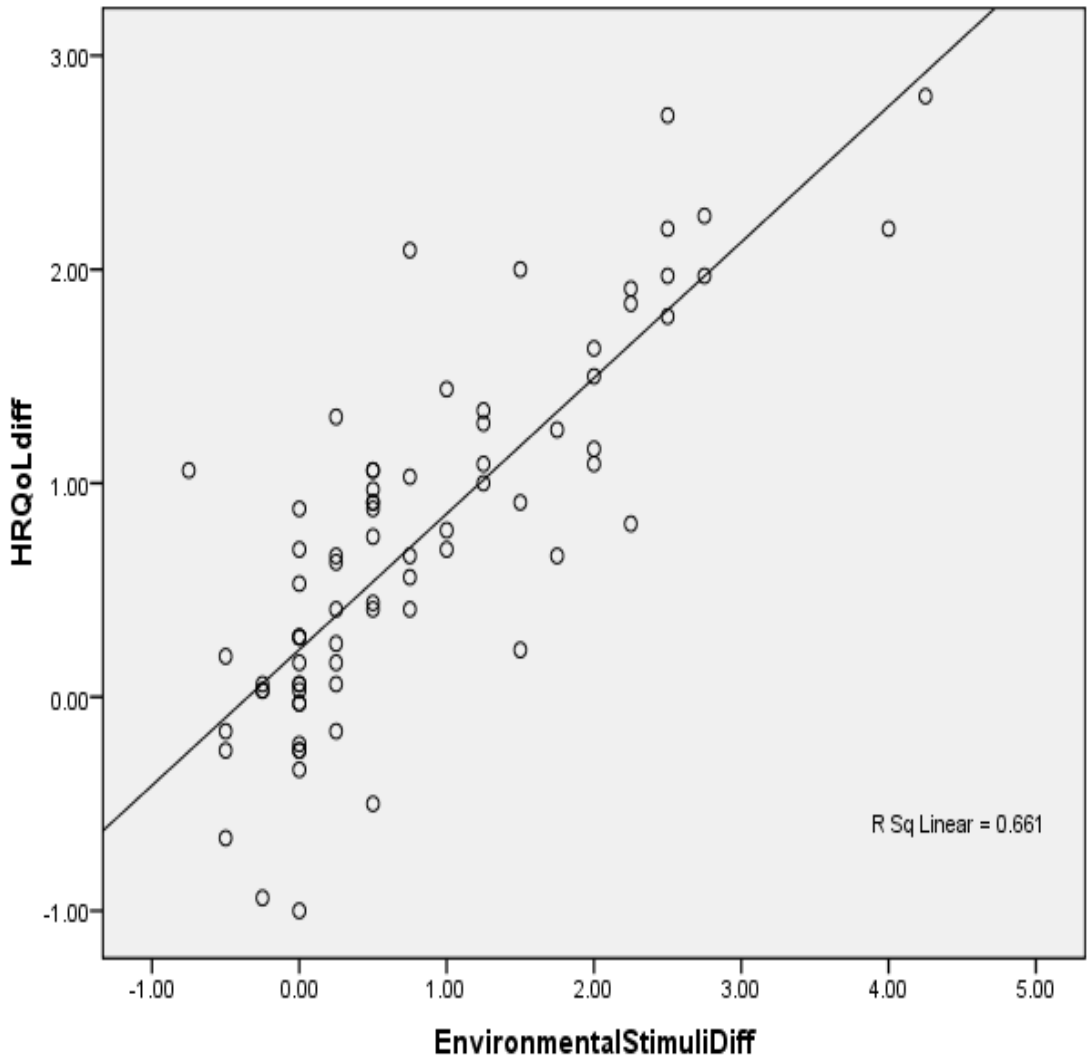


**Chart 3.8:** Scatter Plot of Differences in Health-related Quality of Life vs. Environmental Stimuli Domain

The relationship of variability between differences in the HRQoL and those of the S was positive and linear and 88% of the variability in the differences of the HRQoL values was explained by the differences in the symptoms domain values (Chart 3.9). The points in this relationship were more strongly scattered around the best-fit line than those seen between the difference of the HRQoL and those of the ES, AL and EF.

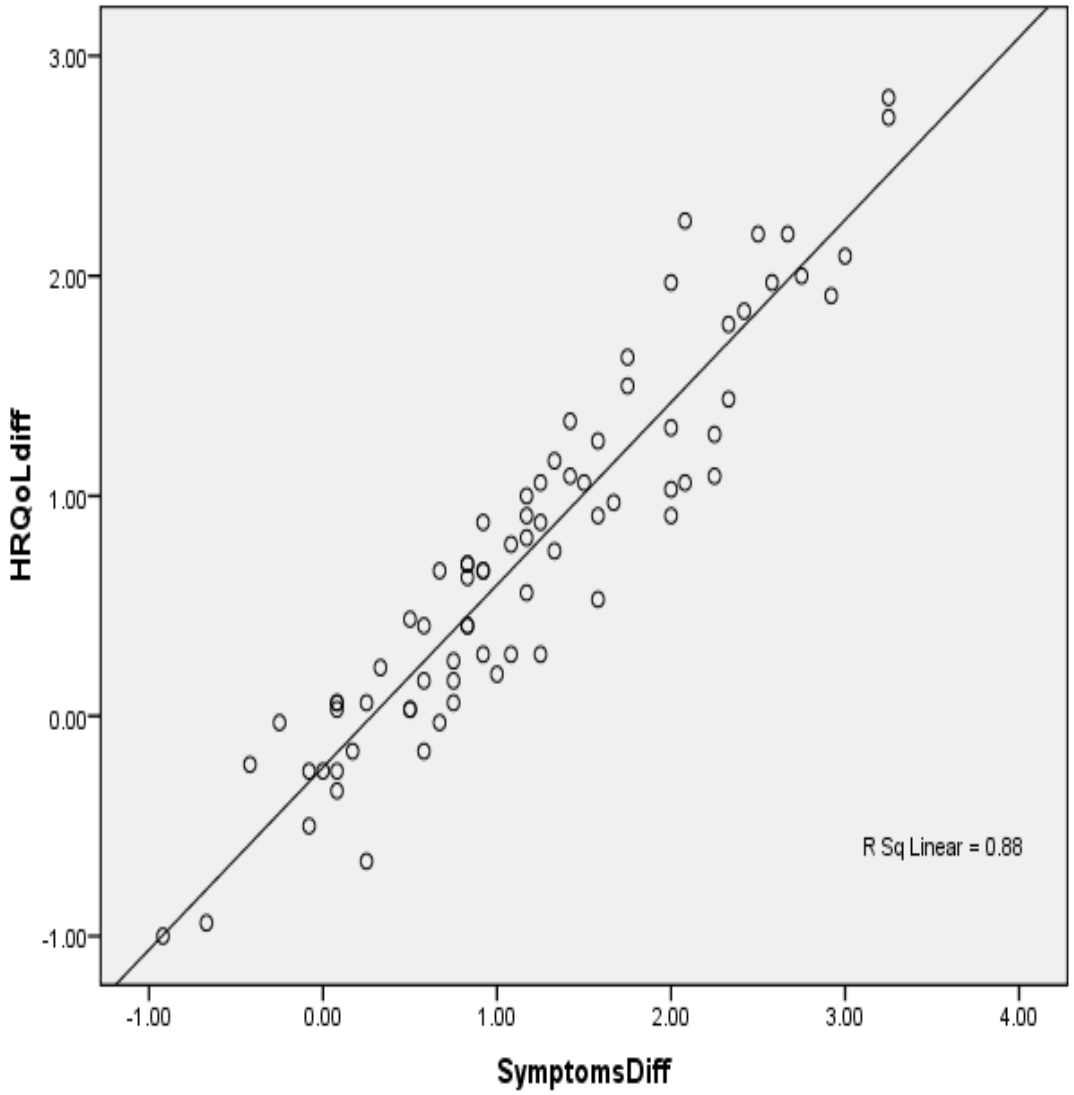


**Chart 3.9:** Scatter Plot of Differences in Health-related Quality of Life vs. Differences in Symptoms Domain

### 3.5.2. Relationship Between Peak Expiratory Flow Rates and HRQoL

In table 3.26, the correlation between the HRQoL and the Peak expiratory flow rates (PEFR) are weak. At a CI 0.01 (2-tailed), the correlation (r) between baseline HRQoL and PEFR was 0.34 ($p<0.05$) and between post-intervention HRQoL and PEFR was 0.431 ($p<0.05$). The correlation (r) at CI 0.01 (2-tailed), between changes in HRQoL and PEFR was 0.268 ($p<0.05$).

**Table 3.26:** Relationships between HRQoL and Peak Expiratory Flow Rates

| **Variables** | **Correlation** | **Sig. (2-tailed) at 0.01** | **N** |
|---|---|---|---|
| PreHRQoL/PrePEFR | 0.340 | 0.003 | 76/75 |
| PostHRQoL/PostPEFR | 0.431 | 0.000 | 75/75 |
| Diff. HRQoL/Diff. PEFR | 0.268 | 0.02 | 76/75 |

### 3.5.3. Modelled Variation of the Composite HRQoL with Symptoms Domain

A regression analysis results of the changes in HRQoL and those of the Symptoms domains presented in tables 3.27, 3.28 and 3.29 to model the variation. In table 3.27, the estimated error of this model was a low 0.30217, with almost all the variation in the Symptoms domain (0.886) explained in the model.

**Table 3.27:** Model Summary of HRQoL Difference vs. Symptom Domain Difference

| **R** | **R square** | **Adjusted R square** | **Standard Error of the Estimate** |
|---|---|---|---|
| 0.942 | 0.887 | 0.886 | 0.30217 |

An ANOVA test results in table 3.28, indicate that 53.1 of about 60 variations were accounted for by this model at an F-static value of less than 0.05.

**Table 3.28:** Model Summary of HRQoL Difference vs. Symptom Domain Difference

| **ANOVA of Model** | | | | | |
|---|---|---|---|---|---|
| | ***Sum of Squares*** | ***Df*** | ***Mean Square*** | ***F*** | ***Significance*** |
| Regression | 53.099 | 1 | 53.099 | 581.535 | 0.000 |
| Residual | 6.757 | 74 | 0.091 | | |
| Total | 59.856 | 75 | | | |

From table 3.29, the coefficients of the HRQoL difference were the constant value of -0.273 and a factor of 0.856 of the Symptom domain difference.

**Table 3.29:** Model Summary of HRQoL Difference vs. Symptom Domain Difference

| **Coefficients of HRQoL Difference** | | | | | | |
|---|---|---|---|---|---|---|
| ***Model*** | ***Coefficients*** | | | | | |
| | ***Unstandardized*** | | ***Standardized*** | ***T*** | ***Significance*** | ***95% CI for B*** |
| | B | Std. Error | Beta | | | |
| Constant | -0.273 | 0.054 | | -5.108 | 0.000 | -0.380 to -0.167 |
| Symptom Difference | 0.856 | 0.036 | 0.942 | 24.115 | 0.000 | -0.785 to -0.927 |

Considering the derived coefficients (Table. 3.29), it can be implied that, at 95% CI, the difference in HRQoL of a patient with asthma can be estimated when the difference in the Symptoms domain (S) is factored by 0.856, and then reduced by a constant of 0.273.

**Difference in HRQoL = 0.856 x Difference in Symptoms – 0.273**

At a t-static less than 0.05, as in table 3.29, this variation was clearly not due to chance.

# CHAPTER 4

# 4. DISCUSSION, CONCLUSION AND RECOMMENDATIONS

## 4.1 Discussion

Phase I of the study was designed to describe the outcomes of counselling and education provided by pharmaceutical service staff to patients. This aspect of the study was necessary in order to understand how patients with chronic or acute disease conditions were managed and to develop a model of care delivery for patients with asthma that would address most of the gaps identified. This section of the study used pharmacy-exit interviews to assess: participant and dispenser communication language and understanding; participant expressed satisfaction in rating of dispensing services; participant information about their health and home medications; and participant knowledge about their pharmacy-exit medicines.

The revelations from these assessments indicated the lack of differentiation in the counselling and education provided to chronically ill patient and acutely ill patients. Secondly, it revealed the fact that patients were somehow satisfied with the services even though they received little of what would be needed to adequately self-manage.

Phase II of the study was designed to assess how asthma medicines were prescribed for study participants. This phase of the study determined the current prescribing patterns for asthma medications to identified gaps that needed to be addressed. The mainstay of asthma management is the use of inhaled medications in additions to asthma self-management education and environmental trigger-factor management. However, the clinical benefits of the medications used can be assessed on how well patients are educated on asthma as a disease

condition and its management and the adherence of the prescriber to standard protocols for asthma management. This phase looked at the adherence to the prescribing protocols.

The findings of these phases created the necessary template for the development of the "Model pharmaceutical Care Plan" (Appendix 4) that was used in phase III of this study.
Chronically ill patients according to Sabate (2003), needed a model of care that paid attention to self-management, prevention and continuity of care, but which received limited attention in acute care models.

Phase III of this study was designed to assess the impact of pharmaceutical services delivery on asthma control, using the model care plan developed based on the findings from phases I and II.
Educating patients with asthma to actively get involved in the management of their condition was currently highly recommended in asthma management (EPR-III, 2007; GINA, 2012). Though clear benefits might be derived from such education, there are no clear indicators to assess the impact of such education beyond those of general asthma control. Certainly, it was not anticipated that all patients might derive the same level of benefits from these diverse educational components.
This section of the study used pharmaceutical care assessment and intervention tools and health-related quality of life instruments to: characterize asthma patients at baseline; make pharmaceutical care intervention; and re-assess the baseline characteristics for comparison after pharmaceutical care intervention.

### 4.1.1 Patient Counselling and Education at Out-patient Pharmacy

Most of the participants in the pharmacy-exit interviews were adults with formal education up to the secondary or tertiary levels and who understood the dispensing communication. Participants in the study understood multiple languages and various languages were used in the counselling and education process. What was not clear from this study was how the communication language was determined and what went into such determination. Since no participants were communicated to Hausa and Ewe, suggested that the language determination might also be limited to a dispenser's inability to communicate in certain other languages. Participants were satisfied with the dispensing activities and almost all of them claimed they understood the dispensing communications. However, most of the participants rated the dispensing activities as "okay"; with about 30% of participants in both the chronic and acute groups rating the dispensing services either as "just right", "alright", "good", "great" or "excellent". The total number of participants who rated the services as "okay", "just right", "alright", "good", "great" or "excellent" was similar to those who claimed initially that they were satisfied with the dispensing services. It could therefore be said from these figures that the terminologies used by participants might be the various ways they wished to express satisfaction.

At the end of the interview, when the issue of satisfaction was raised again, the number of participants initially satisfied with the dispensary services dropped and participants wished for additional information for themselves. The questions posed to participants during the exit interviews might have brought to the fore issues that the participants at the end of the interview now considered relevant but not catered for in the dispensing education and counselling. Participants' requested for education on "side effects from their medications", "how their medicines work", "where to get the un-dispensed medicines" and "an improved relationship with the pharmacy staff. This was an indication that most participants do not

themselves really appreciate the full complement of the information and education that might be required for them to actively and effectively participate in self-management of their health condition. These findings indicated that participants would rate the dispensing services differently than they did, should they have knowledge of what information was important for them to make decisions relating to their health and medications in-between their hospital review periods. These findings agreed to what Yach (2002) considered as the "Micro-level factors" within the ecological frame of factors contributing to patient behaviour. Yach (2002) contended that the quality of the communication between the healthcare professional and the degree of trust the patient had in the healthcare professional could impact patient adherence behaviour. The revelations from this study also indicated that patients needed to also know what information they must have to improve their adherence behaviour.

Sabate (2003) suggested that there are several important variables that are behavioural in nature and are also dynamic and therefore amenable to intervention. The patient request for improved relationship with pharmacy pointed to an uncomfortable situation that might affect trust in the healthcare provider. Though adherence behaviour of patients was said to be amenable to appropriate intervention, it was equally important that it was delivered by pharmacy staff with the right attitude towards the patient. The patient request for better relationship with staff was an indication of a better partnership in which the patient was free to ask and be told what they needed to know beyond what had already been told them.

Participants had challenges with the names of their medications. Though almost all the medicine labels had the names of the medicines, participants had challenges memorizing or reading out the names on the medicine labels. It was not expected that patients should be able to pronounce all the medicine names or easily read out the names of their medications, but to check how easily participants could locate the names and other information relevant to their

medications. In our settings where the population visited different health facilities at various times, it was necessary for patients to have information on their medications or be able to readily locate and provide the information when needed. Participants had more information on things they needed to avoid than was provided for on their current medication labels. However, only a small proportion of participants had any information on things to be avoided. This information was not found on their medicine labels and participants did not mention any as well. The study instrument did not identify the sources of the information that participants had and the study could anecdotally suggest that the information on "things to be avoided" were provided verbally. If the pharmacy staff considered this information important then why was is not stated on the label so that the patient could refer to it occasionally.

Label information on storage of medicines was inadequate and so was participant knowledge on storage. The concern of the pharmacy staff seems not focussed on the time-bound quality of the medications dispensed. It is known that some antibiotic mixtures used in acute care for short periods of time tend to lose potency under various conditions. Patients who were supplied medicines for well over 3 months certainly needed more information on where to store their medications.

The Pharmacy staff did not spend adequate time to explain "the possible side effects", "what to be avoided" and "how best to store medicines" to patients. Participants lack adequate precautionary information on appropriate steps to take when they have adverse drug reactions, or miss a dose, or the things to avoid and the use of other medicines. Of the few participants who had precautionary information, majority of them were from the chronic health condition group. Though an important finding that more participants with chronic health condition had some precautionary information; the overall numbers were relatively smaller than expected. Dunbar-Jacob *et al* (2000) noted that poor adherence attenuates

optimum clinical benefits and this assertion was also supported by a WHO report (2002) that adherence was a primary determinant of effectiveness of treatment. Therefore for a patient's behaviour to correspond with recommendations from the healthcare provider as envisaged by Vitolins and colleagues (2000), the patient must have adequate recommendations to guide their self-management decisions outside the hospitals and between clinical reviews. This type of patient self-management would involve the various actions needed to be performed by patients for themselves in daily life to manage their illness and treatment. There are many cross-roads in self-management and perhaps only the well-motivated and the well-informed patients might make the right turn or choices at each junction.

Participants were not provided information about general and specific approaches regarding steps they needed to take in case of side effects and missed doses. The obvious choices might include infrequent use of medications which were perceived to be the cause of the discomfort or doubling of doses missed. Clinical assessment of a patient's condition is usually based the level of improvement or deterioration noted without much consideration of the patient medication-use behaviour between reviews. Some patients might feel uncomfortable to discuss their medication-use behaviour with their healthcare professional because the possible decisions they needed to take regarding self-management were not initially discussed with them. They would rather keep their behaviour to themselves rather than be reprimanded for an unacceptable approach. The revelations from this study was at variance with the position by Nolte & Mckee (2008) that suffering from chronic condition also implied the adoption of new health behaviour which incorporated adherence to treatment regimens; monitoring health status and making associated care decisions among others. The findings from this study did not indicate much activity from the services rendered by the pharmacy staff as activities directed at supporting the patient with chronic health condition towards the adoption of new

health behaviour. The study findings revealed inadequate information that could empower patient with chronic health conditions towards a new behaviour.

Lack of relevant information might compromise the self-management partnership for patients with chronic health conditions who were usually reviewed infrequently and have to manage themselves for about 3 to 6 months before the next review. Within this period of time, a lot might happen with the patient, which might require the patient to manage their illness and treatment rationally and precisely. The indications from the study did not demonstrate any additional effort in the educational management of chronic health condition participants from that offered to acute health condition participants as envisaged in the EPR-3 (2007) and also as recommended in the WHO-ICCC framework (2002). "That health care provider, public health personnel and those who support health care organizations need new team care models and evidence-based skills for managing chronic health conditions".

These findings agreed with Sabaté (2003) that adherence was a behavioural problem observed in patients, but with causes beyond the patient. In this study the treatment-related demands that the patient must attempt to cope with were not addressed adequately. These demands are characterized by the requirement to learn new behaviours, alter daily routines, tolerate discomforts and inconveniences, and persist in doing so while trying to function effectively in their various life-roles.

### 4.1.2 Prescribing Patterns of Asthma Medications

Information generated from phase I of this study indicated inadequate management of patients with chronic health conditions with regards to self-management education. In phase II, this study demonstrated that prescription patterns varied so much and did not always

followed recommended national treatment protocols for the management of asthma. Many of the patients were on higher therapeutic levels (step III) as compared those on step II. There seem, though anecdotally, to be a quick jump to step III without adequate opportunity to be managed with medications on step II.

The expert panel report (2007) had suggested the addition of Long-Acting Beta-Agonist (LABA) to low-dose inhaled corticosteroids (ICS) in mild to moderately persistent asthma. This according to the EPR (2007) leads to greater improvement in lung function, symptoms, and less use Short-acting Beta-agonist than increasing the dose of ICS or using other adjunctive therapy. The comparatively high number of patients on a combination of LABA to low dose ICS presupposes that these patients had mild to moderate asthma for which reason they needed increment in their ICS doses. If that was the case then prescribing LABA offered the option of additional asthma control. In the study report by Powell & Gibson, (2003), the evidence suggested that in patients who had mild to moderate persistent asthma, the use of higher doses of ICS improved asthma control moderately as compared to the findings of Masoli *et al*., (2004), that indicated improvements at higher doses for patients with severe asthma.

These notwithstanding, the EPR (2007) and the national treatment protocols recommended a step down in pharmacologic therapy were necessary, when the asthma is controlled for a period of time. The findings from this study seem to suggest that hardly were there any situations that warranted pharmacologic therapy step downs.

The addition of LABA to low-dose ICS may have positive effects on the impairment domain of asthma management but may also introduce some level of negative impact on the risk domain. The Expert Panel Report (2007) recommended the use of the lowest dose of ICS that maintained asthma control and further suggested evaluation of patient adherence levels,

inhaler-use technique as well as environmental factors that may contribute to asthma severity before increasing the dose of ICS (EPR, 2007).

In phase II of this study, the reverse was the case. Management of environmental factors and inhaler-use technique were found to be inadequate and therefore there seem to be room to reduce ICS doses by interventions that address the issues of environmental factors and inhaler-use technique in these patients.

Recommended doses for the use of LABA in combination with low-dose ICS were also exceeded in prescriptions reviewed in this study. More than 100 mcg of dry powder Salmeterol were prescribed for patients {2 puffs (100 mcg) twice daily instead of 1 puff (50 mcg) twice daily}.

The study by Nelson and colleagues, (SMART, 2006) noted increases in asthma related deaths in the Salmeterol arm of their study and this has been the basis for the black box warning tag to Salmeterol and its combinations by the FDA (2010). There was no justification for the findings in this study for LABA-containing medications to be used without adequate caution and more so in doses that were not licensed for use (more than 100 mcg per day) and not recommended by the national treatment guidelines.

Even though Sears and colleagues, (2007) found insignificant asthma related number of deaths in the comparative use of Formoterol (LABA) against other agents, there were more asthma related deaths in the Formoterol arm of the study than with the other non-LABA agents. This further makes the FDA caution relevant for all LABA-containing medications and not merely Salmeterol.

This study identified to a small extent the use of oral corticosteroids for the management of asthma that were not recommended in the national treatment protocols. Oral corticosteroid

medications have been indicated for short term use in emergency situations. It is also recommended in situations where addition of leukotriene antagonist and modified-release Theophylline to controller medications (combination of LABA and ICS) had not provided adequate asthma control. Use of oral corticosteroids leads to increased systemic bioavailability of the corticosteroids which in turn negatively affects the risk domain of management of asthma. It may therefore be more appropriate to reduce the high systemic concentration of the corticosteroids by the use ICS that restricts the medication more to the airways where they are mostly needed.

### 4.1.3 Pharmaceutical Care Intervention

Phase III of this study tested the hypothesis that the mean health-related quality of life (HRQoL) score in patients with asthma, a month after pharmaceutical care intervention was the same as at baseline.

According to Junniper and colleagues (1994), a mean difference of 0.5 units in the HRQoL for asthma patients was the minimum difference of clinical importance. Though the quantum change of these units of HRQoL is not directly related to any specific clinical indices, it may contribute to the search for a therapeutic response measure for patients with asthma.

Findings from this phase of the study revealed significant changes in participants' characteristics, especially the health-related quality of life and the peak expiratory flow rates. With such findings the study proceeded to define the relationships between the various domains that constituted the composite HRQoL and the composite HRQoL. Similarly, the study defined the relationships between the HQRoL and the PEFR. Subsequently, because of the very strong relationship identified between the Symptoms domain and the composite HQRoL, the study modelled a variation of the HRQoL with the Symptoms domain.

Further to this, the study performed a prognostic test with the data of study participants to ascertain the relative chance of participants with various environmental trigger-factors that are likely benefit from such interventions as those used in this study.

### 4.1.4 Assessing Impact of Pharmaceutical Care Delivery on Asthma Control

Participants in this phase of the study were all adults on various inhaler medications. A high number of the study participants were either on inhaler Salbutamol and Symbicort® or inhaler Salbutamol with Seretide®. Most participants in the study had used either "preventer" or "reliever" medications for more than a year. Overall participant Inhaler-use technique assessments revealed rather very low figures. Very few of participants had adequate inhaler-use technique to either the dry powder type of inhalers or the metered dose type of inhalers. Over half of participants in this study had used Salbutamol inhaler (a metered-dose inhaler) for more than 5 years, yet very few had adequate inhaler-use technique. Probably most of the participants had progressed on the therapeutic steps to a combination of Salbutamol with Seretide® or Symbicort® due to their inadequate inhaler-use technique. If this assertion was true, then in conformity to both EPR-3 (2007) and Gina (2012) recommendations, after a 3-month consideration and if participants' asthma remained well-controlled then there should have been a possible step down in therapy.

Aburuz and colleagues (2005) have suggested adjustment of therapy based on the level of patient's asthma control but the EPR (2007) and the GINA (2012) suggested that before increasing pharmacologic therapy; one must consider poor inhaler technique, adverse environmental exposures, poor adherence, or co-morbidities as targets for intervention.

The level of poor inhaler-use technique identified among study participants indicated that these considerations were not adequately adhered to in adjusting their therapies. The duration of the study did not allowed for the participants to be followed further to see if their therapies

were subsequently adjusted in the post-interventions months. Agreement is needed on the time needed to assess response to therapy accurately (Zhango *et al*, 2002). Responses to therapy might vary depending principal benefits anticipated (Bousquet *et al*, 2004).

The findings in this study agreed with the position of Dunbar-Jacob and colleagues (2000) as well as that of Rybacki (2002); that poor adherence in patients with chronic illness was the primary reason for suboptimal clinical benefit. Probably some of these participants might have been referred for specialist care as an outcome of poor quality education and counselling received in the past, or lack of adherence to therapy that had contributed to a poorly controlled asthma condition. Participant characteristics at baseline indicated inadequate inhaler-use technique and pharmacy-exit interviews also revealed inadequate patient education and counselling. These revelations from this study could best be explained bythe WHO (2003) review that suggested that health-care providers often tried to supply information to patients and to motivate them, but the evidence in practice was that, they gave limited information and also lacked the skills in motivational enhancement and knowledge in teaching patients behavioural skills. Any education provided to these participants in the past clearly did not adequately impact on their behavioural skills.

On the contrary however, Schatz and colleagues, (2005) had suggested that even though it might be generally hoped that control of impairment would reduce the risk of exacerbations, there seemed to be some disassociation between the two components. Some uncertainty remains with regard to factors that affected the risk of asthma exacerbations. It had however been demonstrated by Sont and colleagues (1999) that reduced airway hyper-responsiveness (AHR strategy) in conjunction with optimized symptoms and lung function was more effective in reducing exacerbations than control based on clinical makers alone. In this study,

because the AHR strategy was not being monitored directly as a targeted intervention in addition the clinical markers, it might have been unanticipated asthma exacerbations that might have affected the level control of asthma in these participants.The considerations for the current therapeutic levels might have been basedsolely on the clinical markers of asthma. Stepping up the therapy wasextra cost to patients and might also increase the occurrence of treatment-related adverse effects and subsequentlyworsenedpatient adherence to treatment.

The common major environmental trigger-factors affecting participants in this study were dust, smoke and perfume/scent. Over 70% of all participants were affected by either dust, or smoke or perfume and about 44 % of participants were affected by all these 3 major trigger-factors. The impression created was that one of the major care-need for intervention was the proper control of dust, smoke and perfume by participants within their environment. This study therefore assessed how the intervention impacted on participants affected by the various common environmental trigger-factors identified in the study.

The relative chance of achieving a clinically important (significant) change in the HRQoL using the intervention was (RR=1.56; at 95% CI 1.03-2.35) for participants who were affected by the combination of all three common trigger-factors found among the study population. A number of 4 participants with all three common trigger-factors needed the study-type of intervention to attain a clinically significant change in HRQoL in one participant.

Post-intervention comparison of participant characteristics with those at baseline indicated significant changes in the HRQoL and the PEFR. Over 55% of participants had a positive clinically significant change in HRQoL while about 35% had no clinically significant change in the HRQoL. Some 9% of participants had a negative clinically significant change in their HRQoL. No factual reasons were revealed by the instruments used in this study, but these

effects of the intervention may anecdotally be partially due to non-adherence on the part of some participants, which was likely associated with unavailability or inaccessibility of asthma medications. It was rather difficult to ascertain what role environmental trigger-factors might have played in the deterioration of the HRQoL of these participants. However, these deteriorations and the non-significant changes in HRQoL might also be associated with the "phenotype of asthma theory". The EPR-3 (2007) suggested that very specific patterns of inflammation in individual patients existed and that required different treatment approaches. No direct association of the deterioration of these participants to the intervention could be identified.

The paired mean difference of the general HRQoL, the Activity Limitation domain, the Symptoms domain, the Emotional Function domain and the Environmental Stimuli domain in this study were all clinically and statistically significant. The Symptoms domain had the highest mean change difference of 1.134 ($\pm$ 0.985)and the Activity Limitation had the lowest of 0.548 (+0.921). This was an indication that even though the intervention significantly impacted on all domains within the composite HRQoL, the various domains were affected to different extents. In other previous studies, Mangiapane and colleges (2005) found significant improvements for all humanistic outcomes including the HRQoL, knowledge, medication adherence, PEFR and knowledge among others, but with limited improvement on clinical outcomes. Mancuso and colleagues (2010) found out that these favourable results from pharmacy interventions tended to wane with time if follow-ups were not pursued with participants. Schulz and colleagues (2001) had similar findings of a positive impact from pharmaceutical care intervention on quality of life. In this study 2 other types of questionnaires, which were different from the AQLQ (s) were used (the SF-36 and the

German version of the Living with asthma Questionnaire) to indicate a positive impact of pharmaceutical care intervention on asthma.

In a systematic review study involving 2157 adults by Tapp and colleagues (2007) to assess the effectiveness of educational interventions administered following an acute exacerbation of asthma leading to presentation in the emergency department. Their findings indicated that education significantly reduced future hospital admissions (RR 0.50; 95% CI 0.27 to 0.91), but did not significantly reduce the risk of re-presentation at emergency departments (ED) during follow up (RR 0.66; 95% CI 0.41 to 1.07). Their findings further indicated the lack of statistically significant differences between asthma education and control groups in terms of peak flow and quality of life. Their findings raised interesting questions on the threshold of the educational intervention impact on hospital admission preventions. The challenge somehow remains as to which markers or indices also changed significantly and by what margins in their participants who had the significant reduction in hospital admissions. In our study the findings indicated clinically and statistically significant changes in both the HRQoL and the PEFR and therefore it can be anecdotally assumed that future hospital admissions will be significantly reduced among study participants. Though the minimal important difference of clinical significance of 0.5 has been established by Junniper and colleagues (1994), future studies may also have to look at what this change implies for the various factors involved in asthma control.

The mixed findings on the pharmaceutical care education impact reported in the EPR (2006) and the non-significant changes reviewed by Tapp and colleagues (2007) may possibly imply methodological challenges in this area of study. Randomised controlled trials are robust in scientific studies, but whether they would do well in these behavioural studies with unconfined participants as against internally controlled trials cannot be explained in this

study. This study used HRQoL and PEFR to assess the levels of asthma control attained at the post intervention stage in comparison to baseline values.

Bateman and colleagues (2004) in a randomized controlled trial of interventions to achieve asthma control (decreased symptoms, decreased use of short-acting beta2-agonist (SABA) for quick relief, improved functioning, improvement in FEV1, reduction in exacerbations, fewer emergency department visits, and decreased side effects from medication) used equally weighted scores to develop a composite score that defined a responder to therapy. The extent to which all of the composite variables responded to therapy may not be similar and may likely affect the composite score. In this study, the correlation between the composite HRQoL at baseline and at post intervention were fairly strong as well as those of the various domains at baseline and post-intervention, whilst the correlation between the composite HRQoL or its domains and the PEFR were very weak. The pre/post changes in the composite HRQoL and PEFR both significant but changes that occurred were not uniform and poorly related to each other ($r=0.268$ at 99% CI, $p< 0.05$). This fact was also underscored in a documentary by Stempel and Fuhlbrigge (2005) that drew attention to wide variations in statistical significance in published trials of responses to therapy that used pre-/post-bronchodilator $FEV_1$ measurements. Such variations could point a composite variable in any direction.

The complementary role of proper environmental trigger-factor management, appropriate inhaler-use technique and medication adherence may impact differently on the composite outcomes of asthma control. A good inhaler-use technique in a patient who did not use the inhalers as recommended might have some challenges with control and so also might the patient who had the right technique and used the inhaler as recommended but paid no proper

attention to environmental trigger-factors. This study was limited in the direct control of participant attitudes towards all the variables that are known to impact asthma control except in the education that modified their behaviour.

These findings of the study are important, because it was not only quality of life and functional lung capacity that improved after the pharmaceutical care intervention, but that the quality of life of most patients with the most common environmental trigger-factors responded positively to the care intervention. Two important issues may emerge from these findings in relation to the asthma cycle. Either pharmaceutical care intervention has positively impacted on the link between environmental trigger-factors and the inflammatory processes or link between the inflammatory processes and the health-related quality of life, or on both links.

What remain outstanding are the economic implications for the impact of the intervention on the cost of asthma management. Further to the clinical significance, patients and health insurance schemes might make savings on asthma-related health care, cost of medications, hospitalization and emergency department visits as envisaged by Teach *et al* (2006), Cicutto e*t al* (2005) and Morgan *et al* (2004). Future studies may need to look at the links between clinical benefits and the economic implications since this would allow health planners and managers to map benefits from HRQoL directly onto the financial implications and assess any cost savings or otherwise.

To harness the findings into clinical asthma management, this study modelled the predicted changes in HRQoL, making use of the strong correlation ($r = 0.942$ at 99% CI, $p<0.05$) that existed between the differences in the HRQoL and those of the Symptoms domain.

The relational analysis between the baseline and post-intervention domains of the HRQoL indicated the weakest correlation ($r=0.674$; at 99% CI, $p<0.05$) in the Symptoms domain, which implied that changes within this domain were quite substantial. It could therefore be said that the changes found in the composite HRQoL are mostly due to changes in the Symptoms domain. A significant correlation at 94.2% indicated that the changes seen in the Symptoms domain were similar to those seen in the composite HRQoL. This might imply that care-providers could receive adequate information from a shorter Symptom domain questionnaire and save time. However, this relationship might need validation.

Other studies demonstrated clinically significant changes in the HRQoL in patients after pharmaceutical care intervention, but this study demonstrated both clinically and statistically significance changes in the HRQoL after pharmaceutical care intervention. This may possibly be due to the use of internally controlled (cohort follow-up) methodology rather than the externally controlled (case-control) methodology used in the other studies.

The findings of this study therefore reject the initial study hypothesis and accept the alternative hypothesis: that the mean health-related quality of life (HRQOL) scores in patients with asthma, a month after pharmaceutical care intervention is not the same as those of the baseline scores.

### 4.1.5 Study Limitations

This study noted some limitations that occurred in the planning and implementation stages of the work.

#### 4.1.5.1 Data Collection Instrument

Some of the tools used in this study were self-administered and available only in English which limited the study to asthma patients who could read and write in English. Therefore the findings in this study represented only asthma patients who could read and write in the English language. The HRQoL instrument cannot be easily translated into the various Ghanaian languages without proper validation before use.

#### 4.1.5.2 Type of Study Participants

The participants involved in this study were recruited from those attending hospital reviews on regular basis. Most of these participants may have been referred from other hospitals and clinics from the primary and secondary levels of health care delivery for specialist care. These participants may not fully represent the characteristics of all asthma conditions. This population may also represent asthma cases that had remained difficult to control. Many stabilized asthma patients would not be referred and their characteristics may be missed out from the study population. Attempts to recruit from general out-patient department were not successful for lack asthma cases. This limits the scope of the participants in this study to mostly those asthma patients who have been referred from primary or secondary levels of health service delivery.

#### 4.1.5.3 Availability and Usage of Current Medications

This study did not provide participants with their current medications and therefore cannot firmly guarantee the level of medication adherence among participants throughout the study period. Except for the claims made by the participants themselves there was no easy way of checking what exactly transpired between the two contact periods. The study noted some

challenges participants reported about access to their medications through the health insurance scheme.

### 4.1.6 Future Works

Since the current study reviewed the impact of pharmaceutical care on HRQoL within a short period, there is the need to cross-check sustainability of this type of intervention and the economic implications for implementation. Studies are also needed for the assessment of impact of a combined educational intervention from all various frontline health care service providers. From this study the changes in the Symptoms domain were strongly related to those of the HRQoL and because physicians also assess their patient using signs and symptoms, studies will be needed to explore the relationship between the changes in the HRQoL and those of the Symptoms domain as well as the symptoms used by physicians and the Symptoms domain.

## 4.2 . Conclusions

This study concludes that content and outcome of patient counselling and education were inadequate and non-discriminatory among patients with acute and chronic health conditions.

There was a widespread use of high dose controller combination medications containing long-acting Beta-agonists and corticosteroids that was not consistent with recommendations in the standard treatment guidelines.

The counselling and educational model developed and used for the intervention study in the asthmatic patients demonstrated a positive impact on asthma control. One month after

pharmaceutical care intervention, patients with asthma showed significant improvements with regard to asthma-specific quality of life, peak flow and knowledge.

This study identified a strong relationship between the changes in the HRQoL and those of the Symptoms domain, suggesting that a predictive HRQoL change can be obtained from changes observed in the Symptoms domain.

The educational intervention impact reflected positively on both the HRQoL and the PEFR,but the relationship between these two variables was very weak.

Subsequent to these, the study was able to model a variation of the observed changes in HRQoL with those of the Symptoms domain.

### 4.3 . Recommendations

In furtherance to the implementation of the findings of this study, the following recommendations are being made for consideration:

1. That the implementation of a well-structured systematic pharmaceutical care delivery as part of the overall management of patients with asthma would improve health-related quality of life.
2. That therapeutic changes and adjustments for patients with asthma must not only be based on clinical judgment but also on the role, impact and management of environmental trigger factors, availability of asthma medications to the patient, patient's inhaler usage , as well as the adequacy of the inhaler-use technique in each individual patient.

3. That conformity to standard treatment guidelines must be continuously reviewed to ensure prescriber adherence.
4. That continuous assessment of Health-related quality of life alongside the peak expiratory flow rates and other clinical measures for asthma should be incorporated as part of patient management.
5. That the estimation of changes in the Symptoms domain can be used to predict changes in the health-related quality of life.
6. That pharmaceutical service should incorporate a chronic care model alongside the acute care model to facilitate adequate education towards self-management for patient with chronic conditions.
7. That the developed Model Pharmaceutical Care Plan used in this study should be adopted for use by pharmacy outlets in the management of patients with asthma.

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Appendix 1

## GHANA HEALTH SERVICE ETHICAL REVIEW COMMITTEE

*In case of reply the number and date of this Letter should be quoted.*

*My Ref. :GHS-ERC: 3*
*Your Ref. No.*


Research & Development Division
Ghana Health Service
P. O. Box MB 190
Accra

*Tel: +233-0302-681109*
*Fax + 233-0302-685424*
*Email: Hannah.Frimpong@ghsmail.org*

October 19, 2011

**PHILIP ANUM, Principal Investigator**

**ETHICAL CLEARANCE - ID NO: GHS-ERC: 08/9/11**

The Ghana Health Service Ethics Review Committee has reviewed and given approval for the implementation of your Study Protocol titled:

**"A Psychometric assessment of the impact of pharceutical care intervention on health-related quality of life in asthmatic patients"**

This approval requires that you submit periodic review of the protocol to the Committee and a final full review to the Ethical Review Committee (ERC) on completion of the study. The ERC may observe or cause to be observed procedures and records of the study during and after implementation.

Please note that any modification of the project must be submitted to the ERC for review and approval before its implementation.

You are also required to report all serious adverse events related to this study to the ERC within seven days verbally and fourteen days in writing.

You are requested to submit a final report on the study to assure the ERC that the project was implemented as per approved protocol. You are also to inform the ERC and your mother organization before any publication of the research findings.

Please always quote the protocol identification number in all future correspondence in relation to this protocol

SIGNED.....

PROFESSOR FRED BINKA
(GHS-ERC CHAIRMAN)

Cc: The Director, Research & Development Division, Ghana Health Service, Accra

**KOMFO ANOKYE TEACHING HOSPITAL**

**RESEARCH AND DEVELOPMENT UNIT (R & D)**

# *CERTIFICATE OF REGISTRATION*

*REG. NO*[a] *RD/CR12/052*

**This is to certify that**

**Prof/Dr/Mrs/Mr/Ms**.....*Anum Philip*.....

**has registered his/her proposed study titled:** *A psychometric assessment of the impact of pharmaceutical care intervention on health related quality of life of patients with asthma*

.....**with the Research and Development Unit.**

**Date**.....*30th March, 2012*.....

**Name of issuing officer**

*Raymond Atiemo Danso (Adm Mgr R&D)*

**Signature**

[a]Must tally with registration number on the registration form

**Appendix 2**

**Pharmacy-exit Questionnaire**

1. **Patient details:**
   Initials: …… Sex: ……. Age: …….. Smokes: Y / N ……...
   Daily alcohol: Y / N…….

   *For females ask: if pregnant: Y /N…… if breastfeeding: Y / N ……

2. Which languages do you understand? English, Ga, Twi, Ewe, Hausa,

   Others languages (state):…….
3. What is your highest educational level?
   a. Uneducated
   b. Primary
   c. Secondary
   d. Tertiary

4. What language did the dispenser used when giving you the medicine(s) or counselling you on your medicine(s)? ……....……

5. Did you understand everything that you were told about your medicines?
   a. Yes, if yes what were you told?.....
   b. No, if no, why?.....
      What did you not understand?.....
      .....

6. Are you satisfied with the way the pharmacy receives you and issues you with your medicines?
   a. Yes
   b. No, if no, what are you not satisfied with?.....
      .....

7. How would you rate the way you were handled at the pharmacy?
   **P**oor; **B**ad; **U**nacceptable; **O**kay; **J**ust right; **A**lright; **G**ood; **G**reat; **E**xcellent
   Other (state).....

8. Were you told by anybody (doctor, nurse, pharmacist) what is wrong or what the treatment is about?
   a. Yes, if yes, who? .....and what did they tell you?.....
   b. No

9. Were you told what to do if you begin to feel bad or react to the medicine(s)?
    a. Yes, if yes, what did they tell you?.....
    b. No

10. Were you told what to do in-case you missed or forgot to take your medicine(s)?
    a. Yes, if yes, what did they tell you?.....
    b. No

11. Were you told about anything(s) to avoid while using this medicine(s)?
    a. Yes, if yes, what did they tell you?.....
    b. No

12. Were you given any any warning or advice against the use of any other medicine(s)?
    a. Yes, if yes, which of them ?.....
    b. No

13. Were you given any warning or advice against operating machinery or driving?
    a. Yes, if yes, what advice?.....
    b. No

14. What other things would you have wished the pharmacy could do for you concerning your health and your treatment /medicines? List them.
    .....

15. Do you have some problems with any of your medicine(s)?
    a. Yes, if yes, list and mention them:.....
    b. No

16. Which medicines do you have at home that you are currently using?
    (Forms and names only)
    a.....
    b.....
    c.....
    d.....

## 17. Pharmacy-exit Questionnaire: Assessment of Medication Education and Patient Knowledge

| | Form | Name of drug | Strength | Dose | Times daily | How long to use | | What to Avoid | | Possible Side Effects | | How to Store | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Medication | | | | | | Told | Not told | Told | Not told | Told | Not told | Told | Not told |
| *Patient knowledge* | | | | | | | | | | | | | |
| Medication | | | | | | | | | | | | | |
| *Patient knowledge* | | | | | | | | | | | | | |
| Medication | | | | | | | | | | | | | |
| *Patient knowledge* | | | | | | | | | | | | | |
| Medication | | | | | | | | | | | | | |
| *Patient knowledge* | | | | | | | | | | | | | |

**Appendix 3**

# Patient Consent Form 1- Counselling and Education

Dear Patient,

We are here today to contribute to your well-being and to find ways that we can work with you to further improve your health. We have some questions for you as part of our research study. This study is to find various ways that your pharmacist can work with you to improve your health.

This questionnaire will find out from you what information was given to you to help you use the medicines properly.

It will help us to know if you have been told about your health and what the medicines will do for you and how to use them properly.

There are 17 questions for which you are being asked to answer all by telling the person interviewing you, what happened this morning when you came into the pharmacy for your medicines.

Information provided by you will help us look at the best ways to work with patients who use the pharmacy. The information you provide will remain confidential, used by the team in codes and not transferable.

We promise that information collected will never be used against you in any form or manner and findings of the study will be published generally in literature without any form of reference to participants.

We wish to inform you that you are free to decide if you want to be part of this study or not and that we would continue with our cordial work relationship and services with you even if you do not wish to be part of this study.

You are also free to ask more questions in case you are not clear with anything. For any further clarification please contact **Mr. Philip Anum on Tel: 020 812 4191**

We wish you well!

Thank you

I,

……

……. do freely agree to provide my information to be used in this study

Signature

……

Date……/……/…….

**Appendix 4**

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PEFR (PRE-)_____

SELF-ADMINISTERED DATE_____

Name_____ Page 1 of 5

Please complete all questions by encircling 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 pet/children, visiting friends/relatives) | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 4. WORK-RELATED ACTIVITIES (tasks you have to do at work*) | 1 | 2 | 3 | 4 | 5 | 6 | 7 |

* if you are nor employed or self-employed, these should be task you have to do most days.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 5. SLEEPING | 1 | 2 | 3 | 4 | 5 | 6 | 7 |

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

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

PEFR (post-).....

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

IN GENERAL, **HOW MUCH OF TIME DURING THE 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 STRESS** HAVE YOU FELT **DURING THE LAST 2 WEEKS**?

| | A Very Great | 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 TIME DURING THE 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 CHEST HEAVINESS? | 1 | 2 | 3 | 4 | 5 | 6 | 7 |

IN GENERAL, **HOW MUCH OF TIME DURING THE 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 in your chest? | 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 |

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S) PATIENT ID_____

SELF-ADMINISTERED DATE_____ 

IN GENERAL, **HOW MUCH OF TIME DURING THE 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 REULT OF BEING EXPOSED TO STRONG SMEEL OF 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 have 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 lLimited Most Not | Very Limited | Moderately Limited Severely Not Done | Slightly Limited | Very Slightly Limited Very Few Not Done | Hardly Limited At All | Not Limited Have Done All Activites |
|---|---|---|---|---|---|---|---|
| 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

**APPENDIX 5**

## MODEL PHARMACEUTICAL CARE PLAN INSTRUMENT

**Background Information – interviewer administered**

Name:……
……
Age:……years
Contact no.: (Mobile)……..
Highest education: Primary☐ Middle school/JSS/JHS☐ Secondary/SSS/SH☐ Tertiary
Address
(office/home):…….……
……

**Pharmaceutical Care – interviewer administered**

Year diagnosed as patient with
asthma:…….……..
Last admission with asthma, (if any): ……..years ago…….months ago
Last contact with doctor in relation to your asthma:……years
ago……months
Name of last hospital visited with
asthma:…….…….
Any known cause that worsens/triggers your
asthma:……..……

Medication Review:

| Current medications (prescription) | Indication | Compliance status (regular/irregular) | Inhaler technique score* | Duration of medication use |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| (self-medication) | | | | |
| | | | | |
| | | | | |

*see assessor information sheet

12. Identify adverse drug reactions in patient: headaches☐ coughs☐ nausea☐ light-headedness ☐ sore throat ☐ dry mouth ☐ oral thrush ☐ others (list) ☐……

13. Identify with patient the frequency of occurrence of the following components

| Components | Frequency 1 | Frequency 2 | Frequency 3 |
|---|---|---|---|
| Symptoms | ≤ 2 days/week ☐ | >2 days/week but not daily ☐ | daily ☐ |
| Night time awakenings | < 2x/month ☐ | 3-4x/month ☐ | >1x/week but not every night ☐ |
| Inhaler Salbutamol use for control | ≤ 2 days/week ☐ | >2 days/week but not daily ☐ | daily ☐ |

14. Going through the checklist with the steps for treatment, where is this patient on the treatment steps…….

**Inhaler Technique**

***Select the correct Inhaler and then score inhaler technique by ticking the steps which patient performs correctly***

**General for Dry Powder Inhalers**

Step 1. Remove the cap or open mouthpiece of inhaler.
Step 2. Hold inhaler in upright position with mouthpiece upwards.
Step 3. Turbohaler – Rotate grip anticlockwise, then back until a click is heard.
Diskhaler – Pull lever to release medicine.
Step 4. Breathe out slowly and completely (not into mouthpiece).
Step 5. Place the mouthpiece between the front teeth and seal the lips around it.
Step 6. Breathe in through the mouth quickly (forcefully) and deeply over two to three seconds.
Step 7. Remove the inhaler from the mouth. Hold breath as long as possible (4 – 10 seconds). Breathe out slowly.

**General for Metered Dose Inhalers**

Step 1. Remove the cap or open the mouthpiece of inhaler
Step 2. Hold the inhaler in upright position, with the thumb on base and index finger on top of canister.
Step 3. Shake the inhaler up and down vigorously.
Step 4. Breathe out slowly and completely.
Step 5. Hold the mouthpiece firmly between lips.
Step 6. Breathe in through the mouth slowly and deeply, whilst the inhaler is pressed to release medication.
Step 7. Remove the inhaler from the mouth. Hold breath as long as possible (4-10 seconds). Breathe out slowly.

15. Do you think the patient is on the correct treatment step? Yes No☐ If n☐ where should he/she be……
Comments:……
……
……
……
……

**Assessor Guidance Information**

**Activity I: Medication review**

1. Identify all prescribed medications and state them as prescribed or on prescription (form, name, strength, regimen)
2. Identify the indications for all the medications (both prescribed and self-medication) and check compatibility with patient's condition and with the other medications in use.
3. Crosscheck compliance status for all medications against prescribed regimens.

**Activity II: Inhaler technique**

4. Assess and score for inhaler technique. Score up to a total of 7, if all the seven steps in the technique are correctly performed. Select the appropriate inhaler type and score on the sheet as patient demonstrates inhaler-use technique. Tick on the sheet directly the steps that the patient performed correctly.

   *Teach the patient to help him/her to score 7 out of 7 score points for inhaler-use technique*

**Activity III: Adverse events and side effects**

5. Identify all possible side effects and adverse reactions to medications and list them out. (Headaches, coughs, nausea, light-headedness, sore throat, dry mouth, oral thrush)

Activity IV: Action plan and environmental exposure

6. Crosscheck if patient has an action plan in place and how well the patient understands it.
7. Identify with patient what environmental factors triggers or worsens his/her asthma.
   *Address management of trigger-factors and identify strategies with patient.*

**Appendix 6**

# Patient Consent Form 2 – Pharmaceutical Care Intervention

Dear Patient,

We are here today to contribute to your well-being and to find ways that we can work with you to further improve your health. We have some questions for you as part of our research study. This study is to find various ways that your pharmacist can work with you to improve your health.

This questionnaire is designed to find out how you have been feeling during the past **two weeks**. You will be asked about ways in which your asthma has limited your activities, the symptoms you have experienced as a result of your asthma, and how these have made you feel.

There are 32 questions for which you are being asked to answer all by circling the number that best describes how you have been during the last 2 weeks as a result of your asthma.

Information provided by you will help us look at the best ways to work with patients with asthma. The information you provide will remain confidential, used by the team in codes and not transferable.

Before you see your doctor, our pharmacists will have a short discussion with you to find out how you are doing with your medications and offer some advice.

You will be asked to answer all the 32 questions again on your next scheduled visit to the clinic.

We promise that information collected will never be used against you in any form or manner and findings of the study will be published generally in literature without any form of reference to participants.

We wish to inform you that you are free to decide if you want to be part of this study or not and that we would continue with our cordial work relationship and services with you even if you do not wish to be part of this study.

You are also free to ask more questions in case you are not clear with anything. For any further clarification please contact **Mr. Philip Anum on Tel: 020 812 4191**

We wish you well!

Thank you

I,

……
……. do freely agree to provide my information to be used in this study

Signature

……

Date……/……/…….

## General Asthma Management Information Tool

1. Name of Patient:
……..Sex:……..…Age:……

2. Type of case: 1. Referred 2. Not referred

a. If Referred, state the following:
From which facility:……date seen:…….……
Referred to: 1. The emergency department 2. The out-patient department
Rank of officer referring case:……..……

b. If not by referral, is it a Direct visit? yes/no:……..date seen:……..……..…

3. Rank of consulting Physician:……

4. Stated the diagnosis:…….……..

If no diagnosis stated, indicate the stated impression:…….……..

**5.** Current prescription details: **Kindly state prescription details the same way as on the prescription form. Indicate all medicines on prescription.**

| No. | Form | Name of Medicine | Strength | Dose | Frequency | How Long |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |
| | | | | | | |

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