DRUG-RELATED HOSPITAL ADMISSIONS AND RESPONSIVENESS OF HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS IN CHILDREN WITH ASTHMA

by

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ABSTRACT

Objective: To evaluate (1) the frequency of drug-related hospital admissions in Canadian children with asthma and (2) the responsiveness to clinical change of the *Pediatric Health Related Quality of Life Questionnaire (PAQLQ)* and a "patient-specific approach" to quality of life assessment in the children.

Sample: Over 12 months, 54 of 61 patients admitted to one of the study hospitals for asthma or asthma-related symptoms participated in the study.

Methodology: Data were gathered by personal interviews with patients, their families, and their health-care providers; reviews of patients' health record; and administration of HRQOL instruments. Drug-related hospital admissions were evaluated by an expert panel using a set of objective criteria to evaluate each case. The investigator administered HRQOL instruments to the patients during their hospital stay while they experienced acute asthma symptoms, and a second time six weeks after hospital discharge when patients were clinically improved.

Results: 84% (95% CI = 73 - 95%) of 44 patients who participated in the drug-related hospital admission component of the study were deemed to have a "definite" relation between drug-intake and dose-related therapeutic failure (DTF), and 16% (95% CI = 5 - 27%) had a "possible" relation between drug intake and DTF. Evidence of inadequate treatment of chronic asthma was found in 43% of cases. Evidence of inadequate treatment of acute asthma was found in 95% of cases. If the presence of a respiratory tract infection were considered as a possible factor that could have explained patients' symptoms on hospital admission, then 52% (95% CI = 36 – 67%) of the 44 patients who participated in the drug-related hospital admission component of the study would have been deemed to have a "definite" relation between drug intake and DTF, and 48% (95% CI = 33 – 62%) would have been considered "possible" therapeutic failures. The PAQLQ was responsive to the change in clinical status that patients experienced when they were hospitalized compared to when they were well (ES = 1.5). The PAQLQ appeared more responsive than a patient-specific approach at assessing HRQOL domains in pediatric patients with asthma.

Conclusion: Problems related to drug therapy may be a common factor in children admitted to hospital for asthma. Most children deemed to have a drug-related hospital admission were sub-therapeutic compared with the recommendations of the National Institutes of Health (NIH) National Heart Lung and Blood Institute Expert Panel Report II Guidelines, and the Canadian Asthma Consensus Conference Summary of Recommendations. The PAQLQ is a HRQOL instrument that has demonstrated responsiveness to changes in patients' clinical status. "Individualized" items did not improve the responsiveness of items in a questionnaire designed to assess HRQOL in children with asthma.

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LIST OF ABBREVIATIONS

ADR	adverse drug reaction
BCCH	British Columbia's Children's Hospital
BP	blood pressure
COPD	chronic obstructive pulmonary disease
DRHA	drug-related hospital admission
DRP	drug-related problem
DTF	dose-related therapeutic failure
GP	general practitioner
HR	heart rate
HRQOL	health-related quality of life
ICC	intra-class correlation coefficient
MCID	minimal clinically important difference[4]
MDI	metered-dose inhaler
MSJ	Mount Saint Joseph Hospital
NA	not available
ND	not determinable
NHLBI	National Heart, Lung and Blood Institute
NIH	National Institutes of Health
PRN	as needed; taking medication liberally

PRN*	regularly as-needed; taking medication as needed and taking it regularly. An example is taking medication three times a day for two weeks upon start of upper respiratory tract infection.
QOL	quality of life
RR	respiratory rate
SD	standard deviation
TF	therapeutic failure
URTI	upper respiratory tract infection
WHO	World Health Organization

LIST OF TRADE NAMES

Listings by brand name are in the following format:

Brand Name (Manufacturer) *generic name*

Advil (Whitehall-Robins) *ibuprofen*

Alupent (Boehringer Ingelheim) *orciprenaline sulfate*

Atrovent Inhalation Aerosol (Boehinger In gelheim) *ipratropium bromide*

Becloforte (Glaxo Wellcome) *betamethasone dipropionate*

Benylin-DM-D For Children (Warner-Lambert Consumer Healthcare) *dextromethorphan hydrobromide/pseudoephedrine hydrocholoride*

Bricanyl Turbuhaler (Astra) *terbutaline sulphate*

Dimetapp (Whitehall-Robins) *brompheniramine maleate, phenylephrine hydrochloride phenylpropanolamine hydrocholoride*

Intal (Rhone-Poulenc Rorer) *sodium cromoglycate*

Pulmicort Turbuhaler (Astra) *budesonide*

Ventolin Inhalation Aerosol (Glaxo Wellcome) *salbutamol sulfate*

Ventolin Nebules P.F/Respirator Solution (Glaxo Wellcome) *salbutamol sulfate*

Tilade (Fisons) *nedocromil sodium*

Tylenol (McNeil Consumer Products) *acetaminophen*

DEFINITIONS

adverse drug reaction	adverse drug reaction; a toxic reaction or a noxious, unintended drug reaction that occurs at doses normally used in man for prophylaxis, diagnosis, or therapy[2]
therapeutic failure	an absence of therapeutic response that could be linked causally either to a prescribed dose that was too low, to drug compliance, recent dose reduction/discontinuation, interaction or inadequate monitoring.[2]
quality of life	A person's sense of well-being that stems from satisfaction or dissatisfaction with the areas of life that are important to him/her.[3]
health-related quality of life	the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient[4]; those parts of QOL that are affected by health only.

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1. INTRODUCTION

Asthma is the most common chronic medical condition in children in Canada and the United States. [5-7] Patients with asthma suffer from a chronic inflammatory disorder of the lungs, which is characterized by inflammation, epithelial damage, bronchiole constriction, obstruction, and hyper-reactivity to environmental stimuli.[8] These patients are more symptomatic when exposed to factors that can trigger their asthma, including respiratory tract infections, ozone, and other environmental irritants. Triggers can often cause patients to exhibit wheezing, shortness of breath, chest tightness, and coughing. Symptoms can be severe enough for patients to be admitted to hospital and some patients with severe exacerbations who are not treated properly can die.

Asthma accounts for approximately 500,000 hospitalizations annually in the United States and approximately 198,000 hospitalizations in the population less than 25 years of age.[13] Furthermore, the incidence of asthma-related mortality and morbidity has been increasing, especially in the North American pediatric population. [9-13] In the USA, asthma-related hospitalizations rates have increased by approximately 4.5% per year among children less than 17 years of age over the last decade.[14] The frequency of asthma related morbidity has also increased among Canadian children. [15-22]

These trends are occurring despite the development of efficacious medications,[23] which reduce the clinical features of an asthma exacerbation by decreasing airway

constriction and inflammation.[24] For example, it has been reported that corticosteroids suppress inflammation in asthmatic airways, improve lung function, reduce symptoms, prevent exacerbations, and reduce the incidence of hospital admissions,[25-29] reduce asthma mortality,[30] reduce the irreversible changes in airway function, and improve patients' health-related quality of life.[31] Furthermore, asthma treatment guidelines, including the *National Institutes of Health (NIH) National Heart Lung and Blood Institute Expert Panel Report II Guidelines*[32] and *the Canadian Asthma Consensus Conference Summary of Recommendations,*[33] have been developed to help patients, physicians, and other members of the healthcare team manage the disease with these drugs. The content of the *National Institutes of Health (NIH) National Heart Lung and Blood Institute Expert Panel Report II Guidelines* reflect the current state of knowledge about the pathophysiology of the disease. Its recommendations to guide the management of asthma have been based on evidence from the scientific literature, the expert judgement and collective opinion of the members of the expert panel, and approval of the Coordinating Committee of the National Asthma Education Program. The Canadian Guidelines have also been based on the evidence from the scientific literature and the input from a panel of specialists and general practitioners in medicine. However, the number of children admitted to hospital for asthma is growing despite the publication of the guidelines and the availability of efficacious medications.

One explanation for the increased frequency of asthma-related hospital admissions in children, despite the availability of efficacious medication in

North America is inadequate treatment. Children's drug regimens may be inconsistent with the recommendations of the published asthma treatment guidelines. Poor management of children's asthma may be contributing to the high incidence of hospital admission of children with asthma in North America. However, the frequency of drug-related hospital admissions in pediatric patients with asthma is not known.

Asthma can also interfere with physical and social activities, disrupt growth and development in children, and consequently have a large impact on children's health related quality of life (HRQOL). Thus asthma-related HRQOL has been recognized as an important endpoint to measure in clinical trials. Current state of the art instruments, the PAQLQ and the CAQ have been shown to be valid and reliable. However, for these instruments to be useful in longitudinal trials, these instruments must also be responsive to change over time. However, the responsiveness to clinical change of these instruments has not yet been evaluated.

The following thesis serves to estimate the frequency of drug-related hospital admissions in children with asthma. The second objective of this thesis was to examine the responsiveness of two health-related quality of life instruments. A final objective was to conduct initial hypothesis testing of an individualized approach to pediatric HRQOL assessment.

The next section of this thesis reviews what is currently known about

drug-related hospital admissions in the pediatric patient population with asthma and the current status of health-related quality of life instruments designed to measure health-related quality of life in pediatric patients with asthma.

2. LITERATURE REVIEW

The following section reviews the existing research in the area of drug-related hospital admissions in the pediatric patient population with asthma (Section 2.1) and the health-related quality of life instruments for pediatric patients with asthma (Section 2.2).

2.1 DRUG-RELATED HOSPITAL ADMISSIONS IN PEDIATRIC PATIENTS WITH ASTHMA

The role drugs play in the causation of hospitalization in children with asthma has not been well studied. More research has been done examining morbidity associated with drug use in patients with asthma, so a description of this literature is appropriate. The linkage between drug use and hospital admission may be stronger in patients with asthma, since they are generally taking multiple medications over long periods of time. Sections 2.1.1 and 2.1.2 provide a description of the epidemiology of problems associated with drug use in adult and pediatric patients with asthma. A description of the epidemiology of drug-related hospital admissions in adults and pediatric patients with asthma follows (Section 2.1.3).

2.1.1 DRUG USE PROBLEMS: ADULT PATIENTS WITH ASTHMA

Problems related to drug therapy are common in patients with asthma. A study of asthma mortality rates found that 61% of asthmatic patients had insufficient medication to control their disease and 54% showed poor compliance before their deaths.[34-35]

Nonadherence to asthma medication ranged from 30% to 70%.[36] Hartert *et al.*[37] examined the adequacy of chronic medication use in adult patients who lived in urban areas with moderate or severe asthma. The investigators examined physician adherence to the guidelines for asthma management published by the National Asthma Education and Prevention Program (NAEP). Only 28% of the patients had been given an action plan by their physicians in the event of an acute exacerbation. Sixty percent of patients who contacted their physicians during the exacerbation that preceded admission had no changes made to their regimen. Only 11% were able to demonstrate proper use of their inhaler.

Tettersell *et al.*[38] investigated patients' knowledge of asthma and compliance with asthma medications using a postal survey among a group of 100 patients with moderate to severe asthma. They reported that 39% of patients in their study did not take their medication as directed and 48% of these patients were non-compliant because they believed their medications were unnecessary or were embarrassed about taking their inhaler medication in public. Furthermore, 76% of patients who reported to be non-compliant claimed that they did not take their prescribed *preventative* medications. Inappropriate use of preventative medications has also been reported by Laumann *et al.*[39] in a larger study of 1,029 adult patients with asthma. Using a disease-based drug utilization review methodology, the investigators compared patients actual drug therapies to the latest international asthma treatment guidelines. About half of patients who should

have been prescribed inhaled steroids based on disease severity did not have such a prescription filled.

2.1.2 DRUG USE PROBLEMS: PEDIATRIC PATIENTS WITH ASTHMA

Children with asthma may be even more prone to drug use problems than adults because younger patients are less likely to comply to asthma drug therapy.[38] Children may also be prone to drug use problems because objective measures of airways obstruction may be more difficult to assess reliably in children than in adults.[40] These measures may also be less reliable in children since many breathing tests are effort dependent and require full cooperation and concentration of the subject performing the test. Furthermore, children are generally less capable of accurately describing their symptoms to clinicians than adults. Thus, clinicians' evaluations of children's subjective perception of disease severity may be less reliable than in adults. However, even among adults, symptoms of asthma such as wheezing, breath sound intensity, forced expiratory time, accessory muscle use, respiratory rate and pulsus paradoxus are known to correlate poorly with airway obstruction in one-third to one-half of asthmatic patients.[41] Clinicians disagree about the presence or absence of respiratory signs 55% to 89% of the time, correctly predict pulmonary function based on history and physical examination only about half the time, and correctly diagnose asthma based on the clinical examination only 63% to 74% of the time.[41] Moreover, many children resent having to take medication chronically for asthma. Children have reported that they would discontinue treatment if they felt well.[42] For all these reasons children with asthma may be prone to develop adverse drug

reactions or dose-related therapeutic failures that may lead to hospitalization.

Milgrom. *et al.*[43] evaluated the adherence of children with asthma to regimens of inhaled corticosteroids and beta-agonists. Data collected electronically by metered-dose inhaler chronolog monitors (devices that record when patients actually use their medications), were compared with data recorded by patients on traditional diary cards. More than 90% of patients exaggerated their use of inhaled steroids and diary entries. Electronic monitoring demonstrated much lower adherence to prescribed therapy than was reported by patients on diary cards. Low rates of compliance with prescribed inhaled corticosteroids were associated with exacerbation of disease. The median compliance with inhaled corticosteroids was 13.7% for those who experienced exacerbations and 68.2 % for those who did not.

In a more recent study, Bender *et al.* reported that children with asthma seldom take all of their medications as prescribed.[44] In their study that utilized electronic monitoring, they found patients failed to take any inhaled corticosteroid doses on 41.8% of days or inhaled β_2-agonists on 28.1% of days despite prescribed daily use. Thus, the extent of non-compliance in the pediatric patient population may be worse than previous estimates suggest.

2.1.3 DRUG-RELATED HOSPITAL ADMISSIONS

Drug-related hospital admissions are hospital admissions caused by adverse drug reactions or therapeutic failure of drugs. The reported rates of drug-related hospital admissions, excluding intentional overdoses, alcohol intoxication, and illicit drug use, range from 0.2 - 22.3%.[45-46] Einarson *et al.*[35] performed a meta-analysis of studies that evaluated this frequency of drug-related hospital admissions. They estimated that 0.2 % to 21.7 %, with a median of 4.9% of hospital admissions are caused by problems related to drug therapy. The differences in reported rates of drug-related hospital admissions may have been caused by differences in prescribing practices, scope of population sampling, the intensity of data collection, methods of evaluating adverse drug reactions and therapeutic failures, and variations in the definitions used to classify adverse drug reactions and therapeutic failures.

Methods of evaluating problems with drugs contributing to hospital admissions have evolved in the last several decades since the first investigations about drug-related hospital admissions were reported in the literature. Before the mid 1970s, studies performed to estimate the frequency of drug-related hospital admissions relied more on subjective opinions of clinical investigators.[47] Without a set of operational criteria to establish the presence of a drug-related hospital admission, the conclusions drawn from these earlier studies have been difficult to interpret and generalize. Since then researchers have begun to use more operationally defined criteria to establish

the presence of drug-related hospital admissions. A number of algorithms have been developed, and the most significant work has been done by Karch *et al.*,[47] Naranjo *et al.*,[48] Bergman *et al.*,[49] Larmour *et al.*[50] and Hallas *et al.*[2] One of the more commonly used methods reported in the current literature is Hallas' algorithm.[2, 51-54]

Hallas *et al.*[2] developed the algorithm for evaluating drug-related hospital admissions using methods originally published by Karch *et al.*.[55] Hallas *et al.*[2] classify drug-related problems as "adverse drug reactions" or "dose-related therapeutic failures." According to their criteria, an adverse drug reaction is any unintended and undesirable effect of a drug. A dose-related therapeutic failure is a lack of therapeutic effect that could be ascribed to non-compliance, inappropriate administration technique, recent dose reduction/discontinuation, interaction, inadequate dose prescribed, or inadequate monitoring. Non-prescription of a drug, or non-compliance unaccompanied by clinical symptoms are not considered dose-related therapeutic failures. Some validity testing of the algorithm has been done.[52]

2.1.3.1 DRUG-RELATED HOSPITAL ADMISSIONS: ADULT PATIENTS WITH ASTHMA

Some conclusions can be inferred about drug-related hospital admissions in the pediatric patient population from studies in the adult population. However, very little work has been done, even in the adult population.

Hallas'[52] work in 1992 suggested that the frequency of drug-related hospital admissions may be high in the population of patients with asthma. In fact, non-compliance with prescribed anti-asthmatic medication was a cause of dose-related therapeutic failure in six of the 16 cases reported in the study.

Previous studies that have examined drug-related hospital admissions in the general adult population have not included illness caused by underprescribing or inappropriate choice of medication. In fact, Einarson's[35] study did not include underprescribing or inappropriate choice of medication. The reason these researchers did not include these important determinants to drug-related hospital admissions was that with the multitude of conditions that patients may admitted to hospital for, it would have been difficult to debate which drugs should have been required for each case. Thus, the frequency of drug-related hospital admissions as a cause of asthma-related hospital admission has not been well quantified in the adult population.

In the case of the patients with asthma, however, explicit treatment guidelines that clearly indicate which medications are recommended have been published. Thus, it would be possible to quantify using Hallas' algorithm, the frequency of drugs being a contributing factor to hospital admission in patients with asthma. However, to date, no such studies have been published, even in the adult population.

2.1.3.2 DRUG-RELATED HOSPITAL ADMISSIONS: PEDIATRIC PATIENTS WITH ASTHMA

Even less is known about the role of drugs as a cause of hospital admissions in *pediatric* patients with asthma. However, some studies suggest that it may be a widespread and important problem that needs to be investigated. For example, Lozano *et al.*[56] have estimated that children with asthma incur twice as many inpatient days (0.23 vs. 0.11/yr) compared to the general population of children and that hospital care for children with asthma accounts for approximately 33% of the total cost of asthma care. A small group of patients with asthma may be heavy users of the acute health-care system. Furthermore, a subgroup of patients appear to have a very high frequency of hospitalizations. Hospital readmission rates among children with asthma has been estimated to be approximately 43 to 47%.[15, 57] If it were true that children admitted to hospital are caused by problems related to drug therapy, then by targeting preventative measures at the select group of patients who are most frequently hospitalized, substantial healthcare dollars may be saved. To achieve this goal, however, it is necessary to understand the true rates of drug-related hospital admissions and to understand the reason why so many children are hospitalized each year for asthma.

A number of reasons for the high frequency of hospitalization in children with asthma have been identified. These include exposure to environmental pollutants, poverty, and drug-related problems.[28] Little can be done about some of these factors. For example, poverty is a social-economic issue. Inappropriate medication use,

however, is a factor that clinicians may be able to address. Thus, it is imperative that a better understanding be gained of the role of drugs in causing hospitalization.

More recently, the discovery that inflammation plays a substantial role in the pathogenesis of asthma has sparked renewed interest in the role of drugs as causative factors of hospitalization in patients with asthma. The incidence of drug-related hospital admissions in the pediatric patient population with asthma may be higher than previously suspected. In 1992, Macarthur *et al.*[15] found that factors related to children's risk of hospital readmission included care by a specialist and prophylactic use of inhaled corticosteroids. Children not prescribed prophylactic steroids were more likely to be readmitted to hospital than children who were prescribed prophylactic steroids. Furthermore, children who were under the care of a specialist were less likely to be admitted than children who were only under the care of a family physician. Surprisingly, asthma severity was not associated with hospital readmissions. These conclusions support the hypothesis that efficacious drug therapies may not be optimized and are thus less effective than they could be in asthma-related hospitalizations in children.

Yosselson-Superstine *et al.*[58] have examined the role of drug-related hospitalizations in pediatric patients. Approximately 18% of the 906 studied admissions in Jerusalem, Israel were found to be drug-related. Eleven percent was as result of inappropriate drug therapy, 3.4 % as a result of patient non-compliance, and 3.2% as a result of adverse reactions. However, their study population included *all* pediatric

patients admitted to hospital and their results may not apply to the subgroup of *asthmatic* pediatric patients.

Prior to this study, only two published studies in the Medline™ database examined the association between drugs and hospitalization in pediatric patients with asthma. Abduelrhman *et al.*[59] examined the adequacy of pre-hospital treatment in pediatric asthmatic patients in Galway, Ireland in 1990. In this prospective study, 105 children between one and 14 years of age who were admitted to hospital for asthma were studied. They reported that "absence of regular prophylaxis despite adequate indication, poor compliance with prescribed regimens, and inappropriate management of the acute attacks"[59] were common characteristics in pediatric asthmatic patients hospitalized. Overall, 10% of patients lacked adequate prophylaxis and 5% of patients were non-compliant with medications.

Several methodological problems of the study, however, make their results difficult to generalize to pediatric patients in Canada. First, the population that they studied consisted of children aged one to 14. However, the definition of asthma is poorly defined in children less than five years of age. Second, the pre-hospital treatments of pediatric patients with asthma in this study were evaluated by a single evaluator. It is not known how reliable this evaluator was or whether the conclusions of this evaluator agree with others. Third, whether or not the evaluator was qualified to make the assessments was not reported. Fourth, the method used to evaluate "inadequate pretreatments," a

type of drug-related problem, was not reported. Abduelrhman *et al.* did not use a formal algorithm to evaluate the how the drugs may have contributed to hospital admissions. Koch-Weser *et al.*[60] have shown that without a standardized algorithm for evaluating a relation between a drug and an adverse event, such as hospitalization, results are highly variable. For example in their study, they examined only one type of problem, adverse drug reactions, and found that disagreements about reported ADRs among evaluators were as high as 56.8%.[60] Fifth, in the study by Abduelrhman *et al.*, the standards of practice from which the therapies were judged inadequate were not described. Finally, in Galway, access to health care, medication available, and patient education are different from Canada's and the USA's. These factors affect the risk of having drug-related hospital admissions. Thus, although the study by Abduelrhman *et al.* suggests that drug-related hospital admissions may exist in Canada, a good estimate of the extent of the problem in the Canadian population is not available.

The second study was done in 1979. Sublett *et al.*[61] found that 98% of 50 children who arrived to the emergency room with an acute asthmatic attack had subtherapeutic theophylline blood levels and 75.5% of the patients admitted that they had not complied with their physicians' instructions. However, the major weakness with this study is that this study occurred over 20 years ago when the modern clinical guidelines for corticosteroid therapy had not yet been established. Considering the scientific evidence of the effectiveness of corticosteroids in reducing the symptoms of acute asthma exacerbations and the effectiveness of these agents at preventing exacerbations, the

frequency of drug-related hospital admissions in the pediatric patient population admitted to hospital may be very high indeed.

The following study fills the gap in knowledge about the frequency of drug-related hospital admissions in pediatric patients with asthma. By using a modification of Hallas'[7] algorithm to estimate the frequency of drug-related hospital admissions, this study focuses primarily on those types of drug-related hospital admissions caused by therapeutic failures rather than adverse drug reactions and includes those types of therapeutic failures that may be related to under-prescribing or inappropriate choice of medication.

2.2 MEASURING HEALTH-RELATED QUALITY OF LIFE IN PEDIATRIC PATIENTS WITH ASTHMA

2.2.1 MEASURING HEALTH RELATED QUALITY OF LIFE

Health related quality of life is loosely defined as the effect of a person's health status on an individual's quality of life. As such an abstract concept, there has been a lack of a consensus in the current literature about the definition of HRQOL and how it should best be measured. The recent literature suggests that HRQOL is a multi-dimensional concept consisting of several "domains."[62] Although the exact number of domains may vary among various definitions, the domains most commonly reported include physical, psychological, social, role functioning, and general health perception. Thus, the current

literature defines health related quality of life as the impact of health on a person's physical, psychological, social and role functioning, and general health perception.

Ware *et al.*[63] have provided a useful analogy to understand HRQOL. The impact of a disease or health is like a rock hitting the surface of a pond, sending ripples over the entire surface. Like the ripples spreading out, disease first affects the biological function of a person and then creates specific symptoms and problems. These in turn affect a person's physical and mental health, social well-being, and role functioning. The total effect, including the impact on the patients' physical and mental health is the complete effect of the disease on the patient. If clinicians or researchers were to measure the impact of a disease by simply assessing its effects on a patient's biological functioning, then they would not be capturing the whole effect of the impact of the disease. Health related quality of life is a more comprehensive concept that captures the entire effect of a disease on a patient.

Thus, HRQOL is an important endpoint that needs to be evaluated.[63] When used with other endpoints, evaluation of HRQOL can help to better understand the full impact of disease on a patient. Furthermore, many chronic diseases today can only be treated but not cured. Therefore, measures of traditional outcomes like mortality rates would not be able to fully capture the full effect of treatments in populations. In addition, many biological markers that have been used as surrogate markers of patients' quality of life may be poorly correlated with how patients actually feel or perform in their daily

activities. Without measuring the HRQOL directly, other measures may not be fully assessing the impact of a medical intervention on patients' lives. Knowing the full effect of medical interventions on patients' lives can help decision makers direct resources to those medical interventions that provide the most benefit to patients.

A large number of instruments have been developed to assess HRQOL. Some of these include the Sickness Impact Profile (SIP), the Nottingham Health Profile (NIH), and the McMaster Health Questionnaire, which comes in several forms (SF-36, SF-20, SF-12). These generic instruments have been found to be useful in many, but not all patient groups. They have been found to be particularly useful in those patients with multiple disease states, severe disease, the elderly, and the handicapped. However, for some specific sub-populations of patients these generic instruments may contain irrelevant questions, which may reduce the sensitivity of the instruments to detect clinical changes.

Disease-specific instruments have been developed to improve the applicability of the HRQOL questionnaires to patients with certain medical conditions. In general, these instruments have been found to be more responsive to clinical change and more useful for monitoring patients over time than the generic instruments. They have also been less of a burden to administer to patients with specific disease. Disease specific instruments have been developed for patients with cancers,[64] rheumatoid arthritis, and asthma.[65]

2.2.2 MEASURING HEALTH-RELATED QUALITY OF LIFE IN *ADULT* PATIENTS WITH ASTHMA

Asthma is a chronic disease where the assessment of HRQOL is especially useful.[65-68] Jones *et al.*[69] have shown that objective clinical measurements correlate poorly with disease severity in patients that suffer from asthma. For example, PEF and FEV_1 are known to correlate poorly with symptom severity or with the effect of the disease on the social and psychological well-being of patients.[70] Furthermore, physicians appear to estimate their patients' health using criteria different from the patients themselves.[71] Thus, HRQOL instruments can provide a more direct assessment of the impact of asthma on patients. Furthermore, the objectives of modern asthma treatment are not only to maintain "normal" pulmonary function, but also to live a life free of restrictions from everyday activities. HRQOL questionnaires can directly assess this outcome. By using HRQOL assessments, clinicians can identify a threshold response to treatment that may be considered "worthwhile", and researchers can obtain a more complete comparison of the effectiveness of therapies.

Some of the more commonly reported instruments in the literature for the assessment of HRQOL in the adult population with asthma include the Asthma Quality of Life Questionnaire (AQLQ), Living With Asthma Questionnaire (LWA), Asthma Symptom Utility Index (ASUI), the Sydney Asthma quality of Life Questionnaire

(Sydney AQLQ), and others. These asthma-specific HRQOL instruments are usually in the form of a series of scales that patients use to rate the effect of asthma on aspects of their lives that are affected by asthma. Patients' scores on these scales are then used to calculate a numerical value to represent the patients' HRQOL status.

2.2.3 MEASURING HEALTH-RELATED QUALITY OF LIFE IN *PEDIATRIC* PATIENTS WITH ASTHMA

It is just as important to evaluate HRQOL in children with asthma as it is in adults with asthma.[72] The HRQOL instruments designed for the adult population, however, are not useful in children. Furthermore, parents' perception of their children's HRQOL may not be accurate.[73] Children require HRQOL instruments designed for their level of comprehension.[74-75]

A review of the Medline™ database from 1966-1998 has revealed that ten instruments have been designed to assess children's or their parents' perceptions about asthma on their lives.[76-77] The names of these instruments and the type of respondent the instruments have been designed for are listed in Table 1. Six of these instruments have been designed for parents as respondents. Only four of the ten have been designed for children as respondents. Of the four instruments that have been designed for children to respond to, only two evaluate HRQOL as a multi-dimensional concept. They are the

Childhood Asthma Questionnaire (CAQ) and the Pediatric Asthma Quality of Life Questionnaire (PAQLQ).

Table 1 **Asthma-Specific Instruments Designed to Measure the Effect of Asthma on Pediatric Patients**

Instrument	Respondent	
	Parents	Children
Asthma Symptom And Disability Questionnaire	X	
Child Health Survey	X	
Functional Status II (R)	X	
Quality of Life Factors	X	
Functional Severity of Asthma Scale	X	
Childhood Attitudes Towards Illness Scale (CATIS)	X	X (8-12 years)
Life Activities Questionnaire For Childhood Asthma	X	X (5-17 years)
Pediatric Asthma Quality of Life Questionnaire	X	X (7-17 years)
Childhood Asthma Questionnaire	X	X (4-16 years)
About My Asthma[77]		X ($\geq 5^{th}$ grade)

2.2.4 MEASUREMENT PROPERTIES OF PEDIATRIC ASTHMA-SPECIFIC HRQOL INSTRUMENTS

Like other tools in the social and behavioural sciences designed to measure abstract concepts, psychometric properties of the instruments are important determinants of the utility of HRQOL instruments. The most important psychometric properties of HRQOL instruments are validity, reliability, and responsiveness. In general, validity refers to the extent that an instrument measures what it is intended to measure. [78] Reliability refers to the extent that an instrument measures the same result on repeated trials.[78] Responsiveness refers to the extent that a measurement is able to detect clinically meaningful change. So far, very little has been done to evaluate the responsiveness of these instruments to clinical change. Responsiveness is a property that can help researchers and clinicians interpret clinically important change in HRQOL measures.

2.2.4.1 CHILDHOOD ASTHMA QUESTIONNAIRE (CAQ)

The Childhood Asthma Questionnaire (CAQ) is a child-centred instrument that examines children's own perception about how asthma affects their HRQOL. The self-administered CAQ has been designed to obtain responses directly from children and to minimize parental influence. Ease of use, children's interests, and children's level of comprehension are factors that have been taken into account in the design of the

instrument. The development of the CAQ has been reported.[79]

The CAQ is comprised of three different age-specific questionnaires, the CAQ-A, CAQ-B, and the CAQ-C as shown in Table 2 and Appendices 1 to 3. The three age-specific questionnaires address the wide range of comprehension levels and lifestyles of pre-school children to teenagers. Each of the three age-specific questionnaires is comprised of different domains, which have been derived by factor analysis. The domains of each of these instruments are summarized in Table 3. Only the responsiveness of the CAQ-C has been investigated. No studies have yet evaluated the responsiveness of the CAQ-A or the CAQ-B.

2.2.5 PEDIATRIC ASTHMA QUALITY OF LIFE QUESTIONNAIRE (PAQLQ)

The PAQLQ[80] (shown in Appendix 4) was designed to evaluate HRQOL in pediatric patients with asthma aged seven to 17. It has shown to be reliable in the age groups for which it was designed.[81] The PAQLQ can be self-administered or interviewer-administered. In addition, it has an optional component designed to assess the impact of asthma on the caregiver (PACQLQ).[82] A unique feature of the PAQLQ is a set of "individualized" questions that assess the impact of asthma on a child's ability to perform physical activities. These individualized questions are supposed to

Table 2 **Age-specific Questionnaires**

The CAQ is comprised of three age-specific formats. The age specific age group of each instrument, and the unique features of each instrument are described in each column.

Instrument	Age	Unique Features
CAQ-A	4-7	• Requires assistance of adult • Children colour-in the questionnaire
CAQ-B	8-11	• Self-administered • Children colour-in the boxes
CAQ-C	12+	• Self-administered • Children insert numbers adjacent to items

Table 3 **The Subscales of the Childhood Asthma Questionnaire**[79]

CAQ-A	CAQ-B	CAQ-C
Quality of Living Enjoyment of daily activities. **Distress** Feelings about asthma	**Active Quality of Living** Enjoyment of running, swimming, PE, etc. **Passive Quality of Living** Enjoyment of reading, watching TV, etc. **Distress** Feelings about asthma symptoms. **Severity** Frequency of asthma symptoms.	**Active Quality of Living** Enjoyment of sports, swimming, PE, etc. **Teenage Quality of Living** Enjoyment of teenage social activities. **Distress** Feelings about asthma symptoms and social impact. **Severity** Frequency of asthma symptoms. **Reactivity** Awareness of environmental triggers.

make the QOL instrument more responsive to changes in HRQOL.

The PAQLQ was developed according to guidelines that have been used in the construction of a dozen validated disease specific quality of life instruments.[83-84] The following are some of the objectives of the questionnaire:

- reflect areas of function that are important to children with asthma
- include both physical and emotional function
- be reproducible when the clinical state is stable
- be responsive to changes that are important to the patient even if the changes are small
- be valid, that is, actually measure HRQOL in children

STRUCTURE

The interviewer-administered form of the questionnaire has 23 items that cover three domains of quality of life: activity (n=5), symptoms (n=10), and emotional function (n=8). Each item of the PAQLQ is evaluated using one of the seven-point scales that measure the degree and frequency of asthma symptoms, impairment of activities, and limitation of emotional function. The minimum scores of each item in each domain is one, which indicates maximum degree of asthma-related symptoms and maximum impairment of activities or limitation of emotional function. The maximum score of each item in each domain is seven, which indicates no degree of asthma-related symptoms and no impairment of activities or limitation of emotional function. The overall HRQOL

score is the mean score of each domain.

A self-administered version of the PAQLQ with the same number of items is also available. However, the measurement properties of this version has not yet been evaluated. In addition, the PAQLQ has a component that can be administered to parents called the Pediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ). Guyatt *et al.* have reported that additional information can be gained about children's HRQOL by parents of children 11 years old or younger who are administered the PAQLQ. However, in children greater than 11 years, parents can provide little information beyond what is provided through questioning the child directly.[73]

2.2.5.1 PSYCHOMETRIC PROPERTIES

Juniper *et al.*[80] evaluated the discriminative and evaluative properties of the PAQLQ in a nine-week prospective study with a cohort of 52 children. The children enrolled in the study had two, four-week study periods (week 2-5 and week 6-9). As they progressed through the study periods, the children were assessed three times; at week 1, 5 and 9. At each assessment, the children were administered the PAQLQ, the Feeling Thermometer, and a clinical asthma control questionnaire. Spirometry was also measured at each assessment period. When the study was completed, children were classified either

as having stayed the same (Group A) or changed (Group B) by one of three methods shown in Table 4. Agreement between the different methods was calculated using a kappa statistic. The overall QOL change within subjects was 0.79 ($p < 0.001$ using a paired t-test). The mean difference in QOL score between the beginning and the end of the treatment period was also compared between the group that changed and the group that did not change, using an unpaired t-test. The mean change in HRQOL score in the population that changed was 0.79 compared to 0.10 in subjects that remained stable ($p < 0.0001$). A responsiveness index[93] was also calculated from the minimal important difference score using the mean difference in score in those who scored -3, -2, +2, or +3 on the global rating of change as the minimal important difference and the pooled within-subject standard deviation from both Groups A and B. The responsiveness index[93] for overall quality of life was reported to be 0.59. The authors concluded that the PAQLQ was responsive to within-subject change in quality of life over a four-week period. In addition, they reported that PAQLQ scores correlated moderately with asthma control, β_2-agonist use, and the Feeling Thermometer,[85] a generic quality of life instrument (see Table 5).

The responsiveness index, however, may not be accurate because the methods may have been biased. The investigators used *three* methods to distinguish patients who changed (Group B) or stayed the same (Group A). However, the kappa (κ) statistic of the inter-

Table 4 Methods of Classifying Change In Patients

Method	Description
Global Rating of Change[86] (Patient Rated)	If patients scored -1, 0, or +1, they were considered to have stayed the same and if they scored between -7 and –2 or between +2 and +7 they were considered to have changed.
Global Rating of Change[86] (Caregiver Rated)	If the caregiver scored -1, 0 or +1, on their perception of whether the child's asthma symptoms have changed, the child was considered stable, for all other scores the child was considered to have changed.
Clinical Evaluation	Using only clinical data (asthma control score, spirometry, peak flow rates, β-agonist use) one of the investigators classified the patients as stayed the same or changed.

Table 5 **Pearson Correlation Coefficients Showing Cross Sectional Construct Validity**

	Asthma Quality of Life		
	Symptoms	Activities	Emotions
Clinical Asthma			
Clinical Asthma Control	-0.61	-0.62	-0.37
β_2-agonist Use	-0.51	-0.49	-0.30
Generic Quality of Life			
Feeling Thermometer[85]	0.41	0.53	0.36

observer ratings of change was only 0.2, which is considered low (κ ranges from 0, considered no better than expected by chance, to 1, considered perfect agreement).[87] In other words, the inter-observer agreement was low. Thus, it is not clear which patients truly experienced a clinical improvement or worsening of their condition. Furthermore, it was decided only *after* the study was complete that only one of the three methods, the *patient's* Global Rating of Change, was to be used to classify change of the patients' true clinical status. Since this decision was made *after* the study was complete, the method used to calculate the index could have been biased. Furthermore, a commonly used index of instrument responsiveness, the effect size, has not yet been reported for the PAQLQ for patients with moderate changes in clinical status or for patients with large changes in their clinical status.

2.2.6 USING PATIENT SPECIFIC ITEMS IN HRQOL INSTRUMENTS TO IMPROVE RESPONSIVENESS

Most HRQOL instruments consist of a standard set of items designed to evaluate the impact of illness on a person's health-related quality of life. Since these instruments are designed to evaluate HRQOL in groups of patients, the items are neither specific nor individualized for each patient. Some HRQOL instruments may assess a patient's ability to perform a particular function that may or may not be important to the patient or essential for the conduct of day-to-day activities. Items that may not be relevant to a patient may reduce the responsiveness of the instrument. For example, an item may

ask a patient, "How has asthma affected your ability to swim?" in order to assess the impact of a patient's disease on his or her physical function. If swimming were not an important activity for the patient to participate in, then the effect of a clinical improvement in health status such that the patient was able to more actively engage in swimming may not be significant for the patient.

It has been reported that patients can generate items for HRQOL that may be more relevant than clinician generated items.[88] Some instruments, like the PAQLQ have items that patients generate. It is hypothesized that a patient-specific instrument would improve the relevance of items to patients, and be more responsive to changes in a patient's clinical status. For example, if an instrument were dynamic in structure and were capable of assessing those unique characteristics important to each individual's HRQOL domains, then the instrument should be more sensitive to changes in clinical status compared to an instrument that includes items that are not relevant.

In order to explore this idea, hypothesis-testing of asthma-specific HRQOL questions was begun. When referring to these questions collectively, the acronym QOLiF (Quality of Life Index for Families) will be used. Although the QOLiF is not a HRQOL instrument, it has a dynamic structure, which can be used to test this hypothesis. The QOLiF consists of interactive questions that first assesses patients' preferences before generating relevant questions. The QOLiF is designed to explore whether or not individualized items can improve their responsiveness to clinical change on

physical functioning, social functioning, and role functioning.

The QOLiF (shown in Appendix 5) consisted of seven sections. The first section is a list of physical activities, social activities, and role functions that the investigators use to help the children identify items that he or she performs. The items have been designed to reflect activities commonly performed by children living in Canada. Section 2 to 4 respectively, consists of the physical domain, social domain, and role function domain questionnaires for the parent or guardian. Section 5 to 7 respectively, consists of the physical domain, social domain, and role function domain questionnaires for the child. After the child identified items that he or she performs, the investigator transcribes these items into the appropriate domains of the questionnaires, which are then administered to the parent and the child. As shown in Appendix 5, all items of the QOLiF consist of a seven-point likert scale. Both parents and children respond to the questionnaires by marking their answers directly on the form provided. Parents are instructed to help the children answer the questions themselves, not to prompt the child, and not to influence the child's responses.

2.2.7 THE NEED TO EVALUATE RESPONSIVENESS OF HRQOL INSTRUMENTS

Studies have shown that HRQOL measures are sensitive to change in groups of patients and are as sensitive or more sensitive than many traditional measures, such as

performance tests, or laboratory evaluations of disease activity.[89] Responsiveness, which is also referred to as "sensitivity," is an important psychometric property of HRQOL instruments because many studies that use these instruments require measurements to be made in populations over periods of time. Responsiveness, is a property that can help researchers and clinicians interpret clinically important change in HRQOL measures.

It is possible that statistically significant change over time may not necessarily represent clinically important change. A measure of responsiveness can help clinicians and researchers of HRQOL instruments interpret numerical results of HRQOL measurement scores in relation to benchmark scores associated with various degrees of clinical change. Furthermore, an index of responsiveness can be used to determine the statistical power of a trial.[90] Several indices for measuring the responsiveness of a HRQOL instruments have been proposed, although no gold standard exists.[89-90] These methods include the effect size, [91] standardized response mean, [92] relative efficiency, [89] and Guyatt's Index. [93]

One of the more commonly reported indexes of responsiveness is the effect size. The use of effect size calculations has been well accepted in the social and behavioural sciences.[94] The effect size is calculated by taking the difference between means before treatment and after treatment and dividing by the standard deviation of the same measure before treatment as shown in Equation 1. In general, a large effect size of 0.8 or more

indicates high sensitivity to change. A moderate effect size of 0.5 to 0.2 is moderate, and an effect size less than 0.2 is considered small.[95] The standardized response mean and the relative efficiency index are similar to the effect size. Studies in the past that have examined the responsiveness of quality of life instruments have obtained similar results regardless of which method was used.

Equation 1 Effect Size Calculation

$$ES = \frac{(\mu_1 - \mu_0)}{\sigma_0}$$

ES = Effect Size
μ_0 = mean before treatment
μ_1 = mean after treatment
σ_0 = standard deviation before treatment

Guyatt's Index[93] measures responsiveness as the ratio between the minimal clinically important difference (MCID) divided by the square root of twice the mean square error in stable subjects.

2.3 OBJECTIVES

Thus, there is a need to evaluate the incidence of inappropriate use of medication in pediatric patients admitted to hospital for asthma. Furthermore, valid, reliable, and responsive instruments are needed to evaluate the benefits of pharmacological treatments on patients with asthma. An estimate of the frequency of drug-related hospital admissions in pediatric patients with asthma and an understanding of the causative factors associated with these admissions would provide data for clinicians and health policy decision makers to target resources at preventing these problems in the future. A better understanding of the measurement properties of health related quality of life instruments for patients with asthma would help clinicians and researchers better interpret the numerical values of health related quality of life measures in relation to patients' clinical status.

The objectives of the study were the following:

(1) evaluate the frequency of drug-related hospital admission in pediatric patients with asthma

(2) evaluate the *responsiveness* of the PAQLQ to change in patients' clinical status using the effect size index of responsiveness

(3) evaluate the merit of an individualized approach to HRQOL assessment

3. METHODS

The study consisted of two components, the evaluation of drug-related hospital admissions, and the evaluation of health-related quality of life instruments. The two parts of the study were conducted concurrently.

3.1 EVALUATION OF DRUG-RELATED HOSPITAL ADMISSIONS

To estimate the frequency of drug-related hospital admissions in the pediatric patient population, patients newly admitted to hospital with symptoms of acute asthma were recruited. On enrollment, data were collected and evaluated using a method that has been used by Hallas *et al.*[2, 51-54] in several previous studies. By recruiting patients with symptoms of acute asthma, this study focused primarily on drug-related hospital admissions caused by therapeutic failures rather than adverse drug reactions.

3.1.1 PATIENT RECRUITMENT

Between August 11th, 1996 and July 15th, 1997, children between five and 17 years of age with asthma or asthma-related symptoms were recruited from Children's and Women's Health Centre of British Columbia (CWHCBC); the Children's Centre, at Mount Saint Joseph Hospital (MSJ); and Burnaby Hospital. CWHCBC is the primary treatment, research and teaching hospital of pediatric residents of the province of British Columbia. Children less than five years of age were not included because the diagnosis of asthma is less clear in this population and the therapeutic approach outlined in both

the Canadian[33] and International[32] asthma treatment guidelines are more explicit in patients five years and older.[96]

Each day, a registered nurse whose position was: Clinical Quality Advisor, Quality Promotion, at CWHBC reviewed all the hospital admission records and reported those children who met the inclusion criteria shown in Table 6 to the investigator. This nurse had access to all the hospital admission records. The list of inclusion criteria was given to the nurse prior to the start of the study. The nurse was instructed to report any child who was admitted to hospital with a diagnosis of asthma or asthma-related symptoms noted in the admission history of the medical chart. The symptoms of asthma include episodes of wheezing, shortness of breath, chest tightness, and coughing. The nurse reported the name of the child to the investigator if the admitting diagnosis on the child's health record included any of these symptoms.

Once a child's name was reported to the investigator, the investigator confirmed the inclusion criteria by examining the child's health record, or speaking with the child's doctor(s), nurse(s), and other members of the healthcare team involved in the care of the patient. An appointment was then made to meet with the child and the parent or guardian to invite them to participate in the study. At the appointment, the purpose of the study was described. Each child and his/her parent was provided with a consent form and had 24-36 hours to decide whether or not to participate in the study. Parents who agreed to

participate and those children who were 12 years of age or older signed the consent form (Appendix 6).

Table 6 **Inclusion Criteria**

The following is a list of inclusion criteria that was used to select those pediatric patients that could be enrolled in the study. This list of criteria was made available to the nurse that reported admissions to the investigator prior to the start of the study. In addition, this list was posted in the medical wards where the study occurred.

- Age between 5 to 17 years at the time of admission
- Admission to hospital ward with a diagnosis of asthma or asthma-related symptoms.
- No symptoms of any serious concomitant diseases such as cancer, AIDS, or coma
- No symptoms of any medically diagnosed abnormal psychological conditions, which may impair the patient's ability to communicate or answer health-related quality of life instruments.

3.1.2 SAMPLE SIZE ESTIMATE

The goal was to recruit 61 patients, a number which was estimated to equal the minimum sample size for both components of the study. To determine sample size for estimating the frequency of drug-related hospital admissions in the pediatric patient population admitted to hospital with asthma, the true population proportion of drug-related hospital admissions was estimated to be between 5% and 20%. This range was based on a recent meta-analysis,[46] which estimated that the frequency of drug-related hospital admissions in the general population is between 2 and 21% (see Section 2.1.3). It was expected that the frequency of drug-related hospital admissions would be relatively high. Thus, to be conservative, a sample size was estimated, based on the upper end of the range and using Equation 2. It was estimated that 61 patients would be sufficient to provide a 95% confidence interval of ± 10% around an estimated population proportion (Π) of 20% for drug-related admissions, as shown in Table 7. Using the same equation, it was estimated that at least 21 patients would be required to obtain a reasonable estimate of the responsiveness of the quality of life instruments, as described in Section 3.2.

Equation 2 Sample Size Estimate For A Population Proportion

$$N = \Pi (1- \Pi) (Z_{\alpha/2}/CI)^2$$

N = the sample size
Π = the population proportion
Z = the standard normal deviate
CI = the desired confidence interval

Table 7 **Sample Size Estimates For 95% Confidence Interval**

The numbers in the second and third columns show the sample size needed for the 95% confidence interval to be ± 5% or ± 10% respectively of the estimated population proportion.

Estimate of Population Proportion (Π)	95% Confidence Interval	
	± 5%	± 10%
5%	73	19
10%	138	36
20%	246	**61**
30%	323	81
40%	369	92
50%	384	96

Over a 12-month period, it was expected that approximately 75 patients would be enrolled. Past records were evaluated for the apparent frequency of asthma-related admissions. These records had indicated that, in 1995, 150 children less than 17 years of age had been annually admitted and discharged from BCCH and the Children's Centre located at MSJ. Approximately half of those children were less than five years of age. Therefore it was expected that between 61 and 75 patients who met the inclusion criteria would be enrolled over the 12 month study period.

3.1.3 DATA COLLECTION

After consent was obtained, data related to the child's admission were gathered from three sources; (1) the patient's medical record from the hospital; (2) interviews with the patient and the family; and (3) interviews with the patient's professional medical staff, including the pediatrician, specialist, nurse, pharmacist, and other members of their health care team. Using the form shown in Appendix 7, the following data were gathered:

- Medication history prior to admission
- Medication compliance
- History of medical problems including allergy
- History of hospital admissions and doctors' visits
- Frequency and severity of asthma symptoms
- Family history of asthma and atopy
- Environmental exposure to asthma trigger factors
- Ability to perform normal activities of daily living, including school, sleep, and social functioning
- Peak expiratory flow rate (PEFR) of the child at hospital admission
- PEFR of the child at hospital discharge or as soon after discharge as was available.

The interviews placed a particular emphasis on the symptoms on admission, current medication use, medication history and extent of compliance with medications. For example, each child and his parent or guardian was asked to describe the events that took place prior to the hospital admission, the child's previous medications, the method of administration, and signs and symptoms of respiratory distress that occurred prior to admission.

3.1.4 DETERMINATION OF DRUG-RELATED HOSPITAL ADMISSION

A team of experts in asthma care evaluated the relation between hospital admission and concurrent therapy using Hallas' algorithm, with some modification.

3.1.4.1 HALLAS' ALGORITHM

Hallas' algorithm is a three-step procedure that examines first, the relation between a drug event and an adverse drug reaction and the drug event and a dose-related therapeutic failure; second, the role of the suspected symptoms to hospital admission; and third, the degree that each drug event was avoidable. To characterize the relation between drug intake and adverse drug reaction, the criteria shown in Table 8 are used. To assign causality of dose-related therapeutic failure, the criteria shown in Table 9 are used. Next, the suspected symptoms' significance for the hospital admission are evaluated using the criteria shown in Table 10.

Table 8 **Criteria Used to Characterize the Relation Between Drug Intake and ADR[2]**

i.	Presence of a known drug reaction or toxic reaction
ii.	Presence of a reasonable temporal relation between the commencement of drug therapy and the onset of the adverse reaction
iii.	The adverse reaction disappeared upon discontinuation or dose reduction of the drug
iv.	The symptom or event could not be explained by any other known condition or predisposition of the patient
v.	The symptoms reappeared upon re-exposure or laboratory tests showed toxic levels or drug-induced metabolic disturbances that explained the symptoms

"Definite" causal relation. All five criteria are satisfied.
"Probable" causal relation. Criteria (i), (ii), (iii) and (iv) are satisfied.
"Possible" causal relation. Criteria (i), (ii), and (iii) are satisfied.
"Unlikely/Unevaluable" causal relation. The relevant information required for evaluation could not be obtained, the temporal sequence was atypical, or other conditions or dispositions are considered far more likely to have caused the symptoms.

The relation was not rated higher than "possible" if the adverse event occurred previously without relation to drug treatment or was an accentuation of symptoms already present before the start of drug therapy.

Table 9 **Criteria Used to Characterize the Relation Between Drug Intake and TF[2]**

i.	Symptoms of the disease are known to reappear at insufficient doses
ii.	The symptoms were not likely to have been caused by a progression of the disease
iii.	A reasonable temporal relation between the start of inadequate dosage and the appearance of symptoms
iv.	The symptoms resolved upon adjustment to an adequate dose
v.	No other condition present could explain the symptoms
vi.	Drug levels were clearly below the therapeutic range or there was clear evidence of intake of an insufficient dose

"Definite" causal relation. All six criteria are satisfied.
"Probable" causal relation. Criteria (i), (ii), (iii), (iv) and (v) are satisfied.
"Possible" causal relation. Criteria (i), (ii), (iii) and (iv) are satisfied.
"Unlikely/Unevaluable" causal relation. The relevant information required for evaluation could not be obtained, or the temporal sequence was atypical, or other conditions or dispositions are considered far more likely to have caused the symptoms.

Table 10 Significance For Hospital Admission[2]

Dominant	The suspected symptoms were the main reason for admission, and no other symptoms contributed significantly.
Partly Contributing	The suspected symptoms played a substantial role in admission, but other factors also contributed significantly.
Less Important	The suspected symptoms played a minor or uncertain role, and the patient would probably have been admitted without them.
Not Contributing	Other symptoms/circumstances were the main reason for hospitalization.

In each case where there is a "definite" or "probable" causal relation between drug intake and the drug event, and in which the symptoms are "dominant" or "partly contributing" to the hospital admission, a further evaluation is made as to whether the event could have been avoided by appropriate measures taken by health service personnel, as described in Table 11.

3.1.4.2 EXPERT PANEL ASSESSMENT/EVALUATION

To perform the evaluation, a panel consisting of two clinical pharmacists (one Ph.D., one post-graduate Pharm.D trained) and one registered nurse all trained in the management of asthma met face-to-face during three eight-hour sessions. Panel members evaluated each case based on all the collected data for each patient. The data were presented to each panel member using a standardized case report. Furthermore, each patient's medical chart was also available. Although the experts had already been familiar with the The National Asthma Education and Prevention Program Expert Panel Report 2 Guidelines For the Diagnosis and Management of Asthma from the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health and the most recent Canadian asthma treatment guidelines, the reports were also made available to the panel members during their evaluation.[32-33] Each panel member read each case history individually and the panelists openly discussed each case before rendering a decision about each step of

Table 11 Classification of Avoidable Admissions[2]

Definitely Avoidable	The drug event was due to a drug treatment procedure inconsistent with present day knowledge of good medical practice or was clearly unrealistic, taking the known circumstances into account.
Possibly Avoidable	The prescription was not erroneous, but the drug event could have been avoided by an effort exceeding the obligatory demands.
Not Avoidable	The drug even could not have been avoided by any reasonable means, or it was an unpredictable event in the course of treatment fully in accordance with good medical practice.
Unevaluable	The data for rating could not be obtained or the evidence was conflicting

the Hallas algorithm. However, each panel member formed his or her own conclusion and the panel members were not required to reach a consensus.

Each case was first evaluated for the relation between drug intake and adverse drug reaction (ADR). The relation between drug intake and ADR or DTF in each case was classified according to the criteria shown in Table 8 and Table 9. However, a modification was made to Hallas' algorithm in relation to the assessment of dose-related therapeutic failure.

In Hallas' previous studies, a DTF was defined as an absence of therapeutic response that could be linked causally either to a prescribed dose that was too low, to drug non-compliance, recent dose reduction/discontinuation, interaction, or inadequate monitoring. Non-prescription of a drug was not considered to represent DTFs. In the present study, Hallas' algorithm was modified, and non-prescription of a drug was included in the classification of dose-related therapeutic failures.

In addition to this modification, an emphasis was made to the panel related to interpretation of Criterion 5 of the algorithm. Criterion 5 of Hallas' classification of DTF is "no other condition present could explain the symptoms." The panel was instructed to interpret this statement to mean "the development of the acute symptoms could not be explained by a recent or concurrent medical condition." With this interpretation, this criterion was not satisfied if the patient had a recent or concurrent medical condition

that could have explained the acute symptoms of asthma on hospital admission. If there was any evidence of a respiratory tract infection, panel members were instructed to score this criterion as "false."

Since it has been estimated that 80 to 85 %[97-98] of children's asthma exacerbations are triggered by upper respiratory tract infections, the purpose of the explicit reference to respiratory tract infections was to reduce the chance that the expert panel would neglect to consider a respiratory tract infection as a potential factor contributing to a patient's symptoms on hospital admission.

Following evaluation of the relation between drug intake and the ADR or DTF, the suspected symptoms' significance for the hospital admission was evaluated according to the criteria shown in Table 10. For "definite" and "probable" drug events in which symptoms were "dominant" or "partly contributing" to the hospital admission, a third evaluation was made as to whether the event could have been avoided by appropriate measures taken by the health service personnel as described in Table 11. During the evaluation of drug-related hospital admissions, the investigator made the hospital health records of each patient available to the panel members for further reference.

The final result for each criterion of Hallas' algorithm was based on the majority vote of the three panel members. Therefore, for each criterion evaluated, the result was either positive or negative—ties were not possible.

3.1.5 COMPARISON OF PATIENTS' DRUG THERAPIES WITH THE RECOMMENDATIONS OF THE NIHLBI GUIDELINES

After the formal evaluation of drug-related hospital admissions by the panel, the investigator reviewed the results of the expert panel's evaluation together with all data collected for each case to examine the extent the patients' drug therapies were consistent with the *National Asthma Education and Prevention Program Expert Panel Report 2 Guidelines For the Diagnosis and Management of Asthma.* The data collected about patients' drug therapies were subjective data based on patients, parents of patients, and physicians' reports of medication use. Objective evidence of patients' actual medication use was not available.

In each case, the investigator estimated the patient's chronic asthma severity prior to the exacerbation based on their reported chronic symptoms (Appendix 8) and types of prescribed medication. Patients were classified as "mild-intermittent," "mild-persistent," "moderate," or "severe" according to the classification system shown in Table 12, which has been incorporated from the Guidelines. Where there were insufficient data about patients' reported symptoms, an estimate of severity was made by considering the types of medications the patient was prescribed. However, in cases where it was not possible to categorize the patients' severity because data were insufficient, patient's symptoms were classified as "non-determinable."

Table 12 Classification of Asthma Severity[32]

Clinical Features Before Treatment			
	Symptoms	Nighttime Symptoms	Lung Function
STEP 4 Severe Persistent	Continual Symptoms Limited physical activity Frequent exacerbations	Frequent	FEV_1 or PEF ≤ 60% predicted PEF variability >30%
STEP 3 Moderate Persistent	Daily symptoms Daily use of inhaled short-acting β_2-agonist Exacerbations affect activity Exacerbations ≥ 2 times a week' may last days	> 1 time a week	FEV_1 or PEF > 60 % <80% predicted PEF variability > 30%
STEP 2 Mild Persistent	Symptoms > 2 times a week but < 1 time a day Exacerbations may affect activity	> 2 times a month	FEV_1 or PEF ≥ 80% predicted PEF variability 20 -30%
STEP 1 Mild Intermittent	Symptoms ≤ 2 times a week Asymptomatic and normal PEF between exacerbations Exacerbations brief (from a few hours to a few days); intensity may vary	≤ 2 times a month	FEV_1 or PEF ≥ 80 % predicted PEF variability < 20%
The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs. The characteristic notes in this figure are general and may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time. Patients at any level of severity can have mild, moderate, or severe exacerbations. Some patients with intermittent asthma experience severe and life-threatening exacerbations separated by long periods of normal lung function and no symptoms.			

The guidelines indicate appropriate treatment for the chronic management of asthma symptoms and for acute episodes for each classification. Based on each patient's classification, a determination was made about whether or not each patient had "inadequate treatment."

- Chronic asthma management: A patient was considered to have had "inadequate treatment" of chronic asthma if drug therapy indicated by the guidelines for the chronic treatment of asthma was not reported in the patient's drug regimen in the last 3 months; or if the patient, parent, or physician reported that the indicated medication was in the regimen but the patient was non-compliant in using it.

- Acute asthma management: A patient was considered to have had "inadequate treatment" if drug therapy indicated by the guidelines for treatment of the *acute episode* was not reported in the patient's drug regimen; or if the patient, parent, or physician reported that the indicated medication was in the regimen but that the patient was non-compliant in using it.

For example, if a patient had "mild-persistent" asthma, but did not report regularly scheduled inhaled corticosteroids in their regimen, then the patient was considered to have had "inadequate treatment." Or if oral steroids were indicated by the guidelines for the management of the patient's acute exacerbation, but the patient did not report having it in the regimen, then the patient was also considered to have "inadequate treatment."

"Inadequate treatment" was not considered present if the patient received drug therapy that was consistent with the recommendations of the Guidelines. In some cases where data about a patient's history of symptoms were insufficient for the investigator to determine whether the patient received drug therapy appropriate for the patients' level of severity, a "not-determinable" designation was made about the presence of "inadequate treatment."

In general, a patient was considered to have had "inadequate treatment" if the patient or parent did not report receiving drug therapy for the chronic or acute asthma in accordance with the Guidelines. Since objective information about prescribed drug therapy and compliance were not obtained, the estimates of inadequate treatment were approximations.

The investigator also examined patients' reported evidence of non-compliance with long-term control and quick-relief medications. During the interview, the investigator asked each patient the following three general questions related to compliance:

- How often does the child forget to take medication?
- Does the child always take medication at the same time each day?
- If he feels better, would he stop taking medication on his own?

The patient and the parent were then asked to expand on the answer provided to each question. Then the investigator asked specific questions about compliance

regarding each medication that was reported in the regimen. Patients were considered non-compliant if the parent, child, or physician(s) reported that the child did not take their medication(s) as directed.

3.2 EVALUATION OF HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS

The collection of pediatric health related quality of life data were performed at the same time drug-related hospital admission data were collected as described in Section 3.1. To measure the responsiveness of the PAQLQ, CAQ, and the merit of using an individualized approach to HRQOL assessment in the three domains of the QOLiF, the investigator administered the questionnaires to the patients in the hospital wards during their acute phase of asthma, and again six weeks after discharge when the patients' symptoms had improved.

3.2.1 PATIENT RECRUITMENT

The patients who participated in the drug-related hospital admission component were invited to participate in the evaluation of quality of life instruments. Only those patients who could understand the age-specific questionnaires were selected. Patients who had difficulty reading or understanding English were excluded from the study.

3.2.2 SAMPLE SIZE CONSIDERATIONS

To determine the sample size for estimating the responsiveness of the quality of life

instruments, Equation 3 and Equation 4 of Cohen's,[95] *Power Analysis for Behavioural Sciences* were used. Assuming a one-tailed α is 0.05 and a correlation coefficient (ρ) between the first and second observation is at least 0.6, the number of patients required to detect effect sizes 0.6 or greater was 21 or fewer, as shown in Table 13. With our target sample size of 61, and based on these considerations it was anticipated that we would have enough patient to estimate the responsiveness of the quality of life instruments.

Equation 3 Estimate of N For Various Effect Sizes

$N = (n_{0.10}) / (100\ d^2)$
$n_{0.10}$ = value effect size table (Table 2.4.1[95]) d = effect size for paired samples (see Equation 4)

Equation 4 Effect Size For Paired Samples

$d = d_4' / (1 - r)^{0.5}$
d_4' = desired effect size r = correlation coefficient

Table 13 **Number of Paired Observations Required (Power = 0.9)**

Using Cohen's[95] method, this table shows the number of paired observations required to detect effect sizes between 0.4 to 1.0, as shown in the first row. The number of paired observations is dependent on the correlation between the paired observations. The number of paired observations based on correlations between 0 and 0.8 are shown. All estimates have been based on 90% power.

ES	0.4	0.5	0.6	0.7	0.8	0.9	1.0
$\rho = 0.0$	109	70	49	36	28	23	19
$\rho = 0.2$	87	56	40	29	23	18	15
$\rho = 0.4$	66	42	30	22	18	14	12
$\rho = 0.6$	44	29	21	15	12	10	8
$\rho = 0.8$	23	15	11	8	7	6	5

3.2.3 ADMINISTRATION OF INSTRUMENTS

During a two-week pilot phase, the investigator administered the health-related quality of life instruments to five children who met the inclusion criteria. The pilot phase allowed the investigator to practice administering the HRQOL instruments and to identify potential problems that might be encountered during administration.

The investigator administered and scored the health-related quality of life instruments according to the guidelines described by the authors of each instrument. An exception however, was made with the administration of the PAQLQ, which requires parents not be present during the interview. In this study, parents were present when the interviewer administered the PAQLQ to the children because having the parent absent during the administration of the PAQLQ, but present during the CAQ and QOLiF, was difficult to coordinate. Unlike the PAQLQ, the CAQ has been designed to be administered with the parent present, to assist the child in completing the questionnaire. In one previous study the CAQ-A has been administered to groups of up to four different children and their parent(s) together.[99]

Although it is possible that the obsequiousness bias may have been present when the PAQLQ was administered, the effect of this bias was reduced by the investigator who ensured that the parents never prompted the children. If a child asked for help from the parent, the investigator ensured that the parents did not influence the child's

response to any of the questions of the PAQLQ by reminding the child that his or her response was all that was needed.

The QOLiF, shown in Appendix 5, was also administered by the investigator with the parent or guardian present. Similarly, if a child asked for help from a parent or guardian, the investigator ensured that the parent or guardian did not influence the child's responses. Parents were instructed to help the children answer the questions themselves, not to prompt the child, and not to influence the child's responses.

To administer the QOLiF, the child was first asked to select from the list of physical activities, social activities, and role functions items that he or she normally performed. Each item was read aloud to each the child, and the investigator recorded the items that the child identified. After the investigator recorded the items, the child was asked to select, the "top three" most important items to them, and the "top three" least important items from the items that were initially identified. The purpose of identifying the top three most important items and the top three least important items was to compare the effect sizes to the responses of these items. After all items were identified, the investigator transcribed each item next to each seven-point likert scale shown in each form corresponding to each domain. The parent or guardian then responded to each domain-specific questionnaire by marking their answers directly on the form. The parents' answers were not made available to the child. After the parent or guardian

responded to each questionnaire, the children responded to his or her own set of questionnaires.

The appropriate set of age-specific health-related quality of life instruments were administered as shown in Table 14. The order that the instruments were administered within each set was randomized. The first administration occurred during the patient's stay in hospital. The follow-up administration occurred six weeks after hospital discharge in the patient's home. Patients were not shown their previous scores during the second administration of the CAQ instruments.

3.3 PRIMARY ANALYSIS

The primary analysis of drug-related hospital admissions consisted of three measures. The first measure was an estimate of the population proportion in which drug events were were classified as "definite," "probable," "possible," or "unlikely/unevaluable." The second measure was an estimate of the proportion of the population in which the suspected drug event's contribution to the admission was classified as either "dominant," "partly contributing," "less important," or "not contributing." The third measure was an estimate of the proportion of the population in which hospital admissions were classified as "definitely avoidable," "possibly avoidable," "not avoidable," or "unevaluable."

Table 14 Quality of Life Instrument Administered By Age Group

Age	5-6	7	8-11	12-16	17
HRQOL Instruments Administered	CAQ-A QOLiF	PAQLQ CAQ-A QOLiF	PAQLQ CAQ-B QOLiF	PAQLQ CAQ-C QOLiF	PAQLQ QOLiF

For the second component of the study, the primary measures were estimates of the effect size for each domain and summary scores of the CAQ, PAQLQ, and QOLiF.

3.4 SECONDARY ANALYSIS

An estimate was made of the proportion of the study sample that had "objective" or "subjective" evidence of an upper respiratory tract infection prior to their hospital admission, evidence of non-compliance with medications, inappropriate management of their acute asthma exacerbation, inappropriate use of preventative or prophylactic therapy, and a lack of a prescription.

3.5 STATISTICAL EVALUATION

To estimate the population proportion of drug-related events, 95% confidence intervals were calculated. Paired t-tests were used to compare health-related quality of life mean scores measured during hospital admission to scores measured six weeks after hospital treatment. An effect size was calculated using Equation 1 in Section 2.2.7 as an index of responsiveness for each of the instruments. All statistical tests were computed using SPSS for Windows™ and Microsoft Excel 97.™ Results were deemed to be significant when p was less than or equal to 0.05.

4. RESULTS

The results are presented in the following three sections. Section 4.1 describes the demographic and clinical features of the patients who participated in either one or both components of the study. Section 4.2 describes the chronic and acute drug regimens of the patients in the drug-related hospital admission cohort. Section 4.3 describes the results of the evaluation of drug-related hospital admissions and Section 4.4 describes the results of the evaluation of the responsiveness of the PAQLQ, and QOLiF to clinical change.

4.1 DESCRIPTION OF THE OVERALL STUDY SAMPLE

Sixty-one consecutive hospital admissions were identified and reported to the investigator for evaluation. In total, 54 of the 61 children and their parents agreed to participate in the study and met all of the inclusion criteria (Table 6). All parents who enrolled their children in the study and those children who were 12 years of age or older enrolled and signed the consent form shown in Appendix 6.

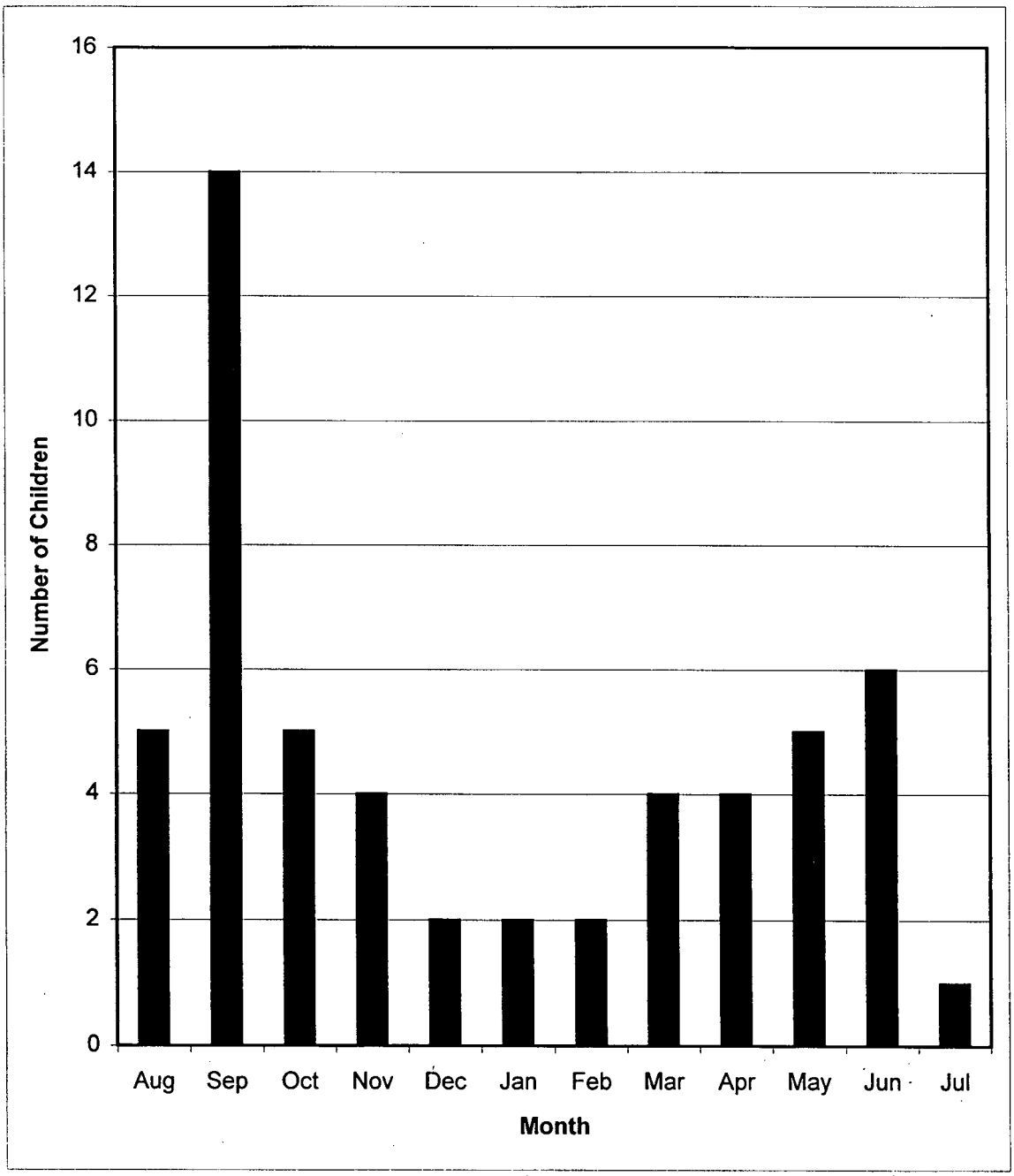
One parent refused to have his child participate, and six children were excluded from both components of the study by the investigator. Patients who were excluded included two children who had a diagnosis of pneumonia on admission rather than asthma, one child who had an admitting diagnosis of croup, two children who had

parents who could not understand or speak English, and one child who did not provide enough information for evaluation for either components of the study. The number of children who met the inclusion criteria and were enrolled each month is shown in Figure 1. The largest number of children was recruited in the month of September. Furthermore, a rise in the frequency of enrollment of children was observed in spring between January and June. The number of children enrolled in the month of July included only those children admitted between July 1st and July 15.th

4.1.1 DEMOGRAPHIC FEATURES OF PATIENTS IN THE STUDY SAMPLE

Of the 54 children who enrolled in the study, 36 (67%) were male and 18 (23%) were female. The mean age was 8.6 ± 3.2 years (median age, 7.8 years). The age distribution is shown in Figure 2. The difference in age between boys and girls was not statistically significant (2-tailed t-test, p = 0.917). Fifteen (28%) were Caucasian; 17 (31%) were Chinese and the rest were other minorities. Forty (74%), were from Vancouver. Furthermore, forty (74%) of the patients were admitted to MSJ. A summary of the demographic and physical features of the study sample is presented in Table 15. Appendix 9 shows the demographic data for each patient enrolled in the study. Each patient's height and weight and the respective percentiles are presented in Appendix 10.

Figure 1 **Number of Children Enrolled Per Month (n=54)[a]**



[a] For August and July, data were collected for only half the month.

Figure 2 **Age Distribution of Patients in the Study Sample (n=54)**

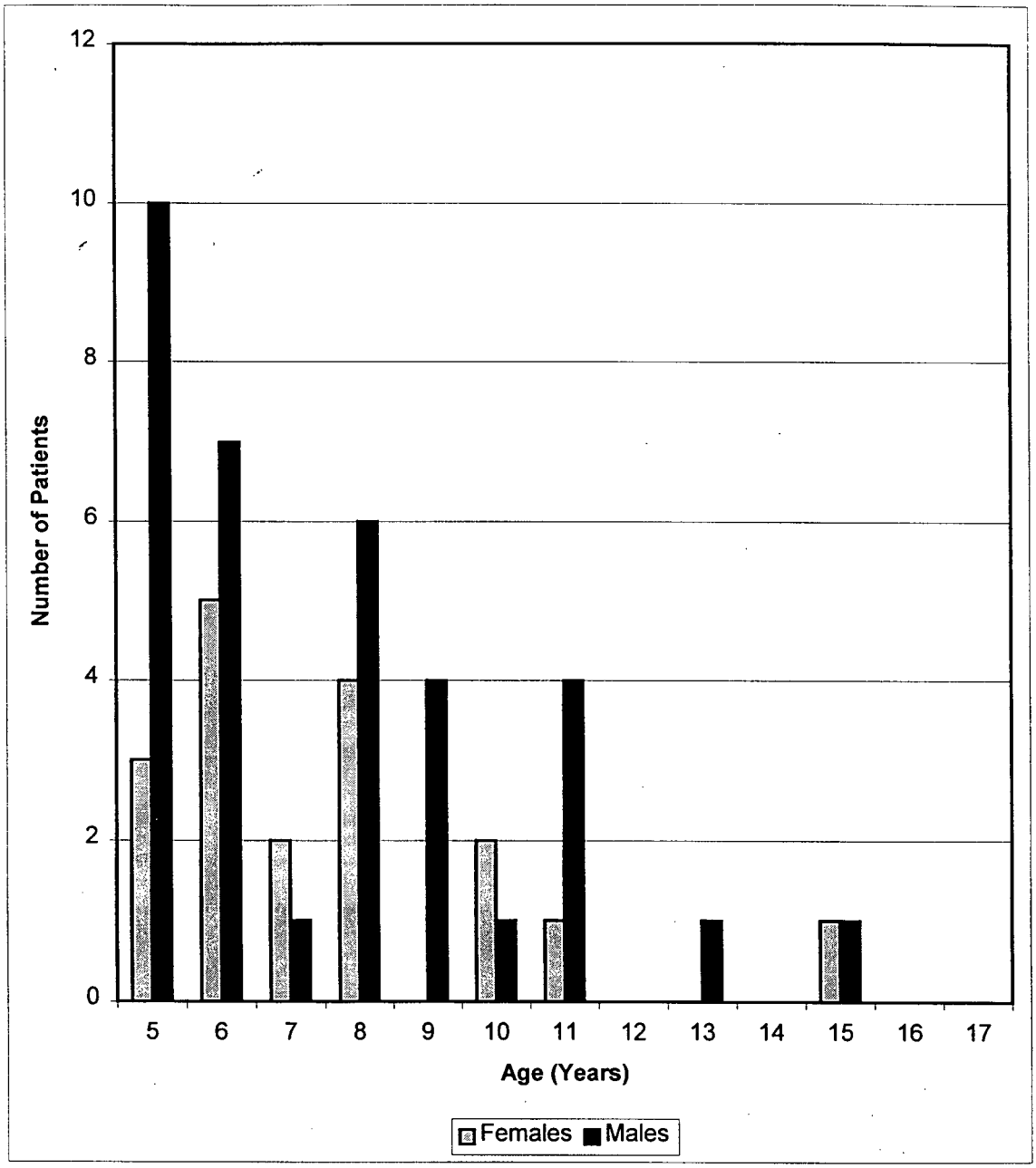


Table 15 **Age, Height, and Weight of the Patients in the Overall Study Sample**[a]

	Males	Females	Total
Age (years) mean ± SD (n)	8.6 ± 3.2 (42)	8.5 ± 3.1 (12)	8.6 ± 3.2 (54)
Height (cm) mean ± SD (n)	129.4 ± 20.9 (30)	114.0 ± 24.3 (12)	125.4 ± 20.9 (42)
Height (percentile) mean ± SD (n)	51.0 ± 32.6 (25)	41.3 ± 22.3 (10)	48.2 ± 30.3 (35)
Weight (kg) mean ± SD (n)	32.4 ± 16.7 (34)	27.5 ± 12.0 (15)	30.9 ± 15.4 (49)
Weight (percentile) mean ± SD (n)	50.3 ± 35.2 (25)	43.4 ± 30.5 (12)	48.1 ± 33.5 (37)

[a] Total sample included 42 males and 19 females. Only data recorded in the patients' hospital medical records were included.

4.1.2 CLINICAL FEATURES OF PATIENTS IN THE OVERALL STUDY SAMPLE

The clinical data for each patient were obtained shortly after hospital admission. Clinical respiratory system data (heart rate, respiratory rate, oxygen saturation at room air, and peak expiratory flow rate) from each patient's health record are shown in Appendix 11. Some data for some patients were not available because they were not recorded in their health records. The mean values, as summarized in Table 16, were consistent with the clinical features of acute respiratory distress. The mean peak flow on admission was 60.6 ± 22.6% of the age and weight-adjusted predicted values. This represented asthma in the moderate range as PEFR is correlated with asthma severity (Appendix 12). In addition, the mean arterial oxygen saturation in room air on admission was reduced, at 93.3 ± 3.3% (normal 94-100%[100]). The patients had a mean heart rate of 129.9 ± 29.4 beats per minute, and all but three of the children had a heart rate higher than their age-adjusted expected value.[101, 102] Expected heart rates in children based on age and weight are shown in Table 17. The mean age-adjusted expected heart rate of the study sample was 92.6 ± 11.5 beats per minute. The children also had an elevated mean respiratory rate of 31.3 ± 7.3 breaths per minute, which is more than two standard deviations above the mean values for children who are five years of age and older.[103] In general, the normal respiratory rate in children is inversely related to age (see Figure 3).

Table 16 **Mean Values of Heart Rate and PEFR on Admission of the Overall Study Sample**[a]

	Males	Females	Total
Heart Rate (beats/min) mean ± SD (n)	130.0 ± 22.5 (33)	126.7 ± 42.9 (15)	129.9 ± 30.0 (48)
Respiratory Rate (breaths/min) mean ± SD (n)	30.8 ± 7.2 (34)	33.5 ± 7.5 (15)	31.6 ± 7.3 (49)
Room Air Oxygen Saturation On Admission (%) mean ± SD (n)	93.1 ± 3.3 (34)	93.9 ± 3.1 (15)	93.3 ±3.1 (49)
Peak Flow On Admission (L/min) mean ± SD (n)	200 ± 100.8 (18)	156.7 ± 32.8 (9)	185.6 ± 88.4 (27)
Peak Flow On Admission[b] (% predicted value) mean ± SD (n)	60.8 ± 24.6 (14)	60.0 ± 13.2 (3)	60.6 ± 22.6 (17)

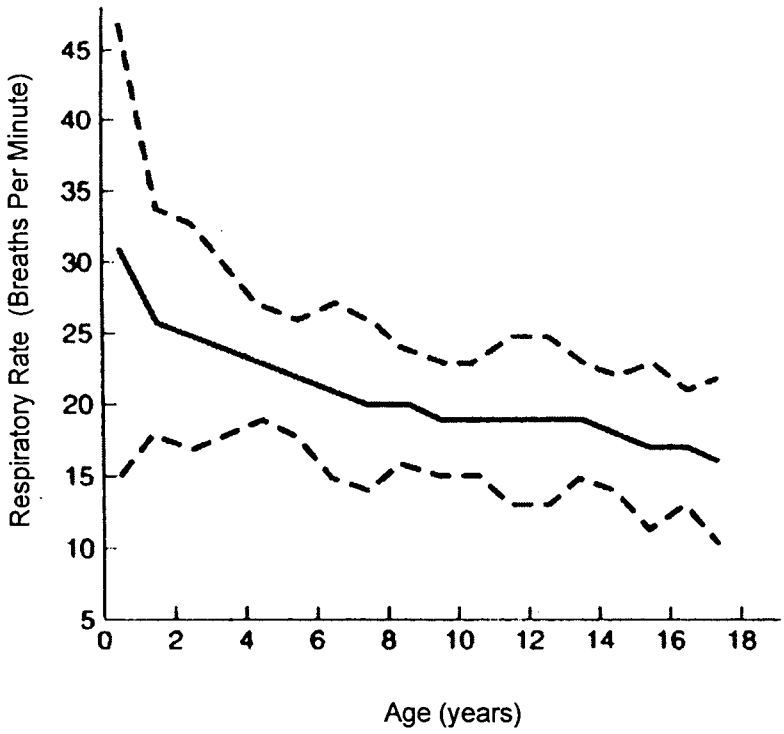
[a] Total sample included 42 males and 19 females. Only data recorded in patient charts were included.
[b] Some values were not available where height and weight data were not available.

Table 17 Expected Heart Rates For Infants and Children[104]

Age Range	Weight	Expected Heart Rate (beats per minute)
4 – 5 years	16 – 18 kg	100
6 – 8 years	20 – 26 kg	100
10 – 12 years	33 – 42 kg	75
> 14 years	> 50 kg	75

Figure 3 **Normal Respiratory Rates At Rest In Relation to Age[103]**

The solid line represents mean respiratory rate and the dashed line represents ± 2 standard deviations from the mean.



Appendix 13 describes each patient's clinical symptoms on admission. Appendix 8 shows details of each patient's chronic symptoms of asthma before hospital admission. As shown in the Appendices, most patients had chronic symptoms of asthma prior to hospital admission. Forty-four (82%) of the patients had a prior diagnosis of asthma and were known to have had asthma for 5.3 ± 3.4 years. Of the 14 children for whom data were available, the parents indicated that the children missed a mean of 11.5 ± 10.6 days of school due to asthma symptoms in the year prior to hospital admission. The mean duration of hospital stay was 2.6 days ± 1.3 days for both genders.

4.1.3 DRUG-RELATED HOSPITAL ADMISSION COHORT

In the first component of the study, 44 of the 54 patients in the study sample were able to be evaluated for drug-related hospital admissions by the expert panel. Four patients were not included in this component of the study because the children or parents did not provide enough data for evaluation by the panel. In these four cases, the hospital stay was too short for data to be collected. Six patients were excluded from the first component of the study because they were diagnosed with asthma for the first time and thus did not have a previous history of asthma.

The mean (±SD) age of the 44 patients in the study sample was 8.6 ± 3.1 years (median age, 8.1 years). Twenty-eight (64%) were males and 16 (36%) were females. Twelve (27%) were Caucasian; 15 (34%) were Chinese and the rest were other

minorities. The mean (±SD) height was 124.0 ± 23.2 cm (n = 34). The mean (±SD) percentile height was 46.1 ± 29.5 percentile (n = 29). The mean (±SD) weight was 30.3 ± 14.5 kg (n = 41). The mean (±SD) percentile weight was 46.3 ± 33.0 percentile (n = 31). The mean (±SD) heart rate was 129.2 ± 31.7 beats per minute (n = 40). The mean (±SD) respiratory rate was 30.9 ± 7.1 breaths per minute (n = 41). The mean (±SD) room air oxygen saturation on admission was 93.3 ± 3.0 % (n = 41). Furthermore, the mean (±SD) PEFR on admission was 169.0 ± 67.4 litres per minute (n = 24), which was estimated to represent 61.9 ± 16.2 % of predicted (n = 14).

4.1.4 PATIENTS DIAGNOSED WITH ASTHMA FOR THE FIRST TIME DURING THE HOSPITAL ADMISSION

Five of the six patients diagnosed with asthma or reactive airways disease for the first time during the hospital admission were males. The mean (±SD) age of these six patients was 6.7 ± 2.6 years. All six patients were from Vancouver and were admitted to MSJ. Two of the six patients had a family history of asthma, and two others had a previous history of eczema. Based on parents' reports, the children had a mean (±SD) of 1.7 ± 0.8 days of asthma-related symptoms prior to being admitted to hospital. The patients' mean (±SD) height was 118.9 ± 9.4 cm. Three of the six were above the 50th percentile in height. The patients' mean (±SD) weight was 23.8 ± 5.3 kg. Four of the six were above the 50th percentile in weight. The mean (±SD) body temperature on admission was 36.7 ± 0.6° C. The mean (± SD) respiratory rate was 35.0 ± 9.1 breaths per minute, the mean

(±SD) heart rate was 138.7 ± 7.7 beats per minute, and the mean (±SD) arterial oxygen saturation in room air was 92.7 ± 3.9%.

4.1.5 HEALTH-RELATED QUALITY OF LIFE ASSESSMENT COHORT

In the second component of the study, 36 patients completed one or more of the health-related quality of life questionnaires. Section 4.4 describes the study population of the second component of the study, and the results of the evaluation of the responsiveness of the PAQLQ, CAQ, and QOLiF to clinical change in this population.

4.2 THE CHRONIC AND ACUTE DRUG REGIMEN OF THE PATIENTS IN THE DRUG-RELATED HOSPITAL ADMISSION COHORT

The panel evaluated 44 of the 54 patients in the study sample for the relation between medication use and hospital admission. Appendix 14 shows a list of the medications that the patients in this study sample reported to be taking before hospital admission. The types of medications the patients reported in their regimen for the management of their chronic asthma before hospital admission are presented in Section 4.2.1. The types of medications the patients reported in their regimen for the acute exacerbations are presented in Section 4.2.2.

4.2.1 MEDICATIONS TAKEN FOR THE CHRONIC MANAGEMENT OF ASTHMA

Figure 4 shows a distribution of the number of prescription medications children reported to be in their regimen for the chronic management of their asthma. The number of chronic medications included both "regularly scheduled" medications and medications taken "as-needed" for symptoms. The median number of chronic medications was one. Twenty-one of 44 patients (48%) did not report having any chronic medications in their regimen prior to their hospital admission. The types of medications the patients reported in their regimen are shown in Figure 5.

Figure 6 shows a distribution of the number of regularly-scheduled medications that the children reported in their regimen for the chronic management of asthma. The parent or the child reported that six of these medications were not used or were

Figure 4 **Distribution of Prescription Medications Prescribed For the Chronic Management of Asthma As Reported By Patients or Parent(s) of Patients**

The number of prescribed medications represents the sum of the number of medications taken on a regular basis and as-needed for symptoms. Included in the figure are ten medications that were prescribed but were not taken or not taken as directed.

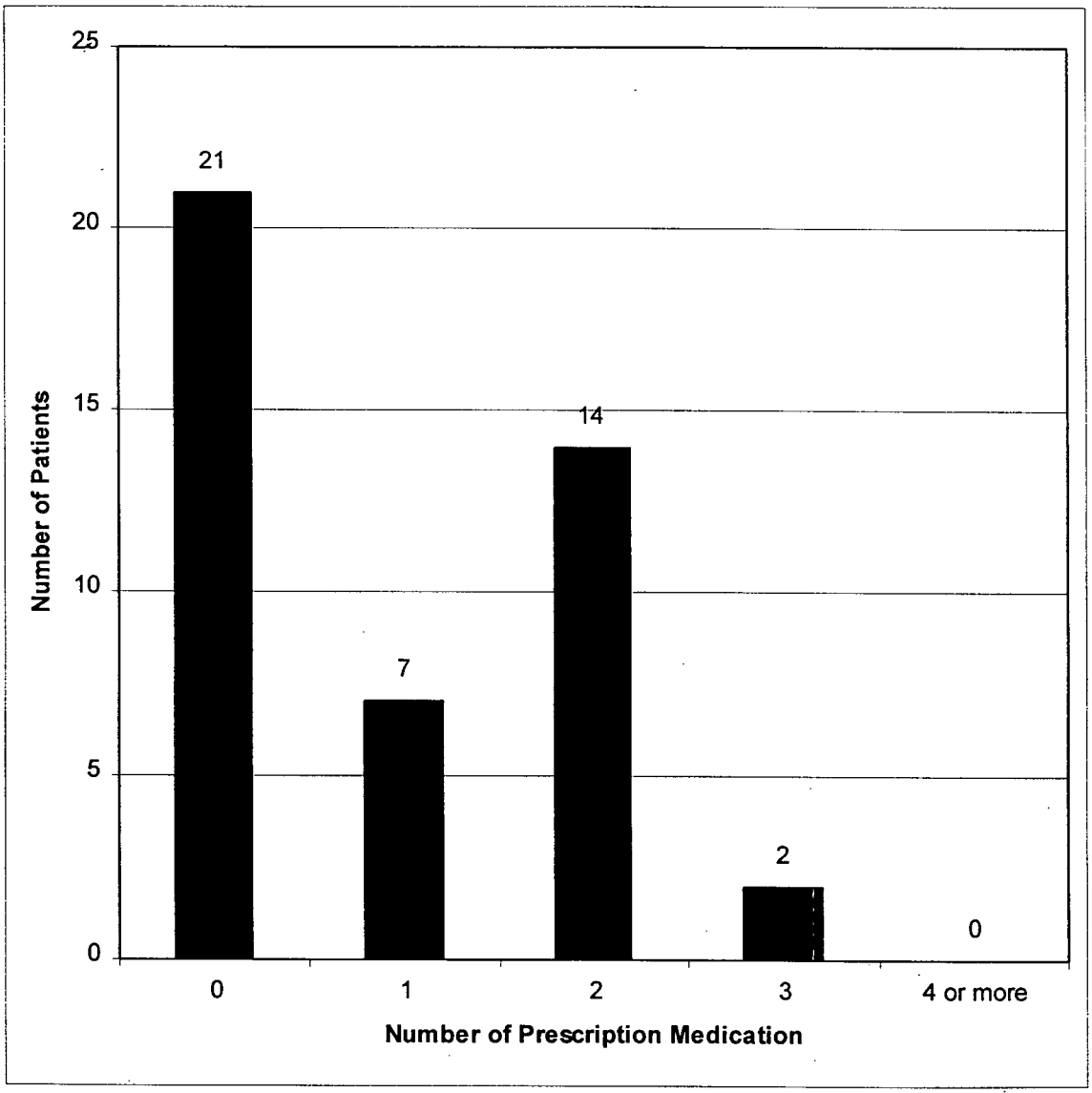


Figure 5 **Types of Medication Prescribed For the Chronic Management of Asthma As Reported By Patients or Parent(s) of the Patients**

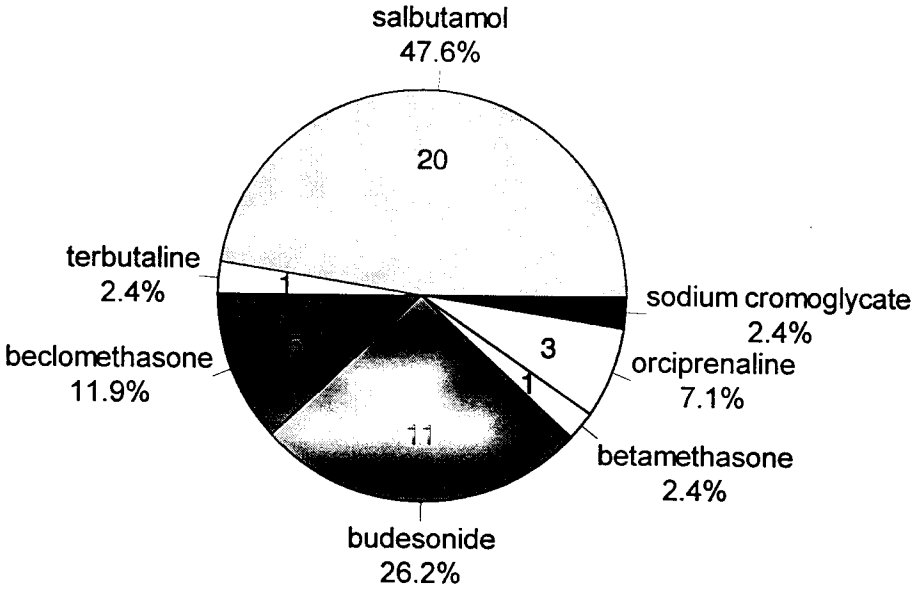
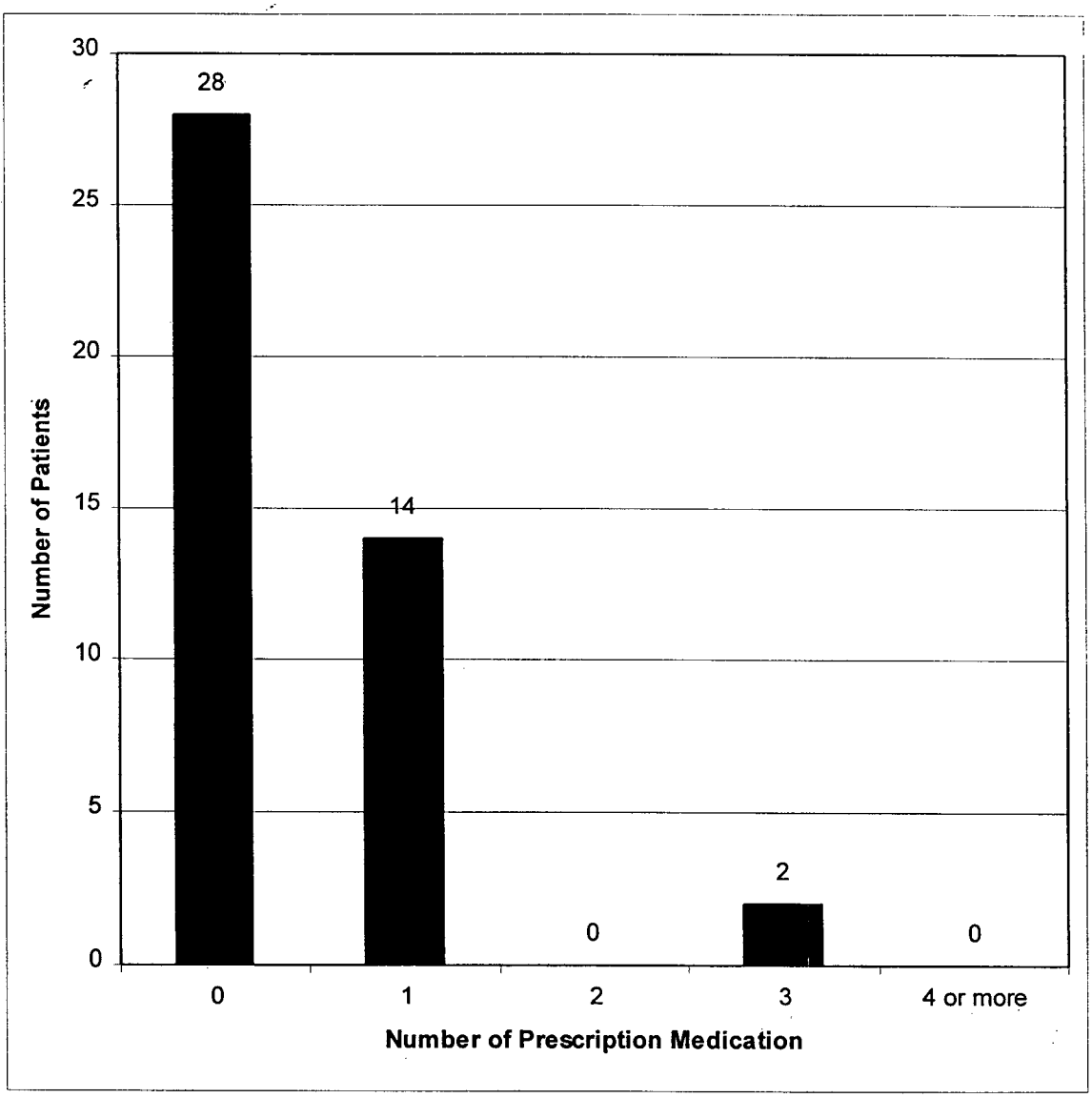


Figure 6 **Distribution of Regularly-Scheduled Medications Prescribed For the Chronic Management of Asthma as Reported by the Patient or the Parent(s) of the Patient.**

The number of prescribed medications represents the sum of the number of regularly scheduled medications. Included are six medications that were prescribed but were not taken or not taken as directed by the physician.



not taken according to the instructions of the prescribing physician. The median number of medications reported in their regimen was zero. Twenty-eight children did not report having any "regularly scheduled" medications. Fourteen of the 44 children reported taking one "regularly scheduled" medication for the chronic management of asthma. Two children reported that they took three "regularly scheduled" medications. Only six of the 44 children reported taking an inhaled corticosteroid on a regular basis for the chronic management of asthma, prior to hospital admission. Eight of the 14 children (57%) reported being prescribed an inhaled corticosteroid but did not take it regularly. The types of regularly scheduled medications that the patient reported in their regimen is shown in Figure 7.

The distribution of "as-needed" medications prescribed for the chronic management of asthma is shown in Figure 8. The parent or child study participants reported that four of these medications were not used. The median number of medications prescribed was zero. The types of "as-needed" medications prescribed for the chronic management of asthma is shown in Figure 9.

4.2.2 MEDICATION TAKEN FOR THE ACUTE EXACERBATION

Some of the children were administered drug therapy in addition to the medication that they were already taking for the management of their chronic asthma. The medication taken for the acute exacerbation included increased doses of their "regularly-

Figure 7 **Types of Regularly-Scheduled Medications Reported by the Patient or the Parent(s) of the Patient to be in the Patient's Regimen for the Chronic Management of Asthma**

The types of regularly-scheduled medications prescribed are shown below. Included in the figure are six medications that were not taken or not taken as directed by the physician.

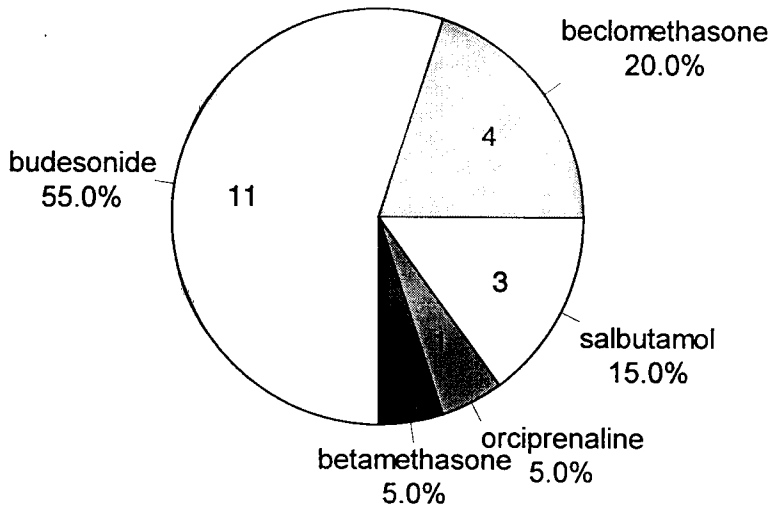


Figure 8 **Distribution of "As-needed" Medications Reported by the Patient or Parent(s) of the Patient to be in the Patient's Regimen for the Chronic Management of Asthma**

Included in the figure are four medications that were prescribed, but were not taken.

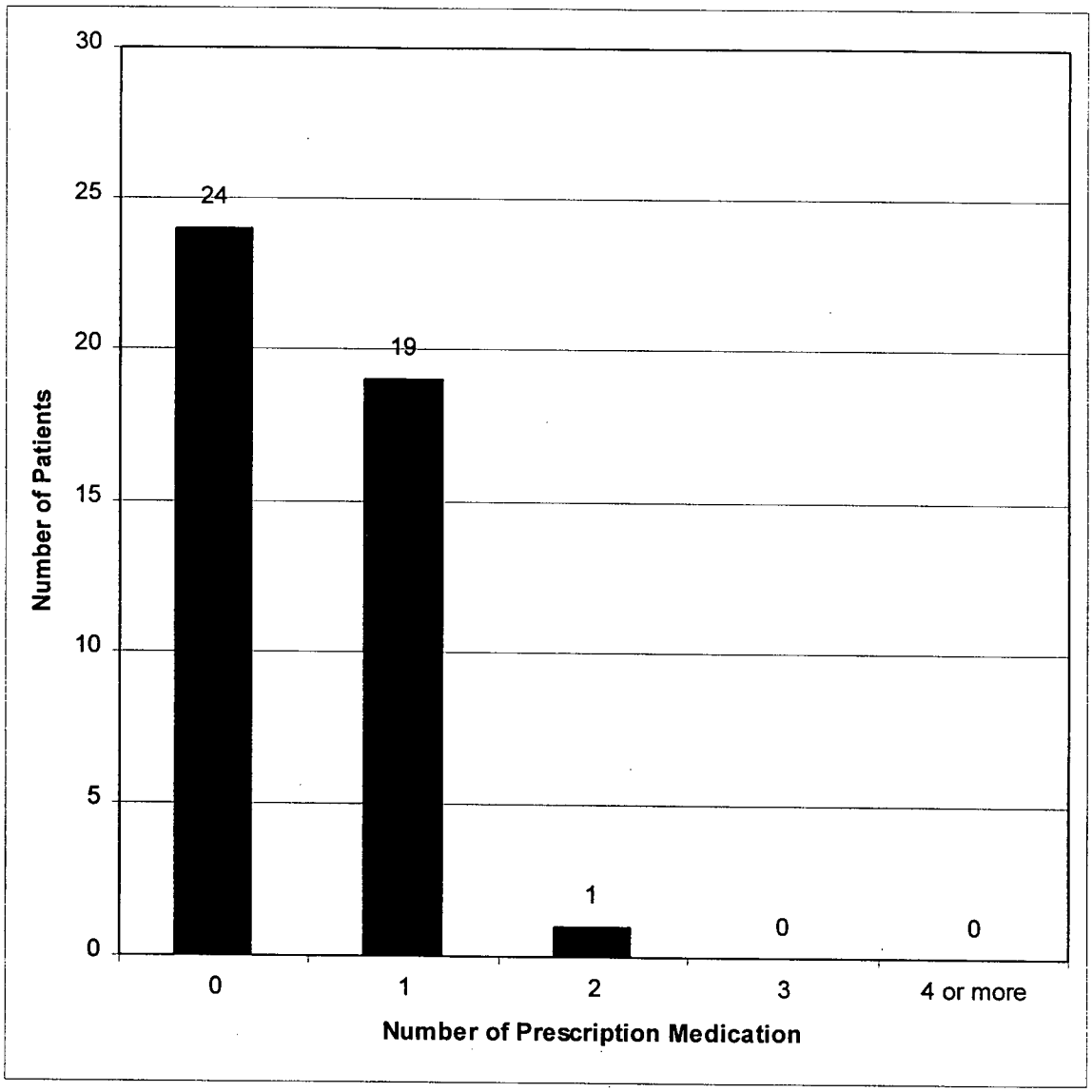
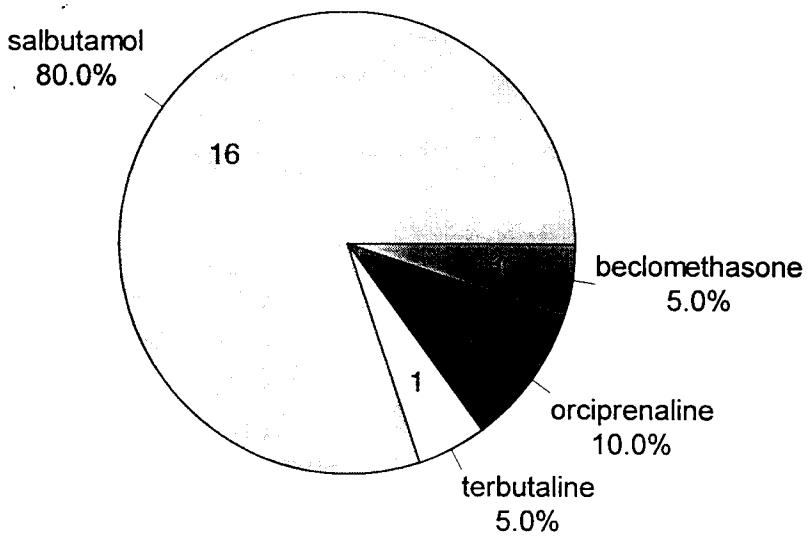


Figure 9 **Types of "As-needed" Medications Reported by the Patient or the Parent(s) of the Patient to be in the Patient's Regimen for the Chronic Management of Asthma**

Included in the figure are four medications reported in the patients' regimen but were not taken at all.



scheduled" chronic medications and different drugs taken specifically for the acute exacerbation. Thirty-one of the 44 patients (70%) reported that they increased the dose of their regularly scheduled chronic medications or reported that they took medications in addition to their "regularly-scheduled" chronic medications. In 14 of these 31 cases (45%), the children reported that they increased the dose of chronic medication and did not add additional drugs. The distribution of the number of medications that the children reported that they took for the acute exacerbation is presented in Figure 10. As shown, 13 patients (30%) did not report increasing the dose of their chronic medications or add additional therapy for their acute exacerbation. The types of medications that the children reported taking specifically for the acute exacerbation, other than what they were already taking for the chronic management of their asthma is shown in Figure 11.

4.3 EVALUATION OF DRUG-RELATED HOSPITAL ADMISSIONS

The results of the panel evaluations to determine the relation between drug intake and the presence of an adverse drug reaction or therapeutic failure, the significance of the symptoms for hospital admission, and the degree that each admission was deemed avoidable for each of the 44 cases is shown in Appendix 15. Appendix 16 shows a summary of the events leading up to each hospital admission for the 44 cases that were evaluated by the expert panel. The method that the panel used and the makeup of the panel have been described in Section 3.1.4.

Figure 10 **Distribution of Number of Medications that Patients Reported Taking for the Acute Episode**

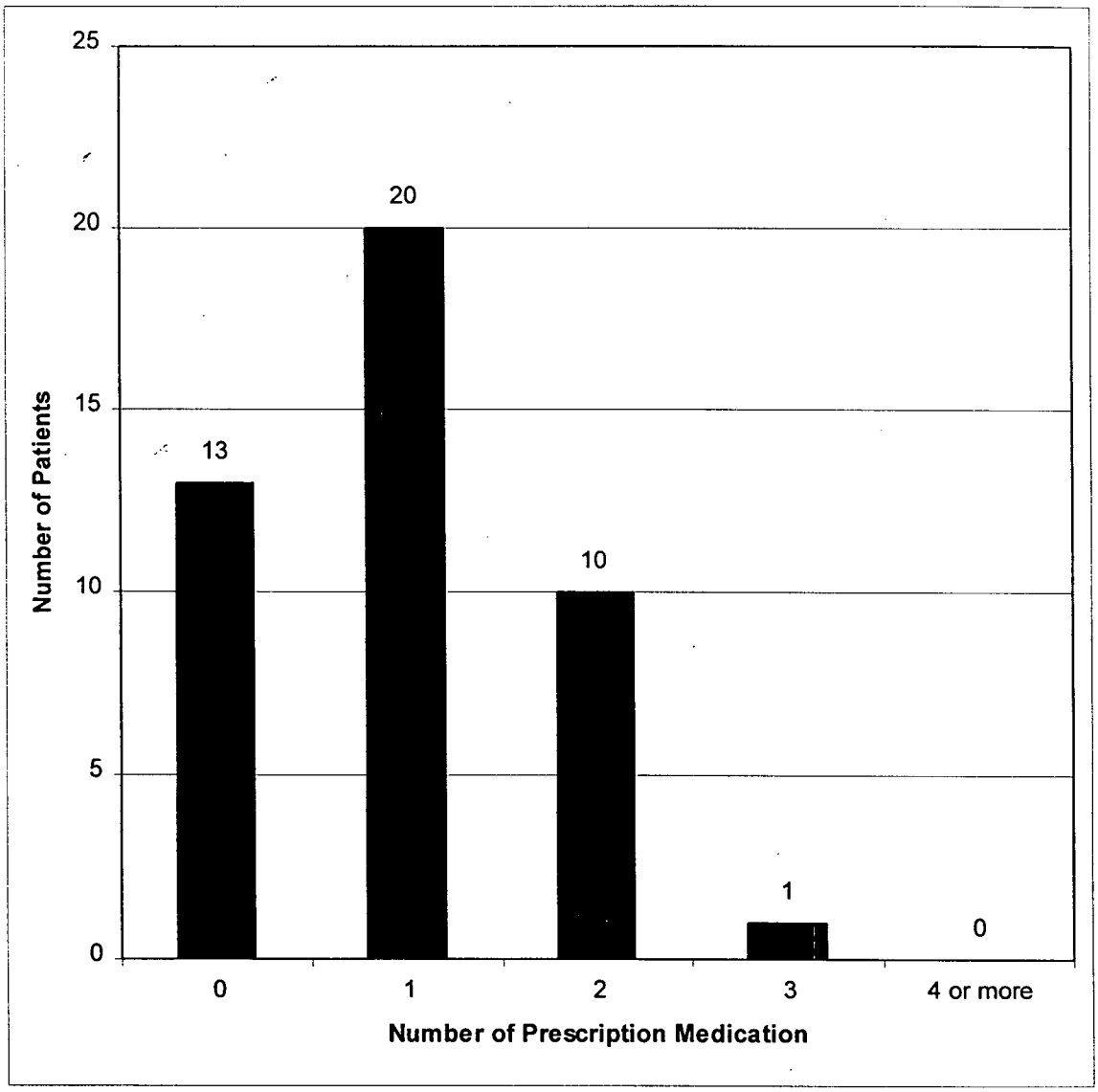
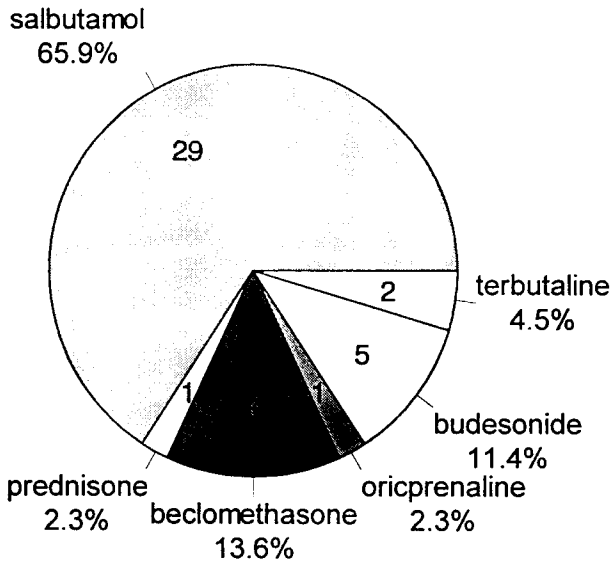


Figure 11 **Types of Medications that the Patients Reported Taking for the Acute Episode**



Of the 44 patient admissions that were evaluated, 37 (84%, 95% CI = 73-95%), were found to be "definitely" drug-related (Figure 12). All 37 cases of drug-related hospital admissions were considered to be therapeutic failures. No adverse drug reactions were found. Furthermore, the panel concluded that in all 37 cases, the symptoms of asthma were the "dominant" reason for admission, and that they were all "avoidable."

Seven of 44 admissions (16%, 95% CI = 5-27%) were deemed to be "possibly" drug-related by the panel. In six of the seven cases, the symptoms of asthma were judged by the panel to be the "dominant" reason for admission. In the remaining case, the symptoms were deemed to be "partly contributing" to the admission. In accordance with Hallas' algorithm, the panel did not evaluate the avoidability of hospital admission in the cases where the probability of adverse drug reaction or therapeutic failure were not deemed to be "definite."

4.3.1 EFFECTS OF SYMPTOMS OF URTI ON DRUG-RELATED ADMISSIONS

The panel reported that evidence that could have explained the symptoms was present in seven of the 44 cases of hospital admissions evaluated. These admissions were therefore rated as "possibly" drug-related. This designation was made because of the presence of a "condition" that could have explained the symptoms. Table 18 summarizes the symptoms found by the panel to be associated with the acute exacerbation. In one case, the child had a diagnosis of bronchitis along with a diagnosis of an acute asthma

Figure 12 Classification of DRHAs

Dark bars indicate the frequency of "definite," "probable," "possible," and "unlikely" therapeutic failures of the 44 cases that were evaluated by the expert panel. Light bars indicate the frequency of therapeutic failures by the investigator who considered 14 additional cases where there was evidence of a condition other than asthma that could have explained the patients' symptoms on admission.

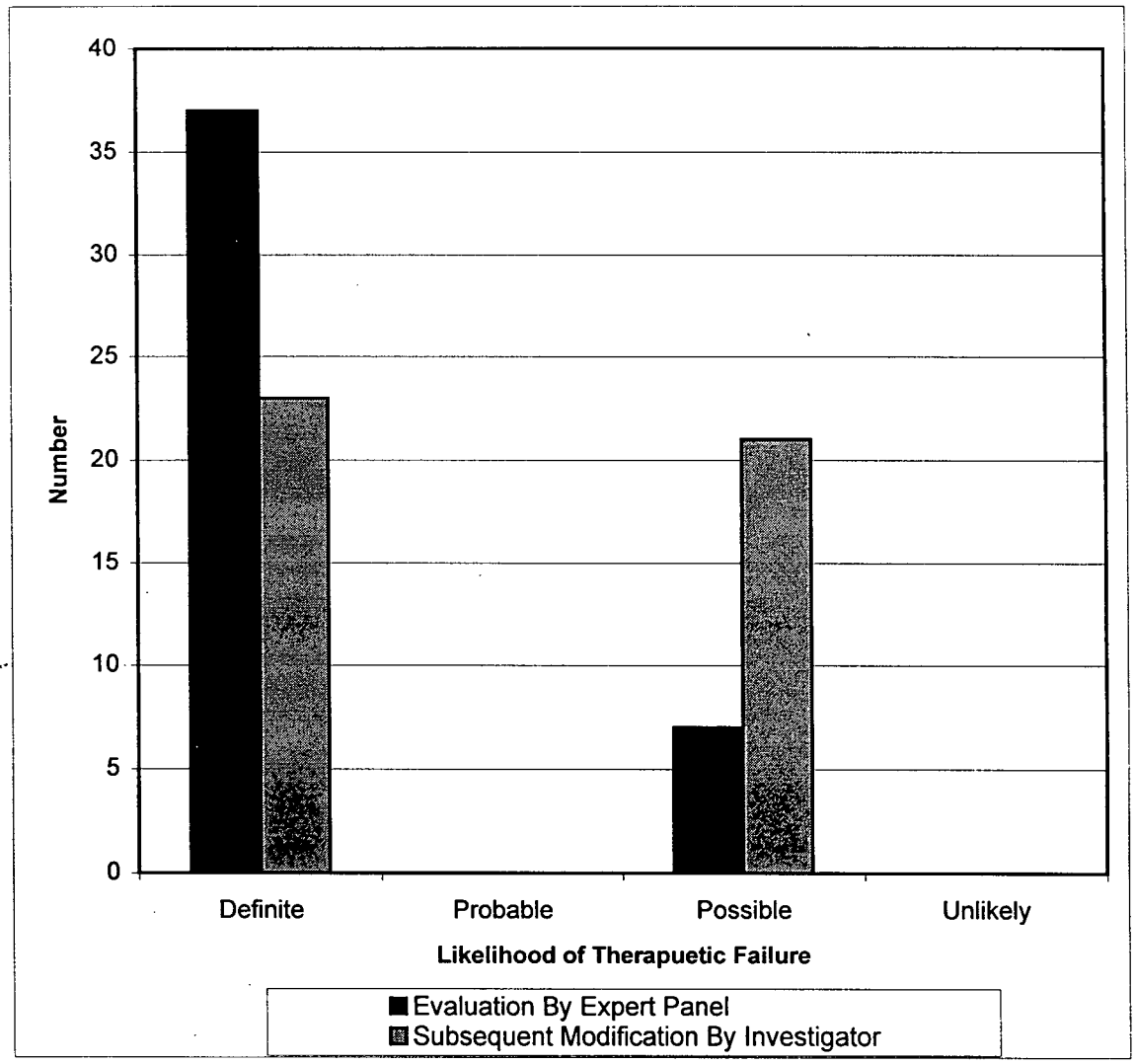


Table 18 **Evidence From Patients' Case Summaries of a Condition That Could Have Explained the Symptoms In the Seven Cases Deemed to Be "Possibly" Drug-related By the Panel**

Patient	Evidence From Each Patient's Case Summary of a Condition that Could Have Explained the Symptoms Related to the Patient's the Hospital Admission
42	Diagnosis of bronchitis
43	A fever of 39°C.
44	Since two weeks he has had sore throat- given amoxicillin but progressed to cough, wheeze and dyspnea. Chest X-ray revealed actelectasis in left lower lobe, suspected atypical pneumonia
45	Right medial lobe pneumonia; treated with intravenous cefuroxime
46	Admitted for fever and cough. Right upper lobe pneumonia, infectious contact with 2.5 years old sister
47	24 hours prior to admission he developed an apparent cold, low grade fever, discharge from nose.
48	Runny nose and cough for three days.

exacerbation noted in the medical chart. In another case, the child had a fever of 39°C and no other symptoms. In three cases, patients had or were suspected of having pneumonia. In two other cases, patients had symptoms of an upper respiratory tract infection prior to admission. In these cases, despite other evidence of drug-related factors leading to admission, criterion 5 of Hallas' algorithm was not satisfied, and in all seven cases, the panel concluded that the relation between drug intake and therapeutic failure was only "possible."

On examination of patients' case summaries after the panel had evaluated the admissions, the investigator found that there was evidence of a condition that could have explained the symptoms in 14 additional cases. The evidence in each of the 14 cases is summarized in Table 19. In two cases, patients had reported experiencing fever prior to admission. In another case, the physician suspected pneumonia and the patient had symptoms of an upper respiratory tract infection. In the remaining cases, the physician or parents noted symptoms consistent with upper respiratory tract infection experienced by the children during the week prior to admission.

Had the panel determined that the symptoms of infection reported for the children provided sufficient evidence for a condition that could have explained the symptoms on admission, then the overall evaluation for drug-related hospital admissions using Hallas' algorithm would have changed accordingly. Figure 12 shows the frequency of drug-

Table 19 **Fourteen Additional Cases of Patients With Evidence of a Respiratory Tract Infection Identified by the Investigator.**

The investigator determined that the following 14 patients had evidence of a respiratory tract infection before their hospital admission. These patients had been deemed to have a definite relation between drug intake and therapeutic failure by the panel. The evidence shown for each case was taken from each patient's hospital record.

Patient	Evidence From Each Patient's Case Summary of A Condition That Could Have Explained the Symptoms of the Hospital Admission
1	Suspected pneumonia. Twenty-four hour cough and fever, runny nose. Fever "98.1 F," [sic] given ibuprofen, and improved.
5	Two day history of runny nose and sore throat.
8	Asthma symptoms started with flu symptoms, coughing.
13	Three day history of URTI
16	Cough and runny nose.
17	Runny nose
19	Sore throat, runny nose
23	Cold started five days ago.
24	Had fever two to three days ago.
32	Fever
33	Two day history of URTI (known trigger)
34	Parents don't [sic] think that she had a cold or the flu, which started two weeks prior to hospital admission.
40	For past three days has had symptoms of cold: slight fever, cough, no runny nose.
41	Sore throat, some runny nose, cough

related hospital admissions; 23 of the 44 cases (52%, 95% CI = 36 - 67%) would have been considered "definite" and 21 of the 44 cases (48%, 95 % CI = 33 - 62%) would have been considered "possible" therapeutic failures.

4.3.2 PATIENTS' DRUG THERAPY IN RELATION TO THE RECOMMENDATIONS OF THE NIHLBI GUIDELINES

The investigator estimated that 16 of the 44 patients (36%) had "mild-intermittent" asthma, 15 of 44 patients (34%) had "mild-persistent" asthma, and seven of 44 patients (16%) had "moderate persistent" asthma on a chronic basis prior to their acute episode. Six cases (14%) were classified as "non-determinable" (see Appendix 17).

4.3.2.1 MANAGEMENT OF CHRONIC ASTHMA

A patient was considered to have had "inadequate treatment" of chronic asthma if drug therapy indicated by the guidelines for the chronic treatment of asthma was not reported in the patient's drug regimen in the last three months; or if the patient, parent, or physician reported that the indicated medication was in the regimen but that the patient was non-compliant in using it. Based on each patient's estimated level of severity and the NIHLBI guidelines, evidence of inadequate treatment of chronic asthma was found in 19 of the 44 cases (43%). Non-compliance was identified in 13 of the 19 cases (68%) of inadequate treatment of chronic asthma. Nine of 23 patients (39%) who were prescribed regularly scheduled medications were reported to be not compliant with therapy.

In most cases, patients had been prescribed inhaled corticosteroids but were not using them. Only 14 of 44 patients (32%) reported taking medications as directed on a regular basis for their chronic asthma.

None of the 16 patients with "mild intermittent" asthma, had "inadequate treatment," and none of the 16 were reported to be non-compliant. Thirteen of the 16 patients (82%) who had "mild persistent" asthma did not receive daily anti-inflammatory medication as indicated by the guidelines, and thus had "inadequate treatment," as shown in Table 20. Five of the 13 patients did not report having a regularly scheduled anti-inflammatory medication in the regimen. Eight of the 13 patients reported a regularly scheduled anti-inflammatory medication in the regimen but were not compliant in using it. Among the seven patients with moderate persistent asthma (Table 21), six had "inadequate treatment" due to non-compliance and one patient (#38) was "non-compliant" with his long-term control medication and also did not receive influenza vaccination as indicated by the guidelines. None of the five patients in whom severity was "non-determinable," had "inadequate treatment" or "non-compliance."

4.3.2.2 MANAGEMENT OF ACUTE EPISODE

A patient was also considered to have had "inadequate treatment" if drug therapy indicated by the guidelines for treatment of the *acute episode* was not reported in the patient's drug regimen; or if the patient, parent, or physician reported that the

Table 20 Presence of Inadequate Chronic Treatment of Patients with "Mild-Persistent" Asthma

Patient	Inadequate Treatment According to the Guidelines	Description of Inadequate Chronic Treatment[a]
1	YES	Daily anti-inflammatory indicated but the patient was non-compliant in using it. Budesonide DPI was prescribed one year ago on twice daily dosing, but the patient misses the occasional dose. Furthermore, the patient forgets to take medication sometimes and does not always take the medication at the same time each day. When the patient feels better, the patient sometimes stops taking medication on his own.
4	YES	Daily anti-inflammatory medication indicated but not reported to be in the regimen. The patient did not receive daily anti-inflammatory medication. The patient was also non-compliant with terbutaline sulphate MDI. The patient had been prescribed terbutaline sulphate MDI one year ago. This was the only medication he had been prescribed and no other medications were reported in the regimen. However, previous to this acute episode, the patient had not used the terbutaline sulphate MDI.
6	YES	Daily anti-inflammatory medication indicated but the patient was non-compliant with prescribed daily anti-inflammatory due to poor inhaler technique.
12	YES	Daily anti-inflammatory medication indicated but the patient did not take prescribed budesonide DPI because it was not available.
13	ND	ND
19	YES	Daily anti-inflammatory medication indicated but not reported to be in the regimen. The patient did not receive daily anti-inflammatory medication.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.
[a] Descriptions of patients' drug therapies were recorded from patients' medical charts or reported by the patient, parent, or health personnel.

Table 20 (cont...) Presence of Inadequate Chronic Treatment of Patients with "Mild-Persistent" Asthma[a]

Patient	Inadequate Treatment According to the Guidelines	Description of Inadequate Chronic Treatment[a]
22	YES	The patient was in the process of weaning off the inhaled corticosteroid during the URTI.
23	ND	ND
25	YES	Daily anti-inflammatory medication indicated but not reported to be in the regimen. The patient did not receive daily anti-inflammatory medication.
29	ND	ND
31	YES	Daily anti-inflammatory medication indicated but not reported to be in the regimen. The patient did not receive daily anti-inflammatory medication. The patient was non-compliant. Patient's reported use of medication was not consistent. Parents did not appear to be very involved in the patient's management of asthma.
40	YES	Daily anti-inflammatory medication indicated but it was noted in the medical record that the patient had poor inhalation technique. The patient did not receive the daily anti-inflammatory medication as directed because of the poor inhalation technique.
41	YES	Daily anti-inflammatory medication indicated but not reported to be in the regimen. The patient did not receive daily anti-inflammatory medication.
42	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the prescribed daily anti-inflammatory medication because the patient was non-compliant. The prescribed anti-inflammatory medication was not used.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.
[a] Descriptions of patients' drug therapies were recorded from patients' medical charts or reported by the patient, parent, or health personnel.

Table 20 (cont...) Presence of Inadequate Chronic Drug Treatment of Patients with "Mild-Persistent" Asthma[a]

Patient	Inadequate Treatment According to the Guidelines	Description of Inadequate Chronic Treatment[a]
45	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the prescribed daily anti-inflammatory medication because the patient was non-compliant. The prescribed anti-inflammatory medication was not used. The patient was also non-compliant with salbutamol MDI.
48	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the prescribed daily anti-inflammatory medication because the patient was non-compliant. The prescribed anti-inflammatory medication was not used. The parent is not compliant with medication because the parent is afraid of the adverse effects.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.
[a] Descriptions of patients' drug therapies were recorded from patients' medical charts or reported by the patient, parent, or health personnel.

Table 21 **Presence of Inadequate Chronic Treatment with Chronic Drug Therapy in Patients with "Moderate-Persistent" Asthma**

Patient	Inadequate Treatment According to the Guidelines	Description of Inadequate Chronic Treatment[a]
5	YES	Daily anti-inflammatory medication indicated but the patient did not receive the medication as directed because the patient was non-compliant. The budesonide MDI was prescribed twice daily. However, the patient only took the medication twice weekly, despite requiring the salbutamol MDI, the beta-agonist rescue medication, three to four times daily.
10	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the medication as directed because the patient was non-compliant. Influenza vaccination indicated but not reported to be in the regimen. The patient did not receive influenza vaccination.
16	YES	Daily anti-inflammatory medication indicated but the patient did not receive the medication as directed because the patient was non-compliant. The budesonide DPI was rarely used.
24	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the medication as directed because the patient was non-compliant. The patient was non-compliant with nedocromil sodium MDI. The patient has stopped using the nedocromil sodium MDI.
32	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the medication as directed because the patient could not afford to purchase the medication.
36	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the medication as directed because the patient was non-compliant.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.
[a] Descriptions of patients' drug therapies were recorded from patients' medical charts or reported by the patient, parent, or health personnel.

Table 21 (cont...) Presence of Inadequate Chronic Treatment of Patients with "Moderate-Persistent" Asthma

Patient	Inadequate Treatment According to the Guidelines	Description of Inadequate Chronic Treatment
38	YES	Daily anti-inflammatory medication indicated but the patient did not receive any doses of the medication as directed because the parent was non-compliant. The parent sometimes forgets to administer the medication. Influenza vaccination indicated but not reported to be in the regimen. The patient did not receive influenza vaccination.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.
[a] Descriptions of patients' drug therapies were recorded from patients' medical charts or reported by the patient, parent, or health personnel.

indicated medication was in the regimen but that the patient was non-compliant in using it. Evidence of inadequate treatment of the acute asthma episode was present in 39 of the 44 cases (95%), which are summarized in Table 22 to Table 25. In four cases, the presence of inadequate treatment was considered non-determinable and in one case, the patient was treated properly. Each patient's acute symptoms on hospital admission are shown in Appendix 13. The actions taken by each patient, the parent, or the guardian of each patient at the first sign of symptoms related to the hospital admission are shown in Appendix 16. Appendix 18 shows which patients did not take inhaled or oral steroids for the acute exacerbation. In six of the 39 cases (14%) of "inadequate treatment", there was evidence of non-compliance with medications for the management of the acute episode. In 37 of the 39 cases, there was evidence of inadequate treatment based on the patients' histories of symptoms and severity of exacerbations.

Overall, 29 of the 44 patients (66%) that were examined had a history of severe exacerbations. Twenty-six of the 44 patients had one or more previous hospital admissions. Furthermore, 14 of the 44 patients reported that they had on average 2.4 previous hospital admissions for asthma. In 10 of the 44 cases (23%), patients failed to start any drug treatment for management of his or her acute exacerbation. In 25 of the 44 cases (57%), patients required oral corticosteroids for the acute exacerbation but did not report the medication in the regimen. Patients reported taking oral corticosteroids in only three of the 25 cases, despite having symptoms severe enough to require hospital admission.

Table 22 Presence of Inadequate Acute Treatment of Patients with "Mild-Intermittent" Asthma

Patient	Inadequate Treatment	Description of Inadequate Acute Treatment
3	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not receive any doses at all. The patient did not receive β_2-agonist because the patient did not know how to use it. The patient has had difficulty using the salbutamol MDI so the patient did not use it at all. No medication were administered for the acute exacerbation.
7	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
8	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
11	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
15	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
17	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
21	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
27	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
30	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.

Table 22 (cont...) Presence of Inadequate Acute Treatment of Patients with "Mild-Intermittent" Asthma

33	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
34	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not receive any doses at all. All medications taken were expired.
35	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
39	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
44	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
46	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.

Table 23 **Presence of Inadequate Acute Treatment of Patients with "Mild-Persistent" Chronic Severity**

Patient	Inadequate Treatment	Description of Inadequate Acute Treatment
1	YES	Doubling the dose on inhaled corticosteroid indicated but not reported in the regimen. The patient did not receive an increased dose of inhaled steroids for seven to ten days after initial β_2-agonist treatment.
4	YES	Oral corticosteroids indicated for the severe exacerbation but the patient did not report having oral corticosteroids in the regimen. Asthma symptoms started seven days before hospital admission and the patient had an incomplete response to β_2-agonist. Therefore, oral corticosteroids were indicated.
6	ND	ND
12	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
13	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
19	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
22	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
23	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
25	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for one day prior to hospital admission.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or the patient, parent, or physician reported noncompliance.

Table 23 (cont...) Presence of Inadequate Acute Treatment of Patients with "Mild-Persistent" Chronic Severity

Patient	Inadequate Treatment	Description of Inadequate Acute Treatment
29	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
31	ND	Patient's reported use of medication is not consistent. Parents do not appear to be very involved in management of the patient's asthma. Failed to take medication as prescribed.
40	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
41	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
42	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
45	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
48	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.

Table 24 **Presence of Inadequate Acute Treatment of Patients with "Moderate-Persistent" Chronic Severity**

Patient	Inadequate Treatment	Description of Inadequate Acute Treatment
5	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
10	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
16	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.
24	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for three days prior to hospital admission.
32	ND	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen. Child reports that the parents couldn't afford to purchase the corticosteroid medications. That is why they only had the salbutamol MDI at home.
36	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for three days prior to hospital admission.
38	NO	NO

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.

Table 25 **Presence of Inadequate Acute Treatment of Patients with "Non-Determinable" Chronic Severity**

Patient	Inadequate Treatment	Description of Inadequate Acute Treatment
18	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen.
26	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
28	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not receive oral corticosteroids in time.
37	YES	Inhaled short-acting β_2-agonist indicated for initial treatment but the patient did not report having β_2-agonist in the regimen. The patient did not receive any treatment for two days prior to hospital admission.
43	ND	ND
47	YES	Oral corticosteroids indicated for the severe exacerbation, but the patient did not report having oral corticosteroids in the regimen.

ND = Non-determinable; insufficient data to determine.
Inadequate Treatment = The patient, patient of the patient did not report a dose indicated by the Guidelines in the regimen; or patient, parent, or physician reported noncompliance.

4.4 HEALTH-RELATED QUALITY OF LIFE

The following sections describe results of the HRQOL scores for the CAQ, PAQLQ, and QOLiF administered to patients and their parents during the hospital stay (Section 4.4.2) and six weeks after discharge from hospital (Section 4.4.3).

4.4.1 DESCRIPTION OF THE STUDY SAMPLE

The patients who participated in this component of the study were recruited from the sample of 61 children admitted to hospital for asthma or asthma-related symptoms as described in Section 3.1.1. In total, 35 of the 61 potential subjects participated in this component of the study. Others were not available during the admission, did not have time during the admission to respond to the questionnaires, or did not complete the questionnaires. Of the 35 patients who responded completely to one of the three HRQOL instruments, 23 (66%) were male and 12 (34%) were female. Their mean age was 8.9 ± 3.3 years (median age, 8.6 years).

The clinical status of this sub-group on admission was similar to the sample of patients who participated in the DRHA component of the study, as described in Section 4.1.2. The mean (± SD) body temperature of these patients on admission was 36.8 ± 0.7 ° C. The mean respiratory rate was 32 ± 6 breaths per minute, the mean (± SD) heart rate was 127 ± 32 beats per minute, and the mean (± SD) oxygen saturation was 93.1 ±

3.2%. The first mean (± SD) PEFR, which was measured at hospital admission, was 64.8 ± 26.6% of the age and weight-adjusted predicted values. The second mean (± SD) PEFR, which was measured at hospital discharge or after being discharged, was 79.2 ± 36.4% of the age and weight-adjusted predicted values.

4.4.2 HRQOL SCORES MEASURED DURING THE HOSPITAL STAY

The CAQ, the PAQLQ and the QOLiF were administered to this study sample in accordance with the age criteria described in Table 2 of Section 3.2.3.

4.4.2.1 CAQ

Fifteen of 28 patients (54%) eligible by age were administered the CAQ-A. The domain scores for each of the 15 children administered the CAQ-A is shown in Table 26. The mean (± SD) score for the CAQ-A "Quality of Living" domain was 31.1 ± 2.7 and the mean (± SD) score for the CAQ-A "Distress" domain was 11.3 ± 2.64. The "Quality of Living" domain has a range of 10 (low Quality of Living, very unhappy about all activities) to 40 (high Quality of Living, very happy about all activities). The "Distress" domain has a range of 4 (low distress) to 15 (high distress).

Fourteen of 18 patients (78%) eligible by age were administered the CAQ-B. The individual domain scores, mean scores, and summary statistics for each of the 14 children

Table 26 CAQ-A Scores Measured During The Hospital Stay

Patient	Quality of Living	Distress
3	32.7	12
13	28	12
21	25.8	12
23	36	14
26	31.5	12
29	32.6	13
35	32	14.5
38	28	11
39	32.7	7
40	30	10
48	34	6
52	28.8	10
53	33	8
54	31	14.7
56	30	13
Mean ± SD	31.1 ± 2.7	11.3 ± 2.6
Range of Scores	25.8 – 36.0	6.0 – 14.7
Possible Range	10 - 40	4 - 15

administered the CAQ-B are shown in Table 27. The mean scores for the "Active Quality of Living," and "Passive Quality of Living" domains were 28.3 and 17.4 respectively. The scores on the quality of living items increase with more enjoyment of the activities. The range for the "Active Quality of Living" domain, which measures physically active pastimes, is 7 (low Active Quality of Living) to 35 (high Active Quality of Living). The range for the "Passive Quality of Living" domain, which measures sedentary pastimes, is 4 (low Passive Quality of Living) to 20 (high Passive Quality of Living). The mean scores for the "Distress," and "Severity" domains were 15.9, and 15.1 respectively. The range for the "Distress" domain, which measures unhappiness about having asthma is 6 (low distress) to 30 (high distress). The range for the "Severity" domain, which measures severity of symptoms, is 6 (low) to 23 (high).

Four of eight patients (50%) eligible by age were administered the CAQ-C. Each patient's domain scores, mean scores and summary statistics are shown in Table 28. The mean scores for the "Active Quality of Living" and "Teenage Quality of Living" domains were 20 and 11 respectively. Similar to the CAQ-B, the scores of the quality of living items are greater with more enjoyment of activities. The range for the "Active Quality of Living" domain is 8 (low AQOL) to 36 (high AQOL). The range for the "Teenage Quality of Living" domain, which measures the extent to which young people are engaged in social activities associated with the teenage years, is 5 (low sociability) to 23 (high sociability).

Table 27 CAQ-B Scores Measured During The Hospital Stay

Patient	Domain			
	Active Quality of Living	Passive Quality of Living	Distress	Severity
1	24.5	15	14	21
4	34	19	19	14
12	30	17	7	15
16	29	20	14	13
17	26	20	21	13
25	23	17	14	15
32	30	18	11	13
33	35	20	23.3	13
34	31	19	20	17
45	31	13	15	12
47	26.8	14	13	17
55	30.3	17	22.8	10
61	26	15	13	22
63	19.8	19	15	16
Mean ± SD	28.3 ± 4.2	17.36 ± 2.3	15.86 ± 4.7	15.07 ± 3.3
Range of Scores	19.8 – 35.0	13.0 – 20.0	7.0 – 23.3	10.0 – 22.0
Possible Range	7 - 35	4 - 20	6 - 30	6 - 23

Table 28 CAQ-C Scores Measured During The Hospital Stay

Patient	Domain				
	Distress	Severity	Reactivity	Active Quality of Living	Teenage Quality of Living
8	55	22	18	19	10
19	50	19	10	21	12
24	44.7	23	12	21	14
60	50	19	14	19	10
Mean ± SD	49.9 ± 4.2	20.8 ± 2.1	13.5 ± 3.4	20 ± 1.2	11.5 ± 1.9
Range of Scores	44.7 – 55	19 – 23	10 – 18	19 – 21	10 – 14
Possible Range				8 - 36	5 - 23

4.4.2.2 PAQLQ

Twenty of 29 patients (69%) eligible by age were administered the PAQLQ. The mean age of the children was 10.8 ± 3.0 years. The scores for each domain for each patient are shown in Table 29 and the overall mean PAQLQ score was 4.0 ± 1.3. The range of scores of each domain of the PAQLQ is one (maximum degree of asthma-related symptoms and maximum limitation of activities and emotional function) to seven (no degree of asthma-related symptoms and no limitation of activities and emotional function). Since the overall score is the mean score of each domain score, the overall HRQOL score is one (poor HRQOL score; maximum degree of asthma-related symptoms and maximum limitation of activities and emotional function) to seven (high HRQOL score; no degree of asthma-related symptoms and no limitation of activities and emotional function). Nine of 29 parents of patients (31%) eligible by age were administered the PACQLQ. The mean score was 5.0 ± 1.4, as shown in Table 30.

4.4.2.3 QOLiF

Nineteen of 54 age-eligible patients and 19 parents/caregivers of children were administered the QOLiF during the hospital stay. The mean (± SD) age of the children was 9.1 ± 3.3 years. The mean scores and standard deviations of the parents' and children's scores for each of the domains of the QOLiF are shown in Table 31 and Table 32. The physical domain scores were calculated using the mean of the patients' top three

Table 29 PAQLQ Scores Measured During the Hospital Stay

Patient	Domain			
	Activity Limitations	Symptoms	Emotional Function	Overall
1	4.4	5.4	4.5	4.8
4	4.2	3.9	3.8	4.0
5	2.1	2.5	2.7	2.4
8	3.7	3.9	2.6	3.4
17	3.7	6.1	3.7	4.5
19	2.9	3.0	3.5	3.2
24	4.2	3.3	3.2	3.6
25	2.8	3.4	2.5	2.9
26	4.1	6.8	5.4	5.4
29	1.4	2.4	1.5	1.8
32	2.9	2.7	3.3	3.0
33	6.4	6.8	6.0	6.4
34	4.6	4.2	4.1	4.3
45	4.6	5.5	5.0	5.0
47	3.0	3.0	2.9	3.0
52	7.0	7.0	6.7	6.9
55	3.6	5.6	5.2	4.8
60	3.7	3.6	2.3	3.2
61	4.5	4.7	2.6	4.0
63	4.0	4.7	3.6	4.1
Mean ± SD	3.9 ± 1.3	4.4 ± 1.5	3.8 ± 1.4	4.0 ± 1.3
Range of Scores	1.4 - 7.0	2.4 – 7.0	1.5 – 6.7	1.8 – 6.9
Possible Range	1 – 7	1 – 7	1 – 7	1 - 7

Table 30 Parents' PACQLQ Scores Measured During the Hospital Stay

Patient	Score
1	5.2
5	5.4
8	4.8
12	2.8
25	6.0
26	7.0
34	3.4
47	4.1
55	6.5
Mean ± SD	5.0 ± 1.4
Range of Scores	2.8 – 7.0
Possible Range	1 - 7

Table 31 Parents' QOLiF Scores Administered During the Hospital Stay

Patient ID	Domain			
	Physical	Social	Role	Overall
1	7.0	6.8	6.8	6.9
8	4.3	6.0	5.2	5.2
12	4.3	3.6	5.5	4.5
17	7.0	6.6	5.7	6.4
25	6.7	6.0	6.3	6.3
33	6.3	6.7	6.5	6.5
34	6.0	4.3	4.0	4.8
38	5.3	3.5	3.0	3.9
40	NA	5.8	2.3	NA
45	6.3	6.3	6.6	6.4
46	3.3	3.5	2.0	2.9
47	NA	1.3	1.0	NA
48	4.3	6.6	5.7	5.5
52	7.0	7.0	7.0	7.0
53	3.7	4.2	1.0	3.0
55	6.0	7.0	7.0	6.7
60	2.5	4.3	5.0	3.9
61	5.5	6.4	5.0	5.6
63	3.6	3.0	1.3	2.6
Mean ± SD	5.2 ± 1.5	5.2 ± 1.7	4.6 ± 2.2	5.2 ± 1.5
Range of Scores	2.5 – 7.0	1.3 – 7.0	1.0 – 7.0	2.9 – 7.0
Possible Range	1 – 7	1 –7	1 – 7	1 - 7

NA = Data not available. Patient 40 did not indicate which three physical activities were most important. Patient 47 did not complete the QOLiF, although it was completed by the parent/caregiver.

Table 32 Children's QOLiF Scores Measured During the Hospital Stay

Patient ID	Domain			
	Physical	Social	Role	Overall
1	5.0	4.0	2.0	3.7
5	3.0	1.3	1.8	2.0
8	5.7	5.0	5.8	5.5
17	7.0	7.0	7.0	7.0
24	4.7	6.5	6.0	5.7
25	2.7	1.5	2.3	2.2
26	6.3	3.3	1.0	3.5
29	4.7	6.0	2.0	4.2
33	6.7	7.0	7.0	6.9
34	6.0	6.3	6.1	6.1
38	5.0	5.5	6.5	5.7
40	NA	1.7	1.7	NA
46	4.0	2.8	3.0	3.3
47	NA	NA	NA	NA
48	6.0	6.8	7.0	6.6
52	4.0	5.0	5.7	4.9
53	7.0	7.0	7.0	7.0
55	5.7	7.0	7.0	6.6
61	7.0	7.0	7.0	7.0
63	6.7	6.7	3.6	5.7
Mean ± SD	5.4 ± 1.3	5.1 ± 2.1	4.7 ± 2.3	5.2 ± 1.7
Range of Scores	2.7 – 7.0	1.3 – 7.0	1.0 – 7.0	2.0 – 7.0
Possible Range	1 – 7	1 – 7	1 – 7	1 - 7

NA = Data not available. Patient 40 did not indicate which three physical activities were most important. Patient 47 did not complete the QOLiF, although it was completed by the parent/caregiver.

rated items. Data were missing for Patient 40 and Patient 47 because Patient 40 did not indicate which were his top three items, and Patient 47 did not complete the first administration of the QOLiF.

4.4.3 CHANGE IN HRQOL SCORES MEASURED SIX WEEKS AFTER HOSPITAL STAY

Six weeks after the hospital stay, the HRQOL instruments were re-administered to the patients available for follow-up to explore changes in measured HRQOL in patients who were well enough to be active at home.

4.4.3.1 CAQ

Only, four of the original 15 patients completed the second administration of the CAQ-A. The others were lost to follow-up. Changes in the CAQ scores are not reported because the sample size was inadequate and the results would not likely have been representative of the changes in the sample.

4.4.3.2 PAQLQ

Eleven of the 18 patients who were assessed with the PAQLQ in hospital completed the second administration of the PAQLQ . The mean age of this group was 11.6 ± 2.7 years. As shown in Table 33, by six weeks after hospital admission, the overall PAQLQ

HRQOL score had increased from 3.8 ± 0.9 to 5.6 ± 1.3 ($p = 0.0011$), which represented a mean change in score of 1.8 points for overall HRQOL. Consistent with a clinical improvement, the effect size for the overall PAQLQ HRQOL score was 1.5, indicating that the PAQLQ was responsive to changes in patients' clinical status. The mean change in score for each of the domains were also similar; the mean change in each domain was 1.7, 1.6, and 1.9 for the activity domain, symptom domain, and emotional function domain, respectively. Effect sizes were similarly large for each of the domains of the PAQLQ as shown in Table 33.

Ten parents were administered the PACQLQ six weeks after hospital stay (Table 34). The mean score was 5.6 ± 1.3. The change in the mean score is not reported because only three of the nine parents who completed the first administration completed the second administration. The other parents were not available. With only three sets of matched scores, the change in mean score is not meaningful.

4.4.3.3 PATIENT-SPECIFIC APPROACH TO HRQOL ASSESSMENT: QOLIF

Only 10 children completed both the first and second administration of the QOLiF. Two of the 12 children who completed the first administration were not available when the investigator met with parents for the follow-up meeting. Furthermore, one child did

Table 33 **Children's PAQLQ Scores Measured During Hospital Admission and Six Weeks After Hospital Stay**

Patient	Domain							
	Activity Limitations		Symptoms		Emotional Function		Overall	
	IH	IC	IH	IC	IH	IC	IH	IC
1	4.4	6.0	5.4	5.9	4.5	5.9	4.8	5.9
5	2.1	6.1	2.5	6.8	2.7	6.7	2.4	6.5
8	3.7	5.9	3.9	6.4	2.6	6.2	3.4	6.2
17	3.7	3.4	6.1	4.6	3.7	3.8	4.5	3.9
19	2.9	4.2	3.0	6.5	3.5	6.6	3.2	5.8
25	2.8	4.4	3.4	4.7	2.5	4.7	2.9	4.6
34	4.6	6.6	4.2	6.5	4.1	6.3	4.3	6.5
45	4.6	6.4	5.5	6.5	5.0	6.7	5.0	6.5
47	3.0	2.5	3.0	3.1	2.9	3.2	3.0	2.9
55	3.6	6.7	5.6	6.7	5.2	6.9	4.8	6.8
60	3.7	6.3	3.6	6.2	2.3	5.9	3.2	6.1
Mean ± SD	3.6± 0.8	5.3± 1.5	4.2± 1.3	5.8± 1.2	3.6± 1.0	5.7± 1.3	3.8± 0.9	5.6± 1.3
Paired t-test (2-tailed)	p = 0.0015		p = 0.0084		p = 0.0003		p = 0.0011	
Effect Size	2.2		1.4		2.1		1.5	

IH = In Hospital
IC = In Community Six Weeks After Hospital Stay

Table 34 PACQLQ Scores Measured 6 Weeks After the Hospital Stay

Patient	Score
5	3.2
8	4.6
17	6.3
19	3.9
29	6.3
34	7.0
45	6.7
47	5.2
52	6.2
55	6.2
Mean ± SD	5.6 ± 1.3
Range of Scores	3.2 – 7.0
Possible Range	1 – 7

not indicate which items were his three most important physical activities. The mean age of this group of 10 children was 9.0 ± 3.1 years. Eight of the 10 children were seven years of age or older. Table 36 show the summary results from the administration of the QOLiF to these children during their hospital admissions and again six weeks later. Although mean scores increased with the corresponding improvement in the children's asthma, none of the changes in domain scores reported by the children was statistically significant, as shown in Table 36. The effect sizes for the physical domain, social domain, role function domain, and overall scores were 0.4, 0.6, 0.3, and 0.3 respectively.

Twelve parents completed the initial and follow-up administration of the QOLiF. As shown in Table 35, only the change in the parents' social domain scores was statistically significant. The effect sizes for the physical domain, social domain, role function domain, and overall score were 0.7, 0.5, 0.5, and 0.7 respectively.

4.4.3.4 RESPONSIVENESS OF THE PAQLQ AND QOLIF TO CHANGES IN PATIENTS' CLINICAL STATUS

To explore the relative performance of the PAQLQ and the QOLiF, the changes in the physical domain scores of the QOLiF were compared to the changes in activity domain scores of the PAQLQ (Table 37) among the six children who completed both instruments. The mean age of this subgroup of children was 11.2 ± 1.9 years. In this group, there was no significant change in either the parents' or the children's physical

domain scores of the QOLiF. The parents' mean physical domain scores increased from 5.8 ± 1.0 to 6.1 ± 0.8 ($p = 0.25$). The children's mean physical domain scores increased from 5.0 ± 1.7 to 6.2 ± 0.5 ($p = 0.11$). However, the mean PAQLQ scores of the children increased from 3.4 ± 0.9 to 5.5 ± 1.3 ($p = 0.016$). The effect size was much larger with the PAQLQ than with the QOLiF in these matched cases.

Table 35 **Parents' QOLiF Scores Measured During Hospital Admission and 6 Weeks After Hospital Stay**

	Domain							
	Physical		Social		Role		Overall	
	IH	IC	IH	IC	IH	IC	IH	IC
5	5.0	5.3	5.7	6.0	6.0	6.0	5.6	5.8
8	4.3	5.0	6.0	5.0	5.2	5.4	5.2	5.1
17	7.0	6.3	6.6	6.8	5.7	5.7	6.4	6.3
25	6.7	7.0	6.0	7.0	6.3	7.0	6.3	7.0
34	6.0	6.7	4.3	6.9	4.0	7.0	4.8	6.9
38	5.3	5.0	3.5	5.0	3.0	4.5	3.9	4.8
40	NA	NA	5.8	6.8	2.3	5.8	NA	NA
45	6.3	7.0	6.3	6.5	6.6	6.6	6.4	6.7
47	NA	NA	1.3	1.7	1.0	1.3	NA	NA
48	4.3	7.0	6.6	7.0	5.7	3.7	5.5	5.9
53	3.7	7.0	4.2	7.0	1.0	7.0	3.0	7.0
55	6.0	6.3	7.0	6.7	7.0	6.5	6.7	6.5
Mean ± SD	5.5 ± 1.1	6.3 ± 0.8	5.3 ± 1.7	6.0 ± 1.5	4.5 ± 2.2	5.5 ± 1.7	5.4 ± 1.2	6.2 ± 0.8
Paired t-test (2-tailed)	p = 0.07		p = 0.037		p = 0.12		p = 0.78	
Effect Size	0.7		0.5		0.5		0.7	

IH = In Hospital
IC = In Community Six Weeks After The Hospital Stay
NA = Data Not Available. Patient 40 did not indicate which activities were most important to him. Patient 47 did not complete the QOLiF, although it was completed by the parent/caregiver. Data that were not available were not included in the analysis.

Table 36 **Children's QOLiF Scores For the Physical, Role and Social Domain Measured During Hospital Stay and 6 Weeks After Hospital Stay**

	Domain							
	Physical		Social		Role		Overall	
	IH	IC	IH	IC	IH	IC	IH	IC
5	3.0	6.3	1.8	6.0	1.3	6.3	2.0	6.2
8	5.7	6.3	5.8	6.2	5.0	7.0	5.5	6.5
17	7.0	7.0	7.0	6.0	7.0	7.0	7.0	6.7
25	2.7	5.7	2.3	5.7	1.5	6.0	2.2	5.8
34	6.0	5.7	6.1	7.0	6.3	6.9	6.1	6.5
38	5.0	4.3	6.5	5.5	5.5	5.5	5.7	5.1
40	NA	NA	1.7	6.7	1.7	6.8	NA	NA
48	6.0	7.0	7.0	4.7	6.8	6.2	6.6	6.0
53	7.0	4.7	7.0	4.3	7.0	4.2	7.0	4.4
55	5.7	6.3	7.0	6.5	7.0	6.9	6.6	6.6
Mean ± SD	5.3 ± 1.6	5.9 ± 0.9	5.2 ± 2.3	5.9 ± 0.9	4.9 ± 2.5	6.3 ± 0.9	5.4 ± 1.9	6.0 ± 0.7
Paired t-test (2-tailed)	p = 0.34		p = 0.14		p = 0.47		p = 0.45	
Effect Size	0.4		0.6		0.3		0.3	

IH = In Hospital
IC = In Community
NA = Data Not Available. Patient 40 did not indicate which activities were most important to them. Patient 47 did not complete the QOLiF, although it was completed by the parent/caregiver.

Table 37 **Comparison of Scores in the Physical Domain of the QOLiF and Activity Domain Scores of the PAQLQ in the Group of Six Children Who Completed Both the PAQLQ and the QOLiF**

	QOLiF Physical Domain Parents' Scores		QOLiF Physical Domain Children's Scores		PAQLQ Activity Domain Children's Scores	
Number	IH	IC	IH	IC	IH	IC
5	5.0	5.3	3.0	6.3	2.1	6.1
8	4.3	5.0	5.7	6.3	3.7	5.9
17	7.0	6.3	7.0	7.0	3.7	3.4
25	6.7	7.0	2.7	5.7	2.8	4.4
34	6.0	6.7	6.0	5.7	4.6	6.6
55	6.0	6.3	5.7	6.3	3.6	6.7
Mean ± SD	5.8 ± 1.0	6.1 ± 0.8	5.0 ± 1.7	6.2 ± 0.5	3.4 ± 0.9	5.5 ± 1.3
Paired t-test (2-tailed)	0.25		0.11		0.016	
ES	0.3		0.7		2.3	

IH = In Hospital
IC = In Community
NA = Data Not Available. Patient 40 did not indicate which activities were most important to them. Patient 47 did not complete the QOLiF, although it was completed by the parent/caregiver.

5. DISCUSSION

5.1 THE OVERALL STUDY SAMPLE

Children who were five years or older with a diagnosis of asthma were included in the study. Children younger than five were excluded because much of the evidence supporting the recommendations of the NIHLBI guidelines have been based on studies in children five years of age and older.[32] As noted in the guidelines,[32] the diagnosis of asthma is not as clear in children less than five years of age because the symptoms of asthma are similar to other respiratory conditions.[105] The respiratory symptoms typical of asthma, including wheezing, coughing, and breathlessness can be caused by respiratory tract infections, congenital anomalies, and mechanical or cardiogenic problems. For example, pneumonitis, cystic fibrosis, gastro-oesophageal reflux, wheezy brionchiolitis,[106] and other conditions may have similar clinical presentations in children.[107] Without a firm diagnosis of asthma, it would have been difficult to determine the presence of a dose-related therapeutic failure, since the guidelines that were used to judge appropriateness of patients' drug therapies applied only to those patients with a firm diagnosis of asthma. Thus, by including only those children five years of age or older, it was possible for the expert panel to judge which patients received inadequate treatment.

A disadvantage of selecting only those children five years or older was that the number of eligible patients that were able to participate was reduced. As can be seen in

Figure 2, the number of children admitted to hospital for asthma was inversely proportional to age. Ambulatory health care visits by children have been reported to vary inversely with age, especially for patients with asthma.[108-109]

The number of children enrolled in the current study was highest in the month of September (Figure 1), and in general fewer children were admitted to hospital and enrolled in the study between December and February. Thereafter, the number increased through the spring season, between March and June. A similar seasonal pattern has been observed in a group of 12,064 patients with asthma admitted to hospital between 1994 and 1995 in Quebec, Canada.[109] The increase in the number of hospital admissions in September may have been associated with the start of school year for the children. At school, children are generally exposed to more infectious contacts. Respiratory tract infections are known to be triggers for exacerbations of asthma[97, 110] and an association between the frequency of hospital admissions during the school period and the presence of respiratory tract infections has also been reported among children.[111] Similarly, the increase in the number of hospital admissions through the spring may have been associated with children's exposure to seasonal allergens, as it has been reported that seasonal allergens can trigger asthma exacerbations.[112-113]

The patients were acutely ill on hospital admission according to their documented clinical status. As described in Section 5.1.2, the patients' mean PEFR (where data were available) on admission was only 60.6% of their predicted values. PEFR is correlated

with respiratory function and can generally be used to serve as an objective measure of lung function in the patient with asthma.[32] However, a number of factors make the PEFR readings difficult to interpret.[114] First, PEFR is very effort dependent, especially among young children. Proper technique and effort are required to obtain accurate and reproducible readings. Second, PEFR readings vary considerably among different brands of the device, and even among different units of the same model.[115] Third, population norms vary among Caucasians, Orientals, and Blacks.[116] In this study, although the investigator used the same PEFR model, the PEFR monitors varied among some patients who already owned a PEFR monitor. In future studies, supplying a standard PEFR monitor to patients and providing the same brand of PEFR monitor to each patient would help to reduce variability among different brands. However, with the same model PEFR readings can be inconsistent.[114] A better approach would be to measure FEV_1 rather than PEFR to provide the best objective measure of lung function, however this is not practical for a large study in hospitalized children.

As shown in Table 16, the mean arterial oxygen saturation in room air on admission was only 93.3%, which is below the normal range (94-100%[117]). Arterial oxygen saturation in room air is generally a good indicator of the severity of exacerbation among patients with asthma.[118]

The mean respiratory rate (Table 16) was 31.6 ± 7.3 breaths per minute, which was more than two standard deviations above the normal population mean.

Furthermore, all of the patients' heart rates were higher than normal on admission to hospital.

In addition, since patients were enrolled in the study, *subsequent* to being admitted to a hospital ward by a medical doctor, their inferred clinical status was poor. The majority of the patients was admitted to the Mount Saint Joseph Hospital site of The Children's and Women's Health Centre of British Columbia, which is the province's primary pediatric teaching hospital affiliated with the University of British Columbia. Thus, this study sample represented a group of children with respiratory symptoms of asthma severe enough to have required hospital admission.

An important feature of the study was the polarized change in health status of the study patients, as patients were admitted for acute exacerbations of asthma, and discharged in control of their asthma symptoms. Thus, the patients' health status during their hospital admission was expected to be poor compared to when they were re-assessed, approximately six weeks after their hospital stay. By prospectively evaluating this cohort of asthmatic patients in the community when their condition was improved it was possible to measure the patients' HRQOL during their worst asthmatic state and compare it to their HRQOL status when they were well in the community.

5.2 DRUG-RELATED HOSPITAL ADMISSIONS

The results of this study indicated that a high proportion of the children admitted to hospital for asthma had a medication-related therapeutic failure associated with the hospital admission. Thirty-seven of 44 (84%) of patients' admissions that were evaluated by the panel of asthma experts were associated with a "definite" therapeutic failure and seven of 44 admissions (16%) were deemed to have been "possibly" drug-related (Figure 12). In all cases, the admissions were associated with therapeutic failures rather than adverse effects. However, if the panel determined that symptoms of infection reported for the children provided sufficient evidence for a condition that could have explained the symptoms on admissions, then 23 of the 44 cases (53%, 95% CI = 36 - 67%) would have been considered "definite" and 21 of the 44 cases (48%, 95 % CI = 33 - 62%) would have been considered "possible" therapeutic failures.

The estimated frequency of drug-related hospital admissions in this study is consistent with the research by Ordonez GA *et al.,* [119] who examined the incidence of "preventable factors" associated with children three to 15 years of age admitted to hospital for acute asthma in Melbourne, Australia. Using a questionnaire, they interviewed 166 children to obtain data related to their hospital admissions. Although they did not use a standardized algorithm, the investigators reported that approximately 72% of the children had "between two and four preventable factors" associated with their hospital admission. They also reported that, although 44% of the patients had been

given an asthma crisis management plan, only 9% of these patients had followed their plan before admission. Other factors contributing to hospital admission included low levels of asthma knowledge (49%), inappropriate preventative treatment (31%), poor compliance with preventative treatment (21%), and failure to use prednisolone and overuse of β_2-agonists before seeking treatment. The investigators identified "preventable factors" related to the children's hospital admissions, but they did not evaluate the contribution of each factor to hospital admissions.[119]

As described in Section 2.1.3.2 few other studies have examined the frequency of drug-related hospital admissions in the pediatric patient population with asthma. Einarson *et al.*[35] performed a meta-analysis of 36 studies that have examine drug-related hospital admissions in industrialized countries, primarily in North America and Europe. Their focus was on adverse drug reactions, defined as "any unintended of undesired consequence of drug therapy," and patient non-compliance leading to hospitalization. Non compliance was defined as deviation from a regimen written (and intended) by the prescriber and included undercompliance (i.e., taking too little) and overcompliance (i.e., exceeding prescribed dosage). They reported that the frequency of adverse drug reactions leading to hospital admission ranged from 0.2 to 21.7%, with a median of 4.9%. In a more recent meta-analysis, Roughhead *et al.*[46] analyzed studies of drug-related hospital admissions in Australia. They reported that 2.4 to 3.6% of all hospital admissions, 12% of all admissions to medical wards, and 15 to 22% of all emergency admissions among the elderly were drug- related. Between 32 and 69% of drug-

related admissions were preventable. Although the diagnoses implicated in the drug-related admissions were reported in some of the studies, the extent of drug-related admissions related to asthma was not established. Furthermore, non-compliance with medications was examined in only four of the 14 studies.

It is likely that these previous estimates have been lower than that observed in the present study because of methodological differences and differences in the study populations. Only four studies in the meta-analysis by Roughhead *et al.*[45] employed a set of objective criteria to assign a degree of causality to each drug-related hospital admission. Furthermore, these previous studies did not specifically evaluate the population of pediatric patients hospitalized for *asthma.* The present study is unique because it is the first one to have examined drug-related hospital admissions in pediatric patients with asthma using a set of objective criteria.

5.2.1 DRUG REGIMEN OF PATIENTS IN THE DRUG-RELATED HOSPITAL ADMISSION COHORT

Twenty-one of 44 patients (48%) reported not taking any medication on a chronic basis for their asthma (Appendix 14). The most common type of "as-needed" medication reported by the patients or the parents for the chronic management of asthma was salbutamol (Figure 9). Fourteen patients were taking only one regularly scheduled medication. The most common types of regularly scheduled medication reported by

patients or parents for the chronic management of asthma were inhaled corticosteroids: budesonide and beclomethasone (Figure 7). However, only 32% of patients reported taking regularly scheduled preventative medication. This was lower than the frequency of preventive medication use reported by Ordonez GA *et al.*[119] In their study of 266 children admitted to hospital for asthma, 42% had been using preventative treatment on a regular basis as prescribed by their physician.

For the acute episode related to the hospital admission in the present study, 31 of the 44 patients (70%) took medications in addition to their "regularly-scheduled" chronic regimen. In 14 of these 31 cases (45%), the children reported that they increased the dose of chronic medication and did not add additional drugs. One-third of patients did not report increasing the dose of their chronic medications or adding additional therapy for their acute exacerbation. In 25 of the 44 patients (57%), oral corticosteroids were required for the acute exacerbation (as described in Section 5.2.5), but only three (7%) of them took oral corticosteroids for the exacerbation related to the hospital admission. In the majority of cases, the patient took salbutamol for the acute exacerbation (Figure 11).

Ordonez GA *et al.*,[119] reported that 18% of children in their study with a previous diagnosis of asthma and an exacerbation lasting more than 24 hours did not take systemic corticosteroids prior to hospital admission, despite requiring bronchodilators more than every three hours. Ninety-five percent of patients failed to use an asthma crisis management plan. Among the 266 children studied, only seven (3%) took oral

corticosteroids prior to hospital admission for acute asthma. The investigators, however, did not classify patients according to severity of symptoms, and thus it was not possible to relate their findings to adherence to the guidelines.

Future work would benefit from having objective evidence of patients' drug regimens. In the province of British Columbia, all prescriptions processed for each resident are recorded in the Pharmanet database. In the future, verification of patients' medication histories with the Pharmanet database would provide more objective evidence of their drug therapy.

A discussion of patients' chronic and acute drug therapy in relation to the NIHLBI guidelines is discussed in Section 5.2.5.

5.2.2 MODIFICATION OF HALLAS' ALGORITHM

Although the set of criteria has been applied by Hallas *et al.* in other studies[2, 51-53] to evaluate drug-related hospital admissions, this is the first study to apply the approach to the population of *pediatric* patients admitted to hospital with *asthma*. In this population, it was necessary to adapt Hallas' approach with a modification related to the assessment of dose-related therapeutic failure (DTF).

In Hallas' previous studies, a DTF was defined as an absence of therapeutic response that could be linked causally either to a prescribed dose that was too low, to drug non-compliance, recent dose reduction/discontinuation, interaction, or inadequate monitoring, as described in Section **2.1.3**. Non-prescription of a drug was not considered to represent DTFs. The reason that Hallas has not considered lack of a therapeutic effect linked to non-prescribing is that for many conditions it is not clear what the best approach to treatment is.[53] However, asthma is a specific condition for which the currently accepted approach to treatment has been generally accepted and made explicit in *The National Institutes of Health (NIH) Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma* (1997)[32] and *the Canadian Asthma Consensus Conference Summary of Recommendations*.[33] These guidelines clearly outline drug and non-drug treatment strategies for all patients with asthma five years of age and older that are supported by published scientific evidence. Furthermore, the recommendations in the asthma treatment guidelines that are related to the early use of corticosteroids are based on evidence suggesting that these drugs can reduce the severity of acute exacerbations of asthma[25-29, 120-128] and the need for hospital admissions.[28-29, 127-128] Therefore, in the present study, non-prescription of a drug was included in the classification of dose-related therapeutic failures.

A limitation of this modification to Hallas' algorithm is that validity of this algorithm with the modification will require further study. Since there is no gold standard, future studies could compare the results of the modified algorithm to other

algorithms, or to decisions of a separate expert panel that assesses each drug-related hospital admission.

5.2.3 INTERPRETATION OF HALLAS' ALGORITHM IN RELATION TO RESPIRATORY TRACT INFECTIONS

Since respiratory tract infections are common in children with asthma, it was necessary to inform the expert panel about the interpretation of Criterion 5 of Hallas' algorithm in relation to respiratory tract infections.

In Hallas' algorithm, a "definite" causal relation is inferred only if all five criteria (Table 9) are satisfied. To make the algorithm clearly applicable to the population of patients with asthma, the "condition" referred to in criterion five was interpreted to include evidence of a respiratory tract infection that could have explained the symptoms. The purpose of the explicit reference to respiratory tract infections was to reduce the chance that the expert panel would fail to consider a respiratory tract infection as a condition present that could explain the symptoms on hospital admission. The expert panel determined that in only six of the 44 admissions, a respiratory tract infection was a condition that could have explained the symptoms. In these six cases, the panel determined that there was only a "possible" causal relation between drug intake and dose-related therapeutic failure. Subsequent to the panel assessments, 14 additional cases

(Table 19) were noted in which some evidence of a respiratory tract infection was found. In these cases, the panel had apparently considered the evidence to be insufficient. If the panel had concluded that the evidence was sufficient in all cases, then it would have estimated that 23 (52%) of 44 of cases were "definite" dose-related therapeutic failures, and 21 (48%) of 44 of cases were "possible" dose-related therapeutic failures.

Respiratory tract infections are common among children hospitalized for asthma.[111, 129-130] In this study some subjective or objective evidence of an upper respiratory tract infection was reported in 25 (45.5%) of the 44 cases. In a recent study of 108 children admitted to hospital for acute exacerbations of their asthma, sensitive polymerase chain reaction assays, in combination with standard virologic techniques on patients' nasal aspirates, indicated that viral infections were associated with 80 to 85% of the observed asthma exacerbations.[97] In the study, "viruses were detected in 80% of reported episodes of peak expiratory flow, 80% of reported episodes of wheeze, and in 85% of reported episodes of upper respiratory symptoms, cough, wheeze, and a fall in peak expiratory flow." Similar results have also been reported with adults.[98] Thus, respiratory tract infections represent a common cofactor associated with children's symptoms leading to asthma related hospitalization. Since Hallas' algorithm takes this factor into account, an underestimation of the frequency of respiratory tract infections could markedly affect the results.

In the present study, it is possible that the frequency of upper respiratory tract infections was underestimated, because determination of the presence of upper respiratory tract infections was based only on patients' or parents' recall of events and a review of the medical records. Had a more intensive method of data collection been used, then the estimated frequency of "definite" dose-related therapeutic failures might have been reduced.

Some studies have shown that symptoms of asthma triggered by respiratory tract infections can be treated, reducing the need for hospitalization.[125, 127, 131-133] For example, in the study by Brunette *et al.*,[131] that occurred between 1980 and 1984, "two groups of children in Montreal, Canada, with a mean age of 36.4 ± 3.9 months and 40.4 ± 4.9 months were monitored during a two-year period. Group 1, considered as the control group, received theophylline preparations and orciprenaline either on a continuous basis or during attacks. During severe attacks, albuterol (salbutamol) was administered by nebulization, with corticosteroids occasionally added for seven to 14 days in cases of poor response to albuterol. Group 2 received the same treatment during the first year. During the second year, however, a short-term course of oral prednisone (1 mg/kg) each day was given as soon as the first symptoms of an upper respiratory tract infection appeared, prior to any signs of wheezing. The results indicated that, whereas morbidity remained constant in the control group during the 2-year observation period, a significant decrease in the number of wheezing days (65%), attacks (56%), visits to the emergency room (61%), and hospitalizations (90%) occurred in group 2. All of these results

were statistically significant. It was concluded that preschool children who suffer from repeated asthma attacks related to upper respiratory tract infections may benefit greatly from the preventive administration of corticosteroids." [131] However, a number of factors may make the results difficult to interpret. First, only 32 children participated in the study. With such a small sample size, it is difficult to generalize these results. Second, the patients in this study by Brunette *et al.* [131] were much younger than the patients in the current study. Since asthma is difficult to diagnose in very young children (as discussed in Section 5.1), improper diagnosis may have confounded the results. Finally, the patients and parents were not randomized or blinded to the treatment, and this could have confounded the results.

In a double-blind randomized placebo-controlled crossover study, Svedmyr *et al.* reached similar conclusions using inhaled glucocorticoid therapy.[125] They investigated whether inhaled budesonide administered during the early phase of URTI, before asthma symptoms developed, could reduce or completely eliminate asthma symptoms in children with well-controlled asthma. The children were randomized in blocks of two, that is each child was treated with inhaled budesonide (Pulmicort Turbuhaler®) during one period and then received placebo during the next, or vice versa. Children were instructed to start treatment at the first sign of an URTI, and to continue treatment for nine days. Sixty-seven treatment periods were completed. Eleven children visited the emergency room, but only three visits occurred during the budesonide therapy. All five children who required oral steroids and two patients who were admitted to hospital were in the

placebo group. Their results showed that inhaled budesonide could attenuate exacerbation of URTI-induced asthma in children. However, this was also a small study with only 26 children participating. Furthermore, inhaled budesonide was administered four times daily in this study. A less rigorous dosing regimen could affect the patients' responses, since it has been reported that four times daily dosing may have a better effect on severe asthma, or on the incidence of relapse than twice daily dosing.[134]

In summary, respiratory tract infections appear to be commonly associated with asthma and can contribute to patients' asthma symptoms. Also, some studies have shown that the severity of exacerbations of asthma triggered by respiratory tract infection may be reduced with preventative medications.[125, 127, 131, 133, 135] However, the evidence is not clear whether full compliance with proper preventative treatment is effective in all patients. Therefore, in the present study, it was necessary to include respiratory tract infections as a factor that could have contributed to asthma symptoms, in accordance to Hallas' algorithm.

If it were true that full compliance with proper preventative treatment were effective in controlling the severity of symptoms of asthma triggered by respiratory tract infection in patients with asthma, then respiratory tract infections could be disregarded as a condition that could have explained the symptoms on admission accordance to criterion five of Hallas' algorithm. Until further evidence is available, it will be necessary to interpret respiratory tract infections as we have done in this study. Prospective

randomized controlled trials will be required to examine the effectiveness of the NIHLBI guidelines on rates of hospital admissions in children whose asthma exacerbations are complicated by respiratory tract infections, in order to determine whether or not patients whose symptoms are triggered by respiratory tract infections and treated according to the recommendations of the NIHLBI guidelines can avoid the need for hospital admissions.

5.2.4 LACK OF INHALED AND ORAL CORTICOSTEROIDS REPORTED IN THE REGIMEN

For many cases in which the expert panel deemed there was a definite relation between drug intake and therapeutic failure, the patients appeared to have received inadequate preventative therapy with inhaled corticosteroids or inadequate treatment with oral corticosteroids during the acute episode. Some patients were inadequately treated chronically *and* during the acute exacerbation.

The NIHLBI guidelines recommend that inhaled corticosteroids be used regularly in patients whose severity are classified as "mild persistent" or worse. Doubling the dose of regularly scheduled inhaled corticosteroids is also indicated in those patients who obtain a good response to short-acting β_2-agonist therapy during an acute exacerbation. Daily oral corticosteroids are indicated in patients with severe persistent asthma, and

in some patients with moderate persistent asthma. Oral corticosteroids are also indicated for patients who do not obtain a good response to short-acting β_2-agonist therapy during an acute exacerbation. For patients with a history of severe exacerbations with viral respiratory tract infections, oral corticosteroids are recommended at the first sign of the infection.[32]

In the present study, 13 of the 16 patients (82%) who appeared to have chronic "mild persistent" asthma (Table 20) did not receive daily anti-inflammatory medication as indicated by the guidelines. Among the seven patients with chronic "moderate persistent" asthma (Table 21), none received anti-inflammatory medications every day. Five of the seven patients did not receive any doses at all. The other two patients took their preventative medication sporadically, despite the guidelines recommendations that preventative medications be used every day in patients with moderate persistent asthma. In 25 of the 44 cases (57%), patients required oral corticosteroids based on the NIHLBI guidelines for the acute exacerbation but did not report the medication to be in their drug regimen. Patients reported taking oral corticosteroids in only three of the 25 cases, despite having symptoms severe enough to require hospital admission.

Studies have provided evidence of the efficacy of corticosteroids in suppressing inflammation in asthmatic airways, inhibiting the inflammatory process, controlling asthma symptoms,[25-29,120-128] improving lung function,[25-29,122-128] preventing

exacerbations,[28-29, 122, 128, 136] reducing hospital admissions,[28-29, 122, 128, 136] and reducing asthma mortality.[25-30]

The data collected about patients' medication use were subjective, based on patients, parents, and physicians' reports. Although patients were asked to report all medication in their regimen, it is possible that some did not disclose all of their medication because they were not compliant with them. Since objective evidence about patients' actual drug use was not available, it is not possible to determine the extent to which inadequate treatment with inhaled or oral corticosteroids was related to non-compliance or lack of a prescription. As well, one patient, (Patient 32), identified that the cost of medications was as a barrier to compliance. This was a surprising observation, considering that social programs are in place in the province of British Columbia, to help low income families purchase essential prescription medications, although it has been reported that asthma-related morbidity and mortality may be related to socioeconomic factors.[137]

5.2.4.1 NON-COMPLIANCE

Compliance was assessed through an interview with each patient, as described in section 3.1.5. In this study, a patient was considered non-compliant with a medication if the patient, parent, or healthcare provider reported that the individual was non-

compliant with his or her medication. The degree of non-compliance reported by patients ranged from not taking regularly scheduled medication at all, to missing the occasional dose (Appendix 19). In many cases, the patients did not take any doses of prescribed preventative medication at all. More than half of the patients were considered to be non-compliant with their prescriptions.

Poor compliance with preventative treatment has been identified as a factor related to hospital admissions in pediatric patients with asthma.[138] In fact, our estimate of the frequency of non-compliance in this study is relatively low compared to another study.[139] This may have been related to the method of data collection, rather than the fact the non-compliance was low in the study population. Since patients generally under-report non-compliance,[43, 140-141] the frequency of non-compliance is probably higher and would likely have been observed to be higher if a more intensive monitoring scheme had been used. In future studies, a standardized method of evaluating compliance with preventative therapy could easily be incorporated into the patient interview with a four-item self reported adherence measure, which has shown concurrent and predictive validity.[142] An assessment of compliance could also be performed by comparing patients' reported drug therapy with medications recorded in the provincial PharmaNet database, which records nearly all prescriptions processed for patients in the province of British Columbia.

5.2.4.2 LACK OF A PRESCRIPTION

Patients may not have reported certain medications in their regimen because they had not been prescribed. However, based on the data collected, it was not possible to determine whether patients simply were not reporting medication because they did not have the medication prescribed, or whether they were actually prescribed the medication, but they did not use it. Future studies should record patients' health profiles through the provincial PharmaNet database to help determine which medications have been prescribed but not reported in their drug regimens. Furthermore, data collected from the family physicians' health records would help to determine which prescriptions were prescribed, but not filled at the pharmacy.

5.2.5 LACK OF ADHERENCE TO EVIDENCE-BASED GUIDELINES

The NIHLBI guidelines make recommendations about the appropriate use of preventative and acute drug therapy based on patients' chronic level of severity. The present study provided an opportunity to study the extent to which patients' chronic and acute asthma management were consistent with the recommendations of the NIHLBI guidelines.

According to the stepwise approach for managing asthma in the NIHLBI guidelines, a patient's level of severity is based on symptoms and lung function

parameters. The NIHLBI guidelines recommend drug therapy based on a patient's level of severity. Thus, it was possible to examine the extent to which patients' drug therapies were consistent with the NIHLBI guidelines by comparing a patient's reported drug regimen with the drug therapy recommended by the NIHLBI guidelines.

5.2.5.1 MANAGEMENT OF CHRONIC ASTHMA

Patients were classified according to a level of severity from the clinical data that were collected from the interviews and from the medical charts. Thus, the accuracy of the classification of severity was dependent on the reliability of the data collected. Furthermore, the ability to determine inadequate chronic treatment was dependent on accurate classification of chronic asthma severity. In this study, classification of severity was conservative, since cases that were questionable were placed in the less severe group. For cases in which it was not possible to categorize the patients' severity because data were insufficient, disease severity was classified as "non-determinable."

A patient was considered to have had "inadequate treatment" of chronic asthma if drug therapy indicated by the guidelines for the chronic treatment of asthma according to the patient's level of severity was not reported in the patient's drug regimen in the last three months; or if the patient, parent, or physician reported that the indicated medication was in the regimen but that the patient was non-compliant in using it. Evidence of

inadequate treatment of chronic asthma was found in 19 of the 44 cases (43%). If the 6 patients in whom severity was "non-determinable" were excluded from the analysis, the frequency of inadequate chronic treatment would have been 58%. These results suggest that, despite the availability of the NIHLBI guidelines, physicians and patients are not managing asthma in a manner consistent with the guidelines.

Only a few studies have examined the extent to which the NIHLBI guidelines have been adopted in North America. The most recent work was published by Halterman *et al.*,[143] and Meng *et al.*[144] Halterman *et al.* investigated whether children less than 16 years of age with asthma took maintenance medication according to the NIHLBI guidelines.[32] The study sample was recruited from respondents of the National Health and Nutrition Examination Survey, a large-scale national survey of 40,000 people conducted from 1988 through 1994. Patients who reported physician diagnosed asthma were contacted and interviewed. Patients were asked about the number of wheezing episodes, the number of acute health care visits for wheezing, the number of hospitalizations for wheezing during the past 12 months, and about medications used during the past month. Five hundred and twenty four children less than 16 years of age with moderate to severe asthma were identified in the study. Among these patients, only 26% had taken maintenance medications in the previous month. Thus, 74% were inadequately treated according to the Guidelines. It is possible that their estimates of the frequency of inadequate treatment was higher than in the present study because they only

studied children with moderate to severe asthma, and they also included children less than five years of age.

In a comparable study by Meng *et al.*,[144] of 6,703 patients 14 years and older, compliance with the NIHLBI guidelines was also consistently low. The patients in their study also had moderate to severe asthma using a classification scheme similar to those in the NIHLBI guidelines. The frequency of inadequate treatment with daily preventative medication as recommended by the guidelines, ranged from 49.5% to 61.0%. Poor compliance with the NIHLBI guidelines was consistent across all seven of the geographical regions in the United States that were evaluated in the study. Furthermore, more than 10% of respondents in the study reported using a bronchodilator more than eight times daily. The primary limitation of this study was the low response rate to the questionnaire. The Health Survey for Asthma Patients, a 10-page, self-administered questionnaire was mailed in 1996 and 1997 to 35,515 members who were identified as having asthma according to the HMO's database. 11,647 members responded, but 3,150 respondents indicated that they did not have asthma. Excluding false positives and those patients with mild intermittent asthma, the final sample size was only 6,703 patients.

The present study and previous studies[143-144] have identified a discrepancy between patients' use of long-term control medications and recommendations of the NIHLBI guidelines. These recommendations are supported by a large body of research that has provided evidence for the efficacy of regularly scheduled inhaled

corticosteroids for symptoms, exacerbations, and incidence of hospital admissions.[25-27] Although the retrospective studies suggest that patient adherence to the NIHLBI guidelines can have an impact on control of asthma symptoms, prospective randomized controlled studies are needed to determine whether or not the NIHLBI guidelines can provide measureable improvements for patients.[145-146]

5.2.5.2 MANAGEMENT OF ACUTE EPISODE

Patients were also considered to have had "inadequate treatment" if drug therapy indicated by the guidelines for treatment of the *acute episode* was not reported in the patient's drug regimen; or if the patient, parent, or physician reported that the indicated medication was in the regimen but that the patient was non-compliant in using it. Evidence of inadequate treatment of the acute asthma episode was present in 39 of the 44 cases (89%), which is summarized in Table 22 to Table 25.

As reported in Section 4.3.2.2, many of the cases involved inadequate treatment with oral steroids during the acute attack, despite evidence that oral steroids given during an acute asthma attack can reduce symptoms[147] and the need for hospital admissions in patients with asthma.[128, 148-150]

The most recent study by Horowitz *et al.*,[128] evaluated the effectiveness of oral

steroids in children with asthma using a prospective double-blind randomized placebo controlled design. Children who received a single dose of steroids, given orally in pediatric community clinics during an acute mild to moderate asthma attack, had reduced symptoms and did not require as many hospital admissions. Corticosteroids are known to suppress inflammation in asthmatic airways, improve lung function, control symptoms, reduce asthma mortality and the irreversible changes in airway function, and improve patients health-related quality of life.[31]

In some cases, the children's acute symptoms were also treated inappropriately with the use of oral antibiotics rather than oral steroids by their physicians. In the present study, two cases of drug-related therapeutic failure involved a general practitioner prescribing antibiotics for an acute asthma exacerbation prior to hospital admission. Furthermore, in both of these cases of acute asthma exacerbations, corticosteroids were not prescribed. This inappropriate practice has been reported by Jones *et al.* [151] who has investigated inappropriate management by general practitioners of acute asthma attacks associated with respiratory tract infections in adults.[151] They reported that antibiotic prescription is a common practice by general practitioners when faced with an acute asthma attack associated with respiratory tract infection. Antibiotics are often prescribed for asthma attacks that are associated with respiratory tract infections, despite the fact that the respiratory tract infections that trigger asthma are mainly viral and antibiotic therapy provides no additional benefit in these cases.[152-154]

5.2.6 UNDER-DIAGNOSIS OF ASTHMA

Although patients without a prior diagnosis of asthma were excluded from the study, under-diagnosis may have contributed to some hospital admissions. One patient (Patient 14) was not formally diagnosed with asthma until she was admitted to hospital. She did have chronic symptoms of asthma for nearly six years prior to the hospital admission and had a chronic dry cough that was worse at night, since she was two years of age. The patient had also been wheezy at her general practitioner's office visits for almost three years and was finally diagnosed with asthma during the hospital admission. The second patient (Patient 9) had been seen by a general practitioner prior to her hospital admission, but a diagnosis of asthma was not made at the time. The general practitioner started the patient on amoxicillin, an antibiotic, earlier in the day of her admission. The patient developed increased respiratory difficulty and was admitted to hospital. These are two possible cases of under-diagnosis of asthma. Underdiagnosis of asthma, especially in female pediatric patients, is a phenomenon that has been reported in the literature.[155-156]

5.2.7 PREVENTION

Using Hallas' algorithm to evaluate each case, all 44 drug-related hospital admissions evaluated by the expert panel were considered to be preventable. However, despite the evidence that medications can reduce symptoms and severity of exacerbations, it is not clear whether strict adherence to the NIHLBI guidelines can truly prevent

hospital admissions in all patients with asthma.

To address this question, Mitchell *et al*[57] examined risk factors for readmission to hospital in 1,034 children in Auckland, New Zealand. The medical records of patients discharged from hospital between 1986 and 1987 were examined for factors related to readmission to hospital. Factors that significantly increased readmission were female sex (relative risk (RR) 1.23; 95% confidence interval (CI) 1.03 to 1.46), young age (age < 5 years RR 1.71; 95% CI 1.41 to 2.08), number of previous admissions (one previous admission RR 1.32; two, RR 1.68; three, RR 2.00; four or more, RR 2.80), and inpatient intravenous treatment (RR 1.29; 95% CI 1.08 to 1.55). They also reported that medical treatment and management did not influence readmissions. However, this statement was misleading. Besides the fact that the study was not randomized or controlled, the investigators did not actually evaluate drug therapy of patients before hospital admission. In their study, "the medical management of the asthma episode in the community could not be assessed because drug treatment before admission to hospital was poorly recorded."[57] The investigators actually examined the "intention to treat," based on whether or not the association between patients having prophylactic therapy prescribed on *discharge* from a previous hospital admission was a factor associated with future hospital readmissions. They did not determine whether prescriptions for preventative medications were filled or taken. Considering the high rate of non-compliance with preventative medications in this study, it is not surprising that the investigators did not find an association between prescribed preventative medications and hospital

readmissions using an "intention to treat" analysis. Again, using an "intention to treat" analysis, they also examined the association between patients having an action plan on discharge from a previous hospital admission and future hospital readmissions. The investigators reported that "the use of action plans" did not predict readmissions. The most likely explanation for this is that since this was an "intention to treat" analysis, the authors did not actually evaluate patients' use of an action plan. Therefore, it was not surprising that they did not find an association.

In an earlier study, Mitchell *et al.*[157] reported that patients followed by an asthma nurse educator actually had an increased frequency of emergency hospital visits compared to those children in a controlled group. This was a randomized controlled study of 360 children aged two to 14 years of age. Every month, a nurse performed a follow-up evaluation with the treatment group. After six months, inhaled corticosteroid use was 34.9% in the treated group compared to 21.0 % in the control group. However, patients in the treated group used hospital services for severe attacks of asthma more than control patients (34.2 vs. 10.5%). A possible explanation for this unexpected result is that the action plan at the time of the study instructed patients to call an ambulance or to seek urgent medical attention if the relief of their bronchodilator was short-lived, or they had difficulty with speaking or were cyanosed. This particular instruction may have shifted the medical care from the community to the hospital.

A more recent study by Mayo *et al.*[158] reported opposite results in an adult

population with asthma. The investigator prospectively randomized 104 adult patients with asthma to treatment and control groups. Patients in the treatment group were taught aggressive self-management strategies in case of marked asthma exacerbation. Patients in the control group received their regular outpatient care. Patients who were in the treated group had a threefold reduction in readmissions and a two-fold reduction in hospital days compared to patients in the control group. Thus, this study showed that improving self management can reduce the incidence of hospital readmissions.

Barnes[26] has reviewed the evidence for the clinical efficacy of corticosteroids in asthma. Studies have shown that corticosteroid therapy is efficacious at reducing asthma symptoms.[122-123] Studies have also shown that they are efficacious in children.[159-160] However, it is not known whether corticosteroids can reduce the incidence of hospital admissions, or whether strict adherence to asthma treatment guidelines that recommend the use of corticosteroids can prevent hospital admissions in patients who are fully compliant. Some retrospective, cross-sectional studies have suggested that hospital admissions can be prevented.[28-29, 122, 128, 136] To address this question, prospective, randomized, controlled trials will be required.

Two major problems make it difficult to properly design randomized controlled trials to answer these questions. First, since the incidence of hospital admission is relatively rare, a very large sample size would be required. Second is the problem of confounding by severity. Generally, inhaled corticosteroids are more likely to be

prescribed for patients who have more severe symptoms. These patients in turn may be at a higher risk of hospital admission. Thus, patients in retrospective studies who are taking inhaled corticosteroids could actually have more hospital admissions than patients who are not treated with inhaled corticosteroids.

Despite these challenges, it is clear that more studies will be needed to determine whether full compliance with the NIHLBI guidelines can reduce hospital admissions and the utilization of other healthcare resources.

5.3 HEALTH-RELATED QUALITY OF LIFE

As discussed in Section 2.2, HRQOL in children with asthma needs to be investigated because asthma is a disease with highly variable symptoms and the effect of the disease on patients lives and their HRQOL is complicated by their social, emotional, and physical needs.[75, 161] By simply capturing physiological parameters, clinicians would not be able to assess the full impact of the disease on patients without measuring their HRQOL. HRQOL instruments can complement conventional measures of physical function (e.g., FVC, FEV_1 and other lung function parameters) in children with asthma to provide a more comprehensive measure of disease impairment. Furthermore, since parents' reports of their children's HRQOL may not be accurate, direct measures of children's HRQOL from a child's own perspective are needed. Currently, the most developed tools to measure HRQOL from a child's perspective include the CAQ and PAQLQ. For these instruments to be useful in determining the effect of change in clinical status for children with asthma, validity, reliability, and responsiveness must be evaluated. So far, only some psychometric properties of these instruments have been tested. The present study provides further evidence of the validity and responsiveness of the PAQLQ and examines the utility of a patient-specific approach to HRQOL assessment.

5.3.1 THE STUDY SAMPLE

The patients who participated in this component of the study were recruited from

the sample of patients who participated in the first component of the study. Thus, these patients were acutely ill during their hospital stay, as discussed in section 5.1. Six weeks after hospital stay, all the patients had already been discharged and were living in the community, thus it was possible to measure these same patients' HRQOL when their condition had improved.

In total, 35 of the 61 potential subjects participated in this component of the study. Others were not available during the admission or did not have time during the admission to respond to the questionnaires. These patients were excluded from the analysis.

5.3.2 HRQOL MEASURED DURING HOSPITAL STAY

A sufficient number of patients completed the CAQ-A and the CAQ-B to provide profiles of HRQOL scores of children with acute asthma symptoms. The CAQ-A has previously been administered to four study samples.

French *et al.*[162] have reported that CAQ-A Quality of Living domain scores do not correlate with disease severity. This study provides further evidence that this may be true. The mean Quality of Living domain score of 15 children who completed the questionnaire in the current study was 31.07 ± 2.67 and the range of possible scores in this domain is 10 (low Quality of Living) to 40 (high Quality of Living). This mean

score was similar to the other scores previously reported, although severity differed among the groups.[99]

French *et al.*[99] previously reported that the DIS domain scores appeared to correlate with disease severity. Although the sample size in the present study was too small to compare the Distress domain scores of patients with less severe asthma with the Distress domain scores of patients with more severe asthma, it has been postulated that the *generic* questions within the CAQ-A may make the instrument less responsive to differences in patients' clinical asthma severity. These generic items may have less discriminative and/or evaluative properties than disease-specific items for two reasons. First, as discussed by Rutishauser *et al.*,[163] the way the generic items are framed in the instrument may not help to focus the children's perception about the importance of asthma symptoms on their HRQOL. For example, generic items in the instrument ask children to evaluate activities without instructing them to interpret the items in relation to their health status. These activities may or may not have been performed by the patient. Since children are not instructed to interpret the activities in relation to their health status, their answers are more likely to have been influenced by personal preference than the status of their disease. Second, some of the items themselves are not expected to be affected by asthma severity. For example, the CAQ includes items related to children's reading books. Since reading books is a physical activity that is not expected to be influenced much by asthma, these items may help explain the instrument's lack of discriminative and evaluative properties. Another explanation is that children's

actual HRQOL may correlate poorly with their clinical status of asthma.[80] However, many instruments have been shown to be responsive to changes in patients. It is also possible that children's HRQOL improves during a hospital admission compared to when they are in the community because parents and healthcare providers may provide more attention to them. Therefore, it would be difficult to measure a subsequent improvement in patients' HRQOL after they are discharged because their baseline HRQOL would have already improved when they were in the hospital. Methods of assessment and procedural differences could also have confounded the results. In the study be French *et al.*,[99] the administration of the questionnaires were not supervised by the investigators. In the present study, the patients were observed during the administration, and the investigator was present to answer any questions about the questionnaires. However, it is not known what effect the presence or absence of a parent or the investigator could have on the children's reported HRQOL. More studies will be needed to examine the effect of parents or investigators on children's HRQOL scores.

In the present study, 14 children who were between eight and 11 years of age completed the CAQ-B. The CAQ-B scores for the Active Quality of Living domain and the Passive Quality of Living domain of patients in the present study (Table 27) were also similar to the scores that have been previously reported.[99] The Active Quality of Living score and the Passive Quality of Living domain score in the present study were 28.3 ± 4.2 (median = 29.5) and 17.4 ± 2.3 (median = 17.5) respectively. These scores were similar to the other median scores previously reported, even though the patients in the

present study were patients with more severe asthma symptoms. It appears from these data that these domains do not correlate well with patients' severity of asthma symptoms and that these domains do not have good discriminative properties.

A possible reason that the Active Quality of Living and the Passive Quality of Living domains correlate poorly with asthma severity is that the items in the CAQ-B do not ask children to answer questions in relation to any particular time frame. For example, one of the items in the Active Quality of Living domain of the CAQ-B is "Which picture describes how you feel when you play games outside (like ball games) with your class?" Since the child is not instructed to answer the question in relation to a particular time frame, the item could be assessing children's enjoyment of these activities, rather than the impact of asthma symptoms on their enjoyment of these activities.

An unexpected observation was reported in Distress and Severity domain scores. In the present study, the Distress domain score was only 15.9 ± 4.7 whereas in previous studies[99] the Distress domain score has been in the range of 23 to 25 among patients with mild to severe symptoms. The Distress domain is designed to measure feelings about asthma symptoms. It was expected that the children in this study with more severe symptoms would report more Distress and have a higher Distress domain score than patients with less mild symptoms. However, patients in this study actually reported less Distress than patients in the previous studies with less severe asthma symptoms.

Although changes in PAQLQ scores have been previously reported, actual PAQLQ scores have not yet been reported in the literature. This is the first study to report PAQLQ scores of children with symptoms of asthma severe enough to require hospital admission. The mean score and the individual domain scores were in the middle of the range, which is 1 (low) to 7 (high), for the PAQLQ. As shown in Table 29, the mean PAQLQ score of the children in the current study with severe asthma symptoms in hospital was 4.0 ± 1.3, and the individual mean domain scores ranged from 3.9 to 4.4. Standard deviations of individual domains also ranged from 1.3 to 1.5.

The children's "QOLiF" scores measured when the children were acutely ill in hospital are shown in Table 31 and Table 32. With this level of severity, the children's and the parent's mean scores were 5.2 ± 1.7 and 5.2 ± 1.5 respectively. The mean scores were already at the higher end of the range, which was 1 (low HRQOL) to 7 (better HRQOL). Although both instruments use a 7-point likert scale for responses to each item, the primary difference between the "QOLiF" and the PAQLQ are that the "QOLiF" incorporates a graphic image with each response choice. It is possible that these graphic images may be interpreted differently compared to the textual response items of the PAQLQ. These differences in interpretation could potentially have skewed the children's responses to the higher end of the scale.

The variability observed in the "QOLiF" scores were also slightly higher

than that observed with the PAQLQ, despite having the same range of possible scores. Again, if the graphical images are less accurate descriptive response items compared to textual descriptions, it is possible that they may have contributed to the increased variance observed in the responses to the "QOLiF." Further studies will need to be done to evaluate the precision of textual descriptions compared to graphical descriptions of response items in HRQOL questionnaires.

5.3.3 CHANGE IN HRQOL SIX WEEKS AFTER HOSPITAL STAY

It was initially intended that the responsiveness of the CAQ would be investigated. However, with such a small sample of patients, it was not possible to examine the responsiveness of the CAQ to changes in patients' clinical status. Further studies will be needed to examine the evaluative properties of this instrument. Since the CAQ has a component for each age sub-group, a sufficient number of patients for each age subgroup will be required.

The PAQLQ scores improved six weeks after hospital discharge compared to scores reported when children were in the hospital. These results (shown in Table 33) are consistent with other studies that have reported that health related quality of life instruments can be sensitive to changes in patients' clinical status. [89]

This is the first study to report the effect size of the change in the overall

PAQLQ score and for each of the domains for a group of children who were acutely ill in the hospital and whose clinical condition improved enough for them to be in the community. The effect size for overall HRQOL in these patients was 1.5. The effect sizes for the symptom domain, activities domain, and the emotional function domain were 1.4, 2.2, and 2.1, respectively.

Juniper *et al.*.[80] have previously reported Guyatt's Index of Responsiveness[93] for the PAQLQ. Guyatt's Index of Responsiveness is calculated by taking the ratio of the minimal clinically important difference (MCID) to the variability in stable subjects, which is the square root of two times the mean square error of scores in stable subjects.[93] The MCID is defined as the "smallest difference in score in the domain of interest which patients perceive as beneficial and which would mandate, in the absence of troublesome side effects and excessive costs, a change in the patient's management."[1] It is estimated by taking the mean change in score for each domain of an instrument where patients had a Global Rating of Change[1] score of 1 to 3. In the study (described in 2.2.5.1), the PAQLQ, the Feeling Thermometer, and a clinical asthma control questionnaire were administered to the children after 1 week, 5 weeks, and 9 weeks. Guyatt's Index of Responsiveness was calculated for the children whose asthma was classified as changed. The index of responsiveness based on the minimal clinically important difference (MCID) and the pooled within subject standard deviation of all patients in the study was 0.59. Although Juniper *et al.*[80] did not report effect sizes, they reported that the mean change in scores for children whose condition changed were 0.79, 0.90, 0.81,

and 0.70 for the overall HRQOL, activity domain, symptom domain, and emotion domain, respectively.

In the current study, the mean changes in scores were 1.8, 1.7, 1.6, and 1.9 for overall HRQOL, the activity domain, symptom domain, emotional domain, respectively. The mean changes in scores for overall HRQOL and for the domains were larger in the present study compared to the changes reported in the study be Juniper *et al.*[80] The larger change was expected because the clinical change experienced by patients in the current study was larger than the clinical change experienced by patients in the study by Juniper *et al.*[80] In the current study, all patients who participated were considered to have had severe asthma initially and all experienced a similar clinical improvement. The children's asthma status generally changed from being very severe (hospitalized) to well (discharged from hospital). On the other hand, in the study by Juniper *et al.* the sample population had a range of asthma severity at the start of the study. The degree of clinical change was not as large as the one in the current study because children were not treated in the same manner. Furthermore, in Juniper's study, children whose condition only changed moderately were included. Thus it was expected that a larger change in score would be observed in the present study. These results provide evidence that the PAQLQ is responsive among patients with severe asthma and that it is an instrument that appears to be responsive to large changes in asthma severity.

Although the current study did not report the MCID, the MCID's for each

domain of the PAQLQ and for the overall PAQLQ has already been reported by Juniper *et al.*[80] They are 0.42, 0.70, 0.54, and 0.28 for the overall HRQOL, the activity domain, symptom domain, emotional domain, respectively. Thus, all of the changes in the present study can be considered to be clinically significant, if we assume that the MCID was properly estimated by Juniper *et al.* However, it is possible that Juniper *et al.* may have inaccurately estimated the MCID and thus obtained an inaccurate estimate of the index of responsiveness using Guyatt's method. In order to calculate the MCID, it was necessary to compare the children's scores with their Global Rating of Change score. However, since there was low agreement about which patients actually improved or stayed the same then the index of responsiveness based on Guyatt's method may also have been inaccurate. The current study is important because it provides an additional measure of instrument responsiveness for the PAQLQ.

It was also observed that variability in children's mean overall PAQLQ scores and PAQLQ scores in each domain increased after hospital discharge, as shown in Table 33. The increased variability observed in the PAQLQ scores after hospital discharge may have represented variability in the children's degree of clinical improvement after being discharged from the hospital. During hospital admission, children were considered to have had severe asthma symptoms and were considered to have been in their worst asthmatic state. Furthermore, the children's daily activities and environments were all very similar in the hospital environment. However, after being discharged, the children returned to their homes, where their environments were not similar. Their

degree of clinical improvement may also have varied. Some children may have had mild intermittent, mild persistent, or moderate asthma in the community.

These effect sizes observed in the PAQLQ scores were also much larger than the effect sizes observed with the "QOLiF." The "QOLiF" was investigated as an interactive approach to HRQOL assessment using individualized items to improve the responsiveness of the instrument. However, in the present study, overall instrument scores, and scores of each domain of the QOLiF did not appear to be as responsive as the PAQLQ individual domains or to the overall HRQOL PAQLQ scores to changes in patients' clinical asthma severity. A possible explanation for the lack of responsiveness exhibited by the QOLiF is that it had a variable number of items. Without a limit to the number of items that a patient could identify as important to him or her, a patient could potentially identify a few relevant items, and a large number of weakly relevant items. Since item domain scores are equally weighted, a large number of weakly relevant items could attenuate a large change in score among the more relevant items. However, even the three most important physical domain items of the QOLiF among a group of matched patients did not seem to be as responsive as the five Activity domain items of the PAQLQ. This was not expected since the five Activity domain items of the PAQLQ are very similar to the items of the QOLiF. In fact, the first three individualized items of the PAQLQ are similar to the physical domain items of the QOLiF. The first three individualized items of the PAQLQ ask the patient to rate how much they have been bothered by asthma in performing each of three patient-identified items. The main

difference between the PAQLQ Activity domain and the QOLiF physical domain is the addition of 2 items in the PAQLQ. One item asks the child to rate how often asthma makes him or her feel angry. The other item asks the child to think about all the activities that he or she did in the last week, and to rate how much he or she had been bothered by asthma doing these activities. The addition of these two items may account for the increased responsiveness of the PAQLQ compared to the QOLiF.

These data suggest that the approach to HRQOL assessment using a large number of individualized items may not improve the responsiveness of questionnaires. It appears that the PAQLQ was more responsive than the QOLiF at measuring changes in HRQOL in children. Another explanation is that children's HRQOL in the current study actually did not change as much as the PAQLQ suggested. Rutishauser *et al.*[163] has commented that the PAQLQ's focus on emotional well-being and symptoms may contribute to the instrument's good responsiveness, but its lack of a social domain as well as other psychosocial issues undermines the validity of the instrument. Perhaps if the instrument included more items related to these issues, it would not be as responsive as it seems. Further studies will be required to provide more evidence of the validity of the PAQLQ to measure HRQOL in pediatric patients with asthma.

6. CONCLUSIONS

Using a standard set of objective criteria for the evaluation of drug-related hospital admissions and an expert panel trained in the therapeutic management of asthma, this study has found that 84% of pediatric patients admitted to hospital for asthma or asthma-related symptoms were drug-related. However, 45.5% of these cases were also associated with some evidence of a respiratory tract infection, which could also have explained the symptoms.

Most children admitted to hospital typically were inadequately treated prior to their hospital admissions according to the National Institutes of Health (NIH) National Heart Lung and Blood Institute Expert Panel Report II Guidelines. The majority of cases involved inadequate use of long-term control medications, and inappropriate management of acute exacerbations. For example, 82% of patients who had "mild persistent" asthma did not report receiving daily anti-inflammatory therapy, and only three of 25 patients who had evidence of requiring oral corticosteroids reported taking them prior to being admitted to hospital. Furthermore, it was found that these drug-related admissions were deemed to be preventable. In the future, prospective randomized placebo controlled trials using more objective evidence about patients drug therapies may provide further evidence of the effectiveness of strict adherence to international guidelines on the incidence of hospital admissions in children with asthma. In future studies, drug therapies should be verified through the use of objective prescription databases.

The responsiveness of the PAQLQ and a more patient-specific approach to HRQOL assessment have been reported. The PAQLQ was responsive to the changes in clinical status that patients with asthma experienced when they were hospitalized as compared to when they were not hospitalized. However, the patient-specific approach to HRQOL assessment did not appear to improve the responsiveness of a questionnaire. Further studies with a larger number of patients will be necessary to assess responsiveness of the CAQ and to assess the responsiveness and validity of the patient-specific approach to HRQOL assessment.

7. REFERENCES

1. Jaeschke, R., Singer, J., Guyatt, G.H. Measurement of Health Status Ascertaining the Minimal Clinically Important Difference *Controlled Clinical Trials*, 10:407-415, 1989.
2. Hallas, J., Harvald, B., Gram, L.F., Grodum, E., Brosen, K., Haghfelt, T., Damsbo, and N. Drug-related hospital admissions: the role of definitions and intensity of data collection, and the possibility of prevention. *Journal of Internal Medicine* 228(2):83-90, 1990.
3. Dedhiya, S. and Kong, S.X. Quality of life: an overview of the concept and measures. *Pharmacy World & Science* 17(5):141-148, 1995.
4 Schipper H, Clinch J, Powell V. Definitions and Conceptual Issues. In: Spilker B, ed. Quality of Life Assessments in Clinical Trials, New York, Raven Press, 1990; pp. 11-35.
5. Anonymous. Forecasted state-specific estimates of self-reported asthma prevalence--United States, 1998. *MMWR.Morb.Mortal.Wkly.Rep.* 47(47):1022-1025, 1998.
6. Nelson, D.R., Sachs, M.I., and O'Connell, E.J. Approaches to acute asthma and status asthmaticus in children. *Mayo Clin.Proc.* 64(11):1392-1402, 1989.
7. Taylor, W.R. and Newacheck, P.W. Impact of childhood asthma on health. *Pediatrics* 90(5):657-662, 1992.
8. Howarth, P.H. What is the nature of asthma and where are the therapeutic targets? *Respir.Med.* 91 Suppl A:2-8, 1997.
9. Mitchell EA International Trends in Hospital Admission Rates For Asthma. *Arch Dis Child* 60:376-378, 1985.
10. Meza, C. and Gershwin, M.E. Why is asthma becoming more of a problem? *Curr Opin Pulm Med* 3(1):6-9, 1997.
11. Arrighi, H.M. US asthma mortality: 1941 to 1989. *Annals of Allergy, Asthma, & Immunology* 74(4):321-326, 1995.
12. Sly, R.M. Changing asthma mortality and sales of inhaled bronchodilators and anti-asthmatic drugs. *Annals of Allergy* 73(5):439-443, 1994.
13. Anonymous. Asthma mortality and hospitalization among children and young adults--United States, 1980-1993. *MMWR - Morbidity & Mortality Weekly Report* 45(17):350-353, 1996.
14. Gergen PJ, Weiss KB. Changing patterns of asthma hospitalization among children: 1979 to 1987. *JAMA* 1990; 264: 1688-92
15. Macarthur, C., Calpin, C., Parkin, P.C., and Feldman, W. Factors associated with pediatric asthma readmissions. *Journal of Allergy & Clinical Immunology* 98(5 Pt 1):992-993, 1996.
16. Mao, Y., Semenciw, R., Morrison, H., MacWilliam, L., Davies, J., and Wigle, D. Increased rates of illness and death from asthma in Canada. *Canadian Medical Association Journal* 137(7):620-624, 1987.

17. Johansen, H., Dutta, M., Mao, Y., Chagani, K., and Sladecek, I. An investigation of the increase in preschool-age asthma in Manitoba, Canada. *Health Reports* 4(4):379-402, 1992.
18. Wilkins K, Mao Y. Trends in rates of admission to hospital and death from asthma among children and young adults in Canada during the 1980s. Can Med Assoc J 1993; 148(2):185-190.
19. Millar W.J., Hill, G.B. Childhood Asthma. *Health Reports* 10(3):9-21, 1998 Winter.
20. Dales RE. Raizenne M. el-Saadany S. Brook J. Burnett R. Prevalence of childhood asthma across Canada. *International Journal of Epidemiology. 23(4):775-81, 1994 Aug*
21. Kesten S. Rebuck AS. Chapman KR. Trends in asthma and chronic obstructive pulmonary disease therapy in Canada, 1985 to 1990. *Journal of Allergy & Clinical Immunology. 92(4):499-506, 1993 Oct.*
22. Infante-Rivard C. Esnaola Sukia S. Roberge D. Baumgarten M. The changing frequency of childhood asthma. *Journal of Asthma. 24(5):283-8, 1987.*
23. Barnes, P.J. Current therapies for asthma. Promise and limitations. *Chest* 111(2 Suppl):17S-26S, 1997.
24. Busse, W.W. Inflammation in asthma: the cornerstone of the disease and target of therapy. *J.Allergy Clin.Immunol.* 102(4 Pt 2):S17-22, 1998.
25. Selroos, O., Pietinalho, A., Lofroos, A.B., and Riska, H. Effect of early vs. late intervention with inhaled corticosteroids in asthma. *Chest* 108(5):1228-1234, 1995.
26. Barnes PJ. Inhaled glucocorticosteroids for asthma. N Engl J Med 1995;332(13):868-75.
27. Mellis CM, Peat JK, Woolcock AJ. The costs of asthma: can it be reduced? Pharmacoeconomics 1993;3:205-19.
28. Gottlieb, D.J., Beiser, A.S., and O'Connor, G.T. Poverty, race, and medication use are correlates of asthma hospitalization rates. A small area analysis in Boston. *Chest* 108(1):28-35, 1995.
29. Wennergren, G., Kristjansson, S., and Strannegard, I.L. Decrease in hospitalization for treatment of childhood asthma with increased use of antiinflammatory treatment, despite an increase in prevalence of asthma. *J.Allergy Clin.Immunol.* 97(3):742-748, 1996.
30. Suissa, S., Ernst, P., Benayoun, S., Baltzan, M., Cai, B. Low-dose Inhaled Corticosteroids and the Prevention of Death From Asthma. *The New England Journal of Medicine* 343(5):332-336, 2000.
31. Barnes, P.J. Efficacy of inhaled corticosteroids in asthma. *J.Allergy Clin.Immunol.* 102(4 Pt 1): , 1998.
32. Guidelines for the Diagnosis and Management of Asthma. NIH Publication 97-4051, National Institutes of Health, National Heart, Lung, and Blood Institute, 1997.
33. Ernst, P., Fitzgerald, J.M., Spier S., Canadian Asthma Consensus Conference Summary of Recommendations. *Canadian Respiratory Journal* 3 (2):89-100, 1996.

34. British Thoracic Association. Death From Asthma in Two Regions in England. *British Medical Journal* 33:1251-1255, 1982.
35. Einarson, T.R. Drug-related hospital admissions. *Annals of Pharmacotherapy* 27(7-8):832-840, 1993.
36. Anonymous. Asthma care in the U.S.: understanding the effectiveness of health care delivery and barriers to good clinical outcomes. Proceedings of a workshop held in San Diego, California, March 1991. *Medical Care* 31(3 Suppl):MS1-130, 1993.
37. Hartert, T.V., Windom, H.H., Peebles, R.S.,Jr., Freidhoff, L.R., and Togias, A. Inadequate outpatient medical therapy for patients with asthma admitted to two urban hospitals. *American Journal of Medicine* 100(4):386-394, 1996.
38. Tettersell, M.J. Asthma patients' knowledge in relation to compliance with drug therapy. *Journal of Advanced Nursing* 18(1):103-113, 1993.
39. Laumann JM, Bjornson DC. Treatment of Medicaid Patients with Asthma: Comparison with Treatment Guidelines Using Disease-Based Drug Utilization Review Methodology. *The Annals of Pharmacotherapy 32:1290-11294, 1998.*
40. Geppert, E.F., Lester, L.A., and Ober, C. Prioritizing asthma research: the need to investigate childhood asthma. *American Journal of Respiratory & Critical Care Medicine* 151(5):1294-1295, 1995
41. Li, J.T. and O'Connell, E.J. Clinical evaluation of asthma. *Annals of Allergy, Asthma, & Immunology* 76(1):1-13; quiz 13-5, 1996.
42. Hilton S: Report on National Asthma Campaign: Asthma in Teenagers Workshop, 2-3, 1991.
43. Milgrom, H., Bender, B., Ackerson, L., Bowry, P., Smith, B., and Rand, C. Noncompliance and treatment failure in children with asthma. *Journal of Allergy & Clinical Immunology* 98(6 Pt 1):1051-1057, 1996.
44. Bender, B., Milgrom, H., Rand, C., and Ackerson, L. Psychological factors associated with medication nonadherence in asthmatic children. *J.Asthma* 35(4):347-353, 1998.
45. McKenney JM. Harrison WL. Drug-related hospital admissions. *American Journal of Hospital Pharmacy. 33(8):792-5, 1976 AUG.*
46. Roughead EE, Gilbert AL, Primrose JG, Sansom LN. Drug-related hospital admissions: a review of Australian studies published 1988-1996. *Medical Journal of Australia.* 168(8):405-8, 1998 Apr 20.
47. Karch, F.E., Smith, C.L., Kerzner, B., Mazzullo, J.M., Weintraub, M., and Lasagna, L. Adverse drug reactions-a matter of opinion. *Clinical Pharmacology & Therapeutics* 19(5 Pt 1):489-492, 1976.
48. Naranjo, C.A., Busto, U., Sellers, E.M., Sandor, P., Ruiz, I., Roberts, E.A., Janecek, E., Domecq, C., and Greenblatt, D.J. A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology & Therapeutics* 30(2):239-245, 1981.
49. Bergman, U. and Wiholm, B.E. Drug-related problems causing admission to a medical clinic. *Eur.J.Clin.Pharmacol.* 20(3):193-200, 1981.

50. Larmour, I. and McGrath, B. Hospital admissions due to drug reactions. *Medical Journal of Australia* 155(3):204, 1991.
51. Hallas, J., Haghfelt, T., Gram, L.F., Grodum, E., and Damsbo, N. Drug-related admissions to a cardiology department; frequency and avoidability. *Journal of Internal Medicine* 228(4):379-384, 1990.
52. Hallas, J., Gram, L.F., Grodum, E., Damsbo, N., Brosen, K., Haghfelt, T., Harvald, B, Beck-Nielsen, J., Worm, J., Jensen, K.B., and et al Drug-related admissions to medical wards: a population based survey. *British Journal of Clinical Pharmacology* 33(1):61-68, 1992.
53. Hallas, J., Davidsen, O., Grodum, E., Damsbo, N., and Gram, L.F. Drug-related illness as a cause of admission to a department of respiratory medicine. *Respiration* 59(1):30-34, 1992.
54. Stanton, L.A., Peterson, G.M., Rumble, R.H., Cooper, G.M., and Polack, A.E. Drug-related admissions to an Australian hospital. *Journal of Clinical Pharmacy & Therapeutics* 19(6):341-347, 1994.
55. Karch, F.E. and Lasagna, L. Adverse drug reactions. A critical review. *JAMA* 234(12):1236-1241, 1975.
56. Lozano, P., Fishman, P., VonKorff, M., and Hecht, J. Health care utilization and cost among children with asthma who were enrolled in a health maintenance organization. *Pediatrics* 99(6):757-764, 1997.
57. Mitchell EA, Bland JM, Thompson JMD. Risk factors for readmission to hospital for asthma in childhood. *Thorax* 1994;49:33-6.
58. Yosselson-Superstine S. Weiss T. Drug-related hospitalization in paediatric patients. *Journal of Clinical & Hospital Pharmacy*. 7(3):195-203, 1982 Sep.
59. Abduelrhman, E.M. and Loftus, B.G. Childhood asthma, can admissions be avoided? *Irish Medical Journal* 86(1):22-23, 1993.
60. Koch-Weser, J., Sellers, E.M., and Zacest, R. The ambiguity of adverse drug reactions. *European Journal of Clinical Pharmacology* 11(2):75-78, 1977.
61. Sublett, J.L., Pollard, S.J., Kadlec, G.J., and Karibo, J.M. Non-compliance in asthmatic children: a study of theophylline levels in a pediatric emergency room population. *Ann.Allergy* 43(2):95-97, 1979.
62. Testa, M.A. and Nackley, J.F. Methods for quality-of-life studies. *Annual Review of Public Health* 15:535-559, 1994.
63. Ware, J.E. Conceptualizing and Measuring Generic Health Outcomes. *Cancer*: 67(suppl):3, 1991.
64 Aaronson, N.K. and Beckmann, J. (eds) (1987). *The Quality of Life of Cancer Patients,* New York: Raven.
65. Jones, P.W. Quality of life measurement in asthma. *Eur.Respir.J.* 8(6):885-887, 1995.
66. Blaiss, M.S. Outcomes analysis in asthma. *JAMA* 278(22):1874-1880, 1997.
67. Juniper, E.F. Effect of asthma on quality of life. *Can.Respir.J.* 5 Suppl A:77A-84A, 1998.

68. McSweeny, A.J. and Creer, T.L. Health-related quality-of-life assessment in medical care. *Dis.Mon.* 41(1):1-71, 1995.
69. Jones, P.W., Quirk, F.H., and Baveystock, C.M. Why quality of life measures should be used in the treatment of patients with respiratory illness. *Monaldi.Arch.Chest Dis.* 49(1):79-82, 1994.
70. Osman, L. and Silverman, M. Measuring quality of life for young children with asthma and their families. *Eur.Respir.J.Suppl.* 21:35s-41s, 1996.
71. Jones, P.W., Quirk, F.H., and Baveystock, C.M. Why quality of life measures should be used in the treatment of patients with respiratory illness. *Monaldi.Arch.Chest Dis.* 49(1):79-82, 1994.
72. Testa, M.A. and *Simonson*, D.C. Assesment of quality-of-life outcomes. *New England Journal of Medicine* 334(13):835-840, 1996.
73. Guyatt, G.H., Juniper, E.F., Griffith, L.E., Feeny, D.H., and Ferrie, P.J. Children and adult perceptions of childhood asthma. *Pediatrics* 99(2):165-168, 1997.
74. Rosenbaum, P., Cadman, D. and Kiplalani, H. (1990). Pediatrics: assessing Quality of Life. In Spilker, B. (ed.). *Quality of Life in Clinical Trials*. Raven Press: New York.
75. Marra CA, Levine M, McKerrow R, Carleton BC. Overview of health-related quality-of-life measures for pediatric patients: Application in the assessment of pharmacotherapeutic and pharmacoeconomic outcomes. *Pharmacotherapy* 1996;16(5):879-888.
76. Bender, B.G. Measurement of quality of life in pediatric asthma clinical trials. *Annals of Allergy, Asthma, & Immunology* 77(6):438-45; quiz 446-7, 1996.
77. Mishoe, S.C., Baker, R.R., Poole, S., Harrell, L.M., Arant, C.B., and Rupp, N.T. Development of an instrument to assess stress levels and quality of life in children with asthma. *J.Asthma* 35(7):553-563, 1998.
78. Carmines, EG., Zeller, RA. Reliability and Validity Assessment, Sage Publications, Newbury Park, 1979.
79. Christie MJ, French DJ, Sowden AJ. Development of Child-Centered Disease-Specific Questionnaires for Living with Asthma. *Psychosomatic Medicine* 55:541-548 (1993).
80. Juniper, E.F., Guyatt, G.H., Feeny, D.H., Ferrie, P.J., Griffith, L.E., and Townsend, M. Measuring quality of life in children with asthma. *Quality of Life Research* 5(1):35-46, 1996.
81. Juniper, E.F., Guyatt, G.H., Feeny, D.H., Griffith, L.E., and Ferrie, P.J. Minimum skills required by children to complete health-related quality of life instruments for asthma: comparison of measurement properties. *Eur.Respir.J.* 10(10):2285-2294, 1997.
82. Juniper, E.F., Guyatt, G.H., Feeny, D.H., Ferrie, P.J., Griffith, L.E., and Townsend, M. Measuring quality of life in the parents of children with asthma. *Quality of Life Research* 5(1):27-34, 1996.
83. Kirsher B., Guyatt G.H., A methodological framework for assessing health indices. *J Chron Dis* 38:27-36, 1985.

84. Guyatt G.H., Bombardier C., Tugwell P.X., Measuring disease specific quality of life in clinical trials. *Can Med Assoc J* 134: 889-95, 1985.
85. Torrance GW. Measurement of health state utilities for economic appraisal. *J Health Economics* 5:1-30, 1986.
86. Juniper, E.F., Guyatt, G.H., Willan, A., and Griffith, L.E. Determining a minimal important change in a disease-specific Quality of Life Questionnaire. *Journal of Clinical Epidemiology* 47(1):81-87, 1994.
87. Landis, J.R. and Koch, G.G. The measurement of observer agreement for categorical data. *Biometrics* 33(1):159-174, 1977.
88. Lomas, J., Pickard, L., Mohide, A. Patient Versus Clinician Item Generation for Quality of Life Measures. *Medical Care* 25(8): 764-769, 1987.
89. Liang, M.H. Evaluating measurement responsiveness. *Journal of Rheumatology* 22(6):1191-1192, 1995.
90. Deyo, R.A. and Centor, R.M. Assessing the responsiveness of functional scales to clinical change: an analogy to diagnostic test performance. *Journal of Chronic Diseases* 39(11):897-906, 1986.
91. Kazis, L.E., Anderson, J.J., and Meenan, R.F. Effect sizes for interpreting changes in health status. *Medical Care* 27(3 Suppl):S178-89, 1989.
92. Liang, M.H., Fossel, A.H., and Larson, M.G. Comparisons of five health status instruments for orthopedic evaluation. *Medical Care* 28(7):632-642, 1990.
93. Guyatt, G., Walter, S., and Norman, G. Measuring change over time: assessing the usefulness of evaluative instruments. *Journal of Chronic Diseases* 40(2):171-178, 1987.
94. Wolf FM. Meta-analysis: quantitative methods for research synthesis. Beverly Hills: Sage Publications, 1986.
95. Cohen J *Statistical Power Analysis for the Behavioural Sciences*, Hillsdale:Lawrence Erlbaum Associates, 1988.pp. 1-566.
96. Warner, J.O., Gotz, M., Landau, L.I., Levison, H., Milner, A.D., Pedersen, S., and Silverman, M. Management of asthma: a consensus statement. *Arch.Dis.Child* 64(7):1065-1079, 1989.
97. Johnston, S.L., Pattemore, P.K., Sanderson, G., Smith, S., Lampe, F., Josephs, L., Symington, P., O'Toole, S., Myint, S.H., Tyrrell, D.A., and et al. Community study of role of viral infections in exacerbations of asthma in 9-11 year old children. *BMJ* 310(6989):1225-1229, 1995.
98. Nicholson, K.G., Kent, J., and Ireland, D.C. Respiratory viruses and exacerbations of asthma in adults. *BMJ.* 307(6910):982-986, 1993.
99. French DJ, Christie MJ, and Sowden, AJ. The Reproducibility of the Childhood Asthma Questionnaires: Measures of Quality of Life for children with Asthma Aged 4 to 16 Years. *Quality of Life Research* 3:215-224, 1994.
100. Illustrated Guide to Diagnostic Tests, *Springhouse Corp, Springhouse, 1994.*
101. Hooker, E.A., O'Brien, D.J., Danzl, D.F., Barefoot, J.A., and Brown, J.E. Respiratory rates in emergency department patients. *J.Emerg.Med.* 7(2):129-132, 1989.

102. Hooker, E.A., Danzl, D.F., Brueggmeyer, M., and Harper, E. Respiratory rates in pediatric emergency patients. *J.Emerg.Med.* 10(4):407-410, 1992.
103. Iliff A, Lee VA: Child Dev 1952; 23:237.
104. Nadas A. *Pediatric Cardiology*, Ed. 3. WB Saunders, Philadelphia, 1976.
105. Martinez, F.D. Definition of pediatric asthma and associated risk factors. *Pediatr.Pulmonol.Suppl.* 15:9-12, 1997.
106. Brugman, S.M. and Larsen, G.L. Asthma in infants and small children. *Clin.Chest Med.* 16(4):637-656, 1995.
107. Aherne W, Bird T, court SDM, et al. Pathological changes in virus infections of the lower respiratory tract in children. *J Clin Pathol* 23:7-18, 1970.
108. Freid, V.M., Makuc, D.M., and Rooks, R.N. Ambulatory health care visits by children: principal diagnosis and place of visit.. Vital.Health Stat. (137):1-23, 1998.
109. Laurier, C., Kennedy, W., Malo, J.L., Par, M., Labb, D., and Archambault, A. Rate and cost of hospitalizations for asthma in Quebec: An analysis of 1988/89, 1989/90 and 1994/95 data. *Chronic.Dis.Can.* 20(2):82-88, 1999.
110. Johnston, S.L., Bardin, P.G., and Pattemore, P.K. Viruses as precipitants of asthma symptoms. III. Rhinoviruses: molecular biology and prospects for future intervention. *Clinical & Experimental Allergy* 23(4):237-246, 1993.
111. Johnston, S.L., Pattemore, P.K., Sanderson, G., Smith, S., Campbell, M.J., Josephs, LK, Cunningham, A., Robinson, B.S., Myint, S.H., Ward, M.E., Tyrrell, D.A., and Holgate, S.T. The relation between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *American Journal of Respiratory & Critical Care Medicine* 154(3 Pt 1):654-660, 1996.
112. Reid, M.J., Moss, R.B., Hsu, Y.P., Kwasnicki, J.M., Commerford, T.M., and Nelson, B.L. Seasonal asthma in northern California: allergic causes and efficacy of immunotherapy. *J.Allergy Clin.Immunol.* 78(4 Pt 1):590-600, 1986.
113. Sears, M.R., Herbison, G.P., Holdaway, M.D., Hewitt, C.J., Flannery, E.M., and Silva, P.A. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin.Exp.Allergy* 19(4):419-424, 1989.
114. Jain, P. and Kavuru, M.S. A practical guide for peak expiratory flow monitoring in asthma patients. *Cleve.Clin.J.Med.* 64(4):195-202, 1997.
115. Jackson, A.C. Accuracy, reproducibility, and variability of portable peak flow meters. *Chest* 1995; 107:648-51.
116. Wall MA, Olson D, Bonn BA, Creelman T, Buist AS. Lung function in North American Indian children: refernce standards for spirometry, maximal expiratory flow volume curves, and peak expiratory flow. *Am Rev Respir Dis* 1982; 125:158-162.
117. Illustrated Guide to Diagnostic Tests, Springhouse Corp, Springhouse, 1994.
118. Holmgren, D. and Sixt, R. Transcutaneous and arterial blood gas monitoring during acute asthmatic symptoms in older children. *Pediatr.Pulmonol.* 14(2):80-84, 1992.
119. Ordonez, G.A., Phelan, P.D., Olinsky, A., and Robertson, C.F. Preventable factors in hospital admissions for asthma. *Arch.Dis.Child* 78(2):143-147, 1998.

120. Verberne, A.A. Managing symptoms and exacerbations in pediatric asthma. *Pediatr.Pulmonol.Suppl.* 15:46-50, 1997.
121. Ernst, P., Spitzer, W.O., Suissa, S., Cockcroft, D., Habbick, B., Horwitz, R.I., Boivin, J.F., McNutt, M., and Buist, A.S. Risk of fatal and near-fatal asthma in relation to inhaled corticosteroid use. *JAMA* 268(24):3462-3464, 1992.
122. Haahtela, T., Jarvinen, M., Kava, T., Kiviranta, K., Koskinen, S., Lehtonen, K., Nikander, K., Persson, T., Reinikainen, K., Selroos, O., and et al. Comparison of a beta 2-agonist, terbutaline, with an inhaled corticosteroid, budesonide, in newly detected asthma. *N.Engl.J.Med.* 325(6):388-392, 1991.
123. Juniper, E.F., Kline, P.A., Vanzieleghem, M.A., Ramsdale, E.H., O'Byrne, P.M., and Hargreave, F.E. Long-term effects of budesonide on airway responsiveness and clinical asthma severity in inhaled steroid-dependent asthmatics. *Eur.Respir.J.* 3(10):1122-1127, 1990.
124. Meltzer, E.O., Orgel, H.A., Ellis, E.F., Eigen, H.N., and Hemstreet, M.P. Long-term comparison of three combinations of albuterol, theophylline, and beclomethasone in children with chronic asthma. *J.Allergy Clin.Immunol.* 90(1):2-11, 1992.
125. Svedmyr, J., Nyberg, E., Asbrink-Nilsson, E., and Hedlin, G. Intermittent treatment with inhaled steroids for deterioration of asthma due to upper respiratory tract infections. *Acta Paediatr.* 84(8):884-888, 1995.
126. van Essen-Zandvliet, E.E., Hughes, M.D., Waalkens, H.J., Duiverman, E.J., Pocock, SJ, and Kerrebijn, K.F. Effects of 22 months of treatment with inhaled corticosteroids and/or beta-2-agonists on lung function, airway responsiveness, and symptoms in children with asthma. The Dutch Chronic Non-specific Lung Disease Study Group. *Am.Rev.Respir.Dis.* 146(3):547-554, 1992.
127. Donahue, J.G., Weiss, S.T., Livingston, J.M., Goetsch, M.A., Greineder, D.K., Platt, and R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA* 277(11):887-891, 1997.
128. Horowitz, L., Zafrir, O., Gilboa, S., Berger, I., and Wolach, B. Acute asthma. Single dose oral steroids in paediatric community clinics. *European Journal of Pediatrics* 153(7):526-530, 1994.
129. Sarafino, E.P. and Dillon, J.M. Relations among respiratory infections, triggers of attacks, and asthma severity in children. *J.Asthma* 35(6):497-504, 1998.
130. Johnston, S.L. Influence of viral and bacterial respiratory infections on exacerbations and symptom severity in childhood asthma.. *Pediatr.Pulmonol.Suppl.* 16:88-89, 1997.
131. Brunette, M.G., Lands, L., and Thibodeau, L.P. Childhood asthma: prevention of attacks with short-term corticosteroid treatment of upper respiratory tract infection. *Pediatrics* 81(5):624-629, 1988.
132. Deshpand A, McKenzie S. Short course of steroids in home treatment of children—a birth cohort study. *BMJ 1986;293:169-71.*
133. Storr J, Berell E, Barry W, Lenney W. Effect of a single dose of prednisolone in acute childhood asthma. *Lancet* 1987;ii:879-81.

134. Dahl R, Johansson SA. Clinical effect of b.i.d. and q.i.d. adminstration of inhaled budesonide. A double-blind controlled study. *Eur J Respir Dis* 67:254-60, 1985.
135. Deshpand A, McKenzie S. Short course of steroids in home treatment of children—a birth cohort study. *BMJ* 1986;293:169-71.
136. Agertoft, L. and Pedersen, S. Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children. *Respir.Med.* 88(5):373-381, 1994.
137. Claudio, L., Tulton, L., Doucette, J., and Landrigan, P.J. Socioeconomic factors and asthma hospitalization rates in New York City. *J.Asthma* 36(4):343-350, 1999.
138. Martin, A.J., Campbell, D.A., Gluyas, P.A., Coates, J.R., Ruffin, R.E., Roder, D.M., Latimer, K.M., Luke, C.G., Frith, P.A., Yellowlees, P.M., and et al. Characteristics of near-fatal asthma in childhood. *Pediatr.Pulmonol.* 20(1):1-8, 1995.
139. Jonasson, G., Carlsen, K.H., Sodal, A., Jonasson, C., and Mowinckel, P. Patient compliance in a clinical trial with inhaled budesonide in children with mild asthma. *Eur.Respir.J.* 14(1):150-154, 1999.
140. Norell, S.E. Accuracy of patient interviews and estimates by clinical staff in determining medication compliance. *Soc.Sci.Med.*. 15(1):57-61, 1981.
141. Cochrane, M.G., Bala, M.V., Downs, K.E., Mauskopf, J., and Ben-Joseph, R.H. Inhaled corticosteroids for asthma therapy: patient compliance, devices, and inhalation technique. *Chest* 117(2):542-550, 2000.
142. Morisky, D.E., Green, L.W., and Levine, D.M. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med.Care* 24(1):67-74, 1986.
143. Halterman, J.S., Aligne, C.A., Auinger, P., McBride, J.T., and Szilagyi, P.G. Inadequate therapy for asthma among children in the United States. *Pediatrics* 105(1 Pt 3):272-276, 2000.
144. Meng, Y.Y., Leung, K.M., Berkbigler, D., Halbert, R.J., and Legorreta, A.P. Compliance with US asthma management guidelines and specialty care: a regional variation or national concern? *J.Eval.Clin.Pract.* 5(2):213-221, 1999.
145. Jatulis, D.E., Meng, Y.Y., Elashoff, R.M., Schocket, A.L., Evans, R.M., Hasan, A.G., and Legorreta, A.P. Preventive pharmacologic therapy among asthmatics: five years after publication of guidelines. *Ann.Allergy Asthma Immunol.* 81(1):82-88, 1998.
146. Nestor, A., Calhoun, A.C., Dickson, M., and Kalik, C.A. Cross-sectional analysis of the relation between national guideline recommended asthma drug therapy and emergency/hospital use within a managed care population. *Ann.Allergy Asthma Immunol.* 81(4):327-330, 1998.
147. Deshpande A, McKenzie S. short course of steroids in home treatment of children with acute asthma. *BMJ* 293:169-71, 1986.
148. Littenberg B, Gluck EH. A controlled trial of methylpredisolone in the emergency treatment of acute asthma. N Engl J Med 314: 150-152, 1986.
149. Weinberger M Antiasthmatic therapy in children. *Pediatr Clin N Am*: 1251-1284, 1989.

150. Storr J, Barry W, Barrell E, Lenney W, Hatcher G. Effect of a single dose of prednisolone in acute childhood asthma. *Lancet* 1:879-881, 1987.
151. Jones, K. and Gruffydd-Jones, K. Management of acute asthma attacks associated with respiratory tract infection: a postal survey of general practitioners in the U.K. *Respir.Med.* 90(7):419-425, 1996.
152. Stott NC, West RR. Randomised controlled trial of antibiotics in patients with cough and purulent sputum. Br Med J. 1976;2:556-9.
153. Brickfield FX, Carter WH, Johnson RE. Erythromycin in the treatment of acute bronchitis in a community practice. J Fam Pract. 1986;23:119-22.
154. Avorn J. Solomon DH. Cultural and economic factors that (mis)shape antibiotic use: the nonpharmacologic basis of therapeutics. *Annals of Internal Medicine. 133(2):128-35, 2000 Jul 18.*
155. Kuhni, C.E. and Sennhauser, F.H. The Yentl syndrome in childhood asthma: risk factors for undertreatment in Swiss children. *Pediatr.Pulmonol.* 19(3):156-160, 1995.
156. Sennhauser, F.H. and Kuhni, C.E. Prevalence of respiratory symptoms in Swiss children: is bronchial asthma really more prevalent in boys? *Pediatr.Pulmonol.* 19(3):161-166, 1995.
157. Mitchell, E.A., Ferguson, V., and Norwood, M. Asthma education by community child health nurses. *Arch.Dis.Child* 61(12):1184-1189, 1986.
158. Mayo, P.H., Richman, J., and Harris, H.W. Results of a program to reduce admissions for adult asthma. *Ann.Intern.Med.* 112(11):864-871, 1990.
159. Gleeson, J.G. and Price, J.F. Controlled trial of budesonide given by the nebuhaler in preschool children with asthma. *BMJ.* 297(6642):163-166, 1988.
160. Bisgaard, H., Munck, S.L., Nielsen, J.P., Petersen, W., and Ohlsson, S.V. Inhaled budesonide for treatment of recurrent wheezing in early childhood. *Lancet* 336(8716):649-651, 1990.
161. Miles, XX. Social and Emotional Impact of Asthma, 458-460.
162. Christie MJ, French DJ, et al. Manual For Childhood asthma Questionnaires.
163. Rutishauser, C., Sawyer, S.M., and Bowes, G. Quality-of-life assessment in children and adolescents with asthma. *Eur.Respir.J.* 12(2):486-494, 1998.

Appendix 1 CAQ-A

CAQ-A

CHILDHOOD ASTHMA QUESTIONNAIRE

STUDY NO	
INVESTIGATOR	
PATIENT	
DATE OF BIRTH (M/D/Y)	
SEX	
DATE OF COMPLETION (M/D/Y)	
VISIT	1 2

INSTRUCTIONS TO PARENTS

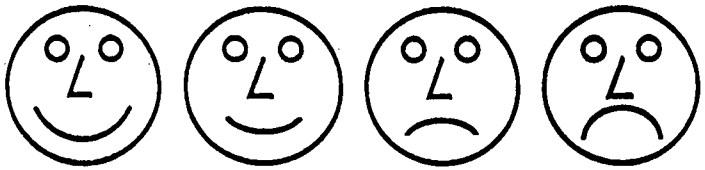
Please read out the section headed 'instructions to child' on the next page and then guide your child through the first 14 items. Please try to encourage your son or daughter to colour in just one face and to decide for themselves how they feel about the various aspects of their life. If your child answers **NO** to part **a** for questions 11,12 or 13, then part **b** of that question should not be attempted.

We are interested in your child's feelings about him or herself, the activities he or she participates in and his or her asthma.

Following this, please complete the questions for parents at the back of the book.

INSTRUCTIONS TO CHILD
(read out)

What I want you to do is to look at each of these faces



The first one is a very happy face
(point to left hand face)

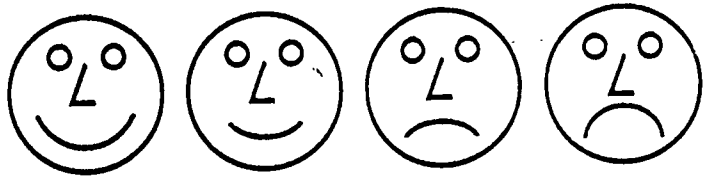
The next one is quite a happy face
(point to the next face to the left)

The next face is quite a sad face
(point to the third face along)

The last one is a very sad face
(point to the face on the right hand side).

When we look at the faces on the next few pages I would like you to colour in the one that is most like you.

1. Which face is you most of the time?
   Colour in one face



For Office Use Onl

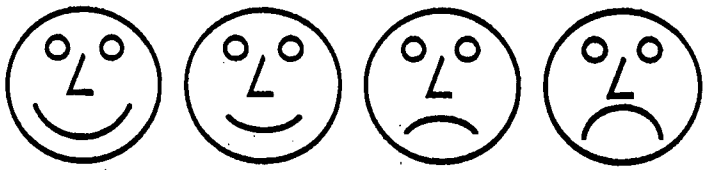
2a. Do you play outside when it is warm and sunny?
Colour in <u>one</u> box

Yes ☐

No ☐

For Office Use Only ☐

2b. Which face is <u>you</u> when you are playing outside when it is warm and sunny?
Colour in <u>one</u> face



For Office Use Only ☐

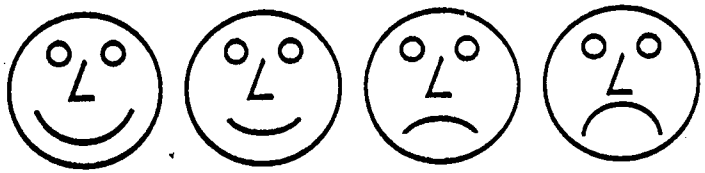
3a. Do you play outside when it is cold?
Colour in <u>one</u> box

Yes ☐

No ☐

For Office Use On ☐

3b. Which face is <u>you</u> when you are playing outside when it is cold?
Colour in <u>one</u> face



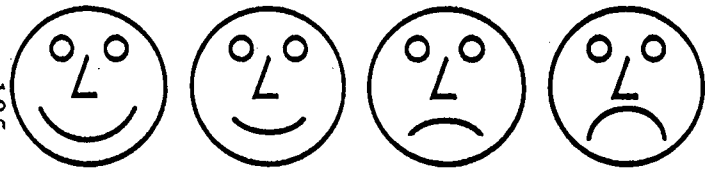
For Office Use On ☐

4a. Do you run around outside?
Colour in <u>one</u> box

Yes ☐

No ☐

4b. Which face is <u>you</u> when you are running around outside?
Colour in <u>one</u> face



185

For Office Use Only

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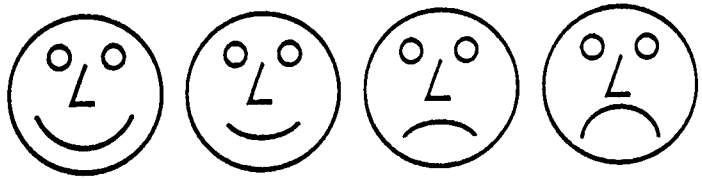
5a. Do you play inside with toys?
Colour in <u>one</u> box

Yes ☐

No ☐

5b. Which face is <u>you</u> when you play inside with toys?
Colour in <u>one</u> face



For Office Use Only

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6a. Do you listen to stories?
Colour in one box

Yes ☐

No ☐

For Office Use Only

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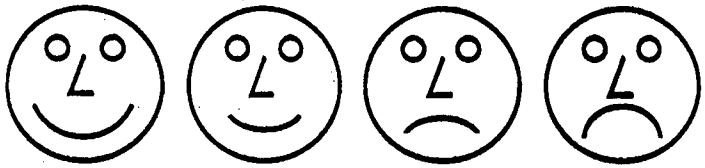
6b. Which face is you when you listen to stories?
Colour in one face



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186

7a. Do you draw pictures?
Colour in one box

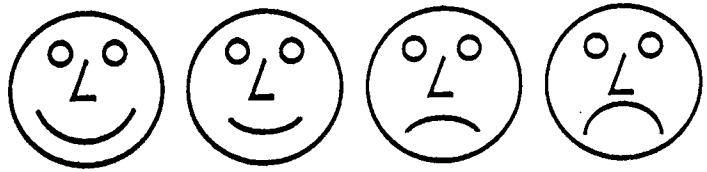
Yes ☐

No ☐

For Office Use On

☐

7b. Which face is you when you draw pictures?
Colour in one face



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8a. Do you watch television?

Colour in <u>one</u> box

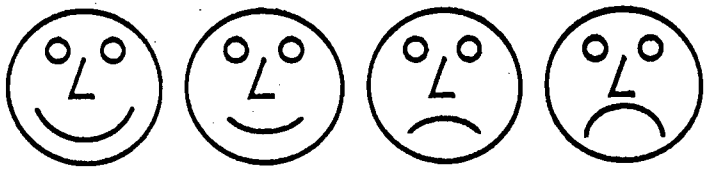
Yes ☐

No ☐

For Office Use Only ☐

8b. Which face is <u>you</u> when you watch television?

Colour in <u>one</u> face



187

For Office Use Only ☐

9a. Do you go to the swimming pool?

Colour in <u>one</u> box

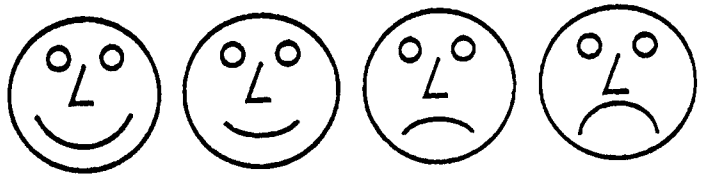
Yes ☐

No ☐

For Office Use On ☐

9b. Which face is <u>you</u> when you go to the swimming pool?

Colour in <u>one</u> face



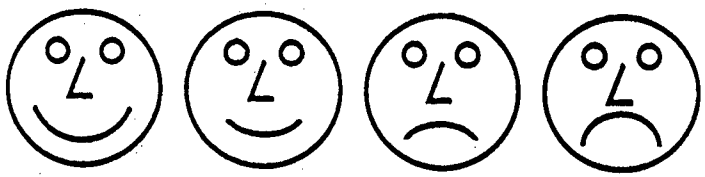
10a. Do you go to . . ?
Colour in <u>one</u> box

School ☐

Nursery ☐

Playgroup ☐

10b. Which face is <u>you</u> when you go to school, nursery or playgroup?
Colour in <u>one</u> face



188

For Office Use Only

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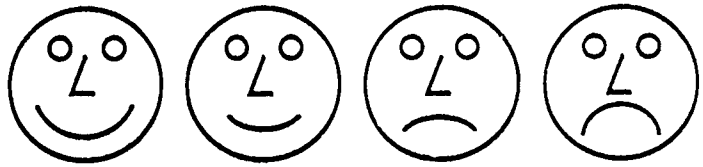
11a. Do you wheeze (get a whistling noise in your chest)?
Colour in <u>one</u> box

Yes ☐

No ☐

11b. Which face is <u>you</u> when you wheeze?
Colour in <u>one</u> face



For Office Use Or

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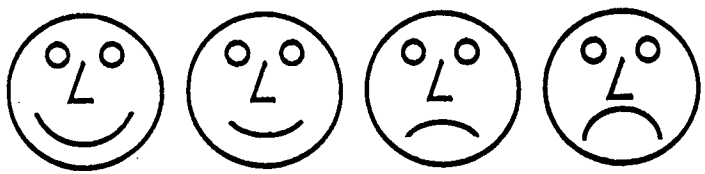
2a. Do you cough?
Colour in one box

Yes ☐

No ☐

2b. Which face is you when you cough?
Colour in one face



189

For Office Use Only

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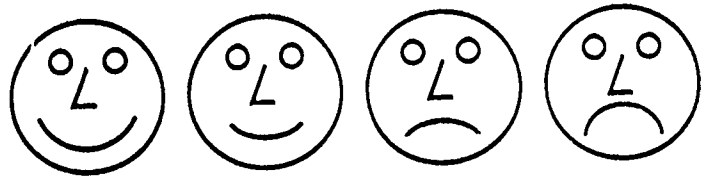
13a. Do you have asthma attacks?
Colour in one box

Yes ☐

No ☐

13b. Which face is you when you are having an asthma attack?
Colour in one face



For Office Use Only

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14. Do you think your asthma is . . ?
Colour in one box

- Very bad ☐
- Quite bad ☐
- Not too bad ☐

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INFORMATION TO BE COMPLETED BY PARENT

1. Does your child go to . . ?
Please tick one box

- School ☐
- Nursery/Nursery class ☐
- Playgroup ☐

2. How many times has he/she been absent from school/nursery/playgroup through illness in the past **TWO** months?

- None at all ☐
- 1 or 2 days ☐
- 3 to 5 days ☐
- 5 to 10 days ☐
- More than 10 days ☐

For Office Use On ☐ ☐

3. How many times has he/she been absent from school/nursery/playgroup in the last **TWO** months because of his/her asthma?
Please tick one box

- None at all ☐
- 1 or 2 days ☐
- 3 to 5 days ☐
- 5 to 10 days ☐
- More than 10 days ☐

For Office Use Only ☐

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4. How often have you been woken at night by your child's asthma in the last **TWO** months?
Please tick one box

- Not at all ☐
- Once a week or less ☐
- Several nights a week ☐
- Almost every night ☐

For Office Use Only ☐

5. How would you rate the severity of your child's asthma at the moment?

- Mild ☐
- Moderate ☐
- Severe ☐

For Office Use Only ☐

6. How well controlled is your child's asthma at the moment?

- Very well controlled ☐
- Quite well controlled ☐
- Not at all well controlled ☐

For Office Use Only ☐

7. How much would you say that your child's asthma is affecting the rest of the family at the moment?

- Not at all ☐
- A little ☐
- Quite a lot ☐
- A great deal ☐

For Office Use Only ☐

8. Does anyone in your close family have asthma? Please tell us how they are related to your child.

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_____

_____

_____

_____

_____ ☐

9. Does your child get tummy aches?
Please tick one box

- Less than once a month ☐
- Between once a week and once a month ☐
- More than once a week ☐

For Office Use On ☐

10. Does your child get headaches?
Please tick one box

- Less than once a month ☐
- Between once a week and once a month ☐
- More than once a week ☐

☐

Appendix 2 CAQ-B

CAQ-B

CHILDHOOD ASTHMA QUESTIONNAIRE

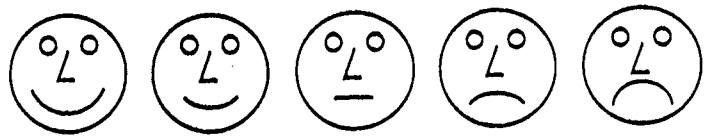
STUDY NO	
INVESTIGATOR	
PATIENT	
DATE OF BIRTH (M/D/Y)	
SEX	
DATE OF COMPLETION (M/D/Y)	
VISIT	1 2

INSTRUCTIONS

We would like to find out how you feel about the things you do at home and at school.

What we'd like you to do is colour in faces to show how you feel about these things or colour in boxes to show how often you do things.

Here are the faces you are going to be looking at:



The first one is a very happy face; the next face is quite a happy face and the one in the middle is neither happy or unhappy. The fourth face is quite an unhappy face, and the one on the far right is a very unhappy face. When you answer the questions we'd like you to colour in the face which describes how you feel.

Here are the boxes you are going to be looking at. Sometimes they ask how often you do something and sometimes they ask how often you feel unwell with your asthma.

A lot	☐☐☐☐
Sometimes	☐☐☐
Hardly ever	☐☐
Not at all	☐

If I have been doing something a lot, or something (like getting wheezy) has happened to you a lot recently, then fill in the top line, four boxes. If it has happened sometimes, or you have done something sometimes, then fill in the three boxes on the second line. If you have hardly ever done that thing recently or have hardly ever had that problem with your asthma then colour in the two boxes marked 'hardly ever', and if it has not happened to you at all or you have not done that thing, then fill in the last line with only one box.

If you get stuck on a word, then please ask someone for help, but answer the questions yourself – we are interested in how you feel.

HOW YOU FEEL

1. Which picture describes how you feel most of the time?

For Office Use ☐

2a. How often do you play outside when it is warm and sunny?

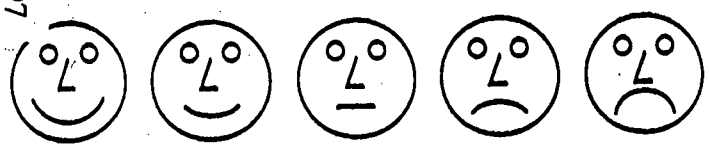
A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

2b. Which picture describes how you feel when you play outside when it is warm and sunny?



For Office Use Only

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3a. How often do you play outside when it is cold?

A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

3b. Which picture describes how you feel when you play outside when it is cold?

For Office Use Only

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4a. How often do you play inside with your toys?

A lot ☐

Sometimes ☐

Hardly ever ☐

Not at all ☐

4b. Which picture describes how you feel when you play inside with your toys?

198

For Office Use Only

☐

☐

5a. How often do you read books?

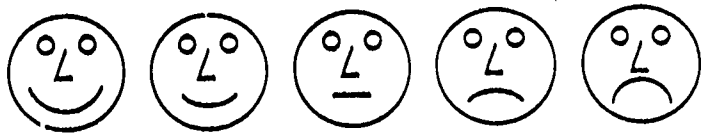
A lot ☐

Sometimes ☐

Hardly ever ☐

Not at all ☐

5b. Which picture describes how you feel when you read books?



For Office Use Only

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☐

6a. How often do you draw pictures?

A lot

Sometimes

Hardly ever

Not at all

For Office Use Only

6b. Which picture describes how you feel when you draw pictures?

199

7a. How often do you watch television?

A lot

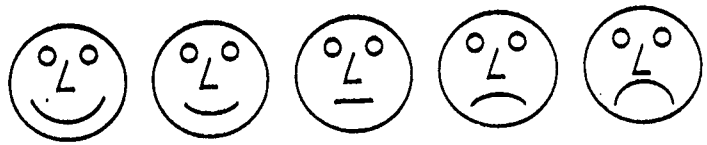
Sometimes

Hardly ever

Not at all

For Office Use Only

7b. Which picture describes how you feel when you watch television?



8a. How often do you go to the swimming pool?

A lot

Sometimes

Hardly ever

Not at all

For Office Use Only

8b. Which picture describes how you feel about going to the swimming pool?

200

9a. How often do you do P.E. at school?

A lot

Sometimes

Hardly ever

Not at all

For Office Use Only

9b. Which picture describes how you feel when you do P.E. at school?

10a. How often do you play games outside (like ball games) with your class?

A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

10b. Which picture describes how you feel when you play games outside (like ball games) with your class?

For Office Use Only

☐

☐

11. Which picture describes how you feel about running around at playtimes?

For Office Use O

☐

12. How often have you had headaches recently?

A lot

Sometimes

Hardly ever

Not at all

13. How often have you had tummy aches recently?

202

A lot

Sometimes

Hardly ever

Not at all

For Office Use Only

14. How often have you had coughs or colds recently?

A lot

Sometimes

Hardly ever

Not at all

15. How often have you missed school because you were not feeling well?

A lot

Sometimes

Hardly ever

Not at all

For Office Use C

ABOUT YOUR ASTHMA

16a. How much have you been wheezing (or getting tight in the chest) recently?

A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

203

16b. Which picture describes how you feel when you are wheezy or tight-chested?

For Office Use Only

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☐

17a. How much have you been coughing recently?

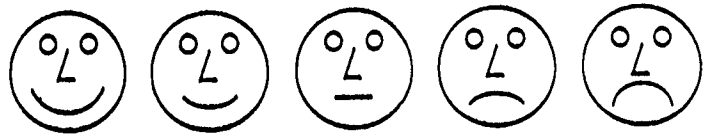
A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

17b. Which picture describes how you feel when you cough?



For Offi Use

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18a. How much have you been waking up at night with your asthma recently?

A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

For Office Use Only ☐

18b. Which picture describes how you feel when you wake at night with your asthma?

For Office Use Only ☐

19a. How often have you had asthma attacks recently?

A lot ☐☐☐☐

Sometimes ☐☐☐

Hardly ever ☐☐

Not at all ☐

For Office Use ☐

19b. Which picture describes how you feel when you are having an asthma attack?

For Office Use ☐

20a. How often have you missed school because of your asthma recently?

A lot ☐

Sometimes ☐

Hardly ever ☐

Not at all ☐

For Office Use Only ☐

20b. Which picture describes how you feel when you miss school because of your asthma?

☐

205

21a. Do you use your inhaler (your medicine) when you're supposed to?

A lot/always ☐

Some imes ☐

Hardly ever ☐

Not at all ☐

For Offic Use (☐

21b. Which picture describes how you feel without your inhaler if you're feeling wheezy?

☐

22a. How bad do you think your asthma has been recently?

Not too bad ☐

Quite bad ☐☐

Very bad ☐☐☐

22b. How do you feel about having asthma?

206

For Office Use Only

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☐

INFORMATION TO BE COMPLETED BY PARENT

1. How many school days has your child lost in the past **TWO** months because of his/her asthma?

None at all ☐

1 or 2 days ☐

3 to 5 days ☐

5 to 10 days ☐

More than 10 days ☐

2. How often have you been woken at night by your child's asthma in the past **TWO** months?

Not at all ☐

Once a week or less ☐

Several nights a week ☐

Almost every night ☐

For Offic Use (

☐

☐

3. How would you rate the severity of your child's asthma at the moment?

Mild ☐

Moderate ☐

Severe ☐

4. How well controlled is your child's asthma at the moment?

Very well controlled ☐

Quite well controlled ☐

Not at all well controlled ☐

For Office Use Only

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☐

5. How much would you say that your child's asthma is affecting the rest of your family at the moment?

Not at all ☐

A little ☐

Quite a lot ☐

A great deal ☐

6. Does anyone else in your close family have asthma? Please tell us how they are related to your child.

_____

_____

_____

_____

For Office Use On

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☐

Appendix 3 CAQ-C

CAQ-C

CHILDHOOD ASTHMA QUESTIONNAIRE

STUDY NO	
INVESTIGATOR	
PATIENT	
DATE OF BIRTH (M/D/Y)	
SEX	
DATE OF COMPLETION (M/D/Y)	
VISIT	1 2

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INSTRUCTIONS

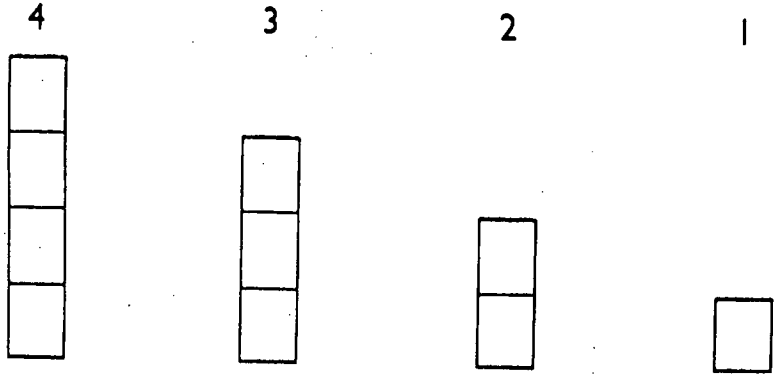
We are interested in how young people who have asthma feel about themselves and the things that they do, how they feel about having asthma and if they think it affects their lives. Your answers will be kept completely confidential so please do your best to answer all of the questions truthfully.

Over the page is an example of how to answer the questions. When a question asks 'How often?', you should place a number between one and four in the box – 4 if you do that thing often or very often; 3 if you do it sometimes, 2 if you hardly ever do it, and 1 if you do not do it at all or it never happens. When you are answering the questions that ask 'How often?', think about the last couple of weeks.

When a question asks 'How do you feel?', you should place a number between one and five in the box, as if you were giving it marks out of five for how much you like it – 5 if you like it a lot, 4 if you quite like it, 3 if you don't mind or don't care one way or the other, 2 if you don't really enjoy it, and 1 if you hate it. When you are answering the questions that ask 'How do you feel?', think how you feel about it at the moment. There will be a reminder on every page of what the numbers mean in case you need it.

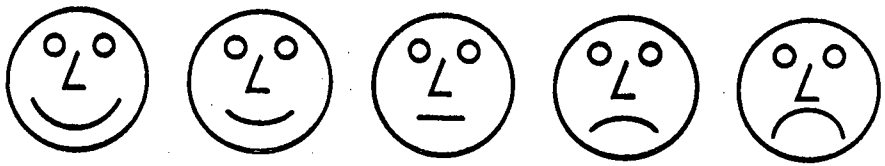
Now turn the page and try the example.

How often?



4	3	2	1
A lot or very often, or all of the time.	Sometimes, or some of the time.	Hardly ever or not very often.	Never or not at all.

How do you feel?



5	4	3	2	1
Great! or I really like it or I am very happy when I am doing this.	OK or I quite like it or I am fairly happy doing this.	I don't mind, I don't like or dislike it.	I don't really like this or it makes me a bit unhappy.	I hate this or it makes me very unhappy to do this.

How often do you watch television?

How do you feel about watching television?

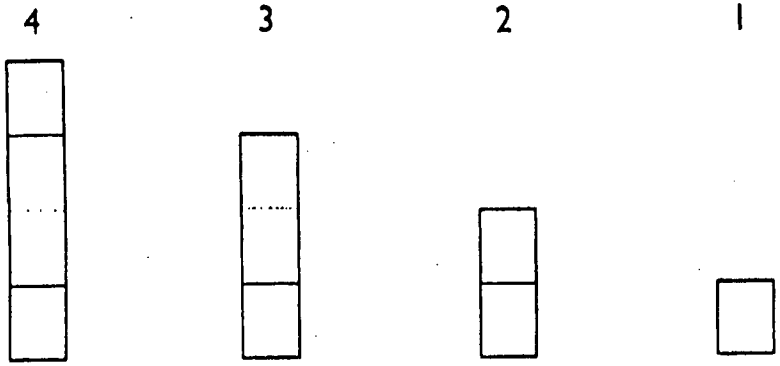
If you think that you watch television a lot and it is something that you really like to do then you would answer 4 to the first question and 5 to the second.

If you only watch sometimes and don't really mind whether you do or not, you don't like or dislike it, then you would answer 3 to the first question and 3 to the second.

If you really hate watching TV then you would answer 1 to the second question.

Are you happy that you know how to answer the questions? If not ask someone to help you with the example. If you feel that you understand then turn the page and answer the questions. On every page there will be a reminder of what the numbers mean in case you need it.

How often?



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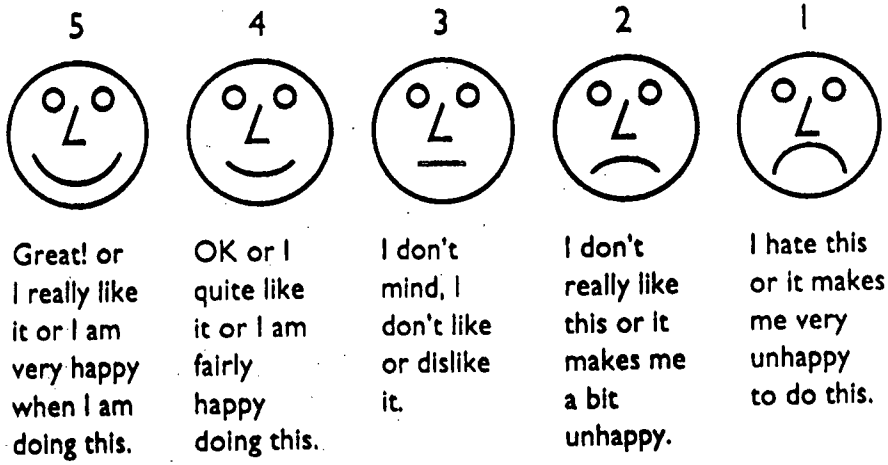
How do you feel?



1a. How often do you read books or magazines?

b. How do you feel about reading books or magazines?

2a. How often do you go to the swimming pool?

b. How do you feel about going to the swimming pool?

3a. How often do you go to discos or parties?

b. How do you feel about going to discos or parties?

4a. How often do you dance at discos or parties?

b. How do you feel about dancing at discos or parties?

5a. How often do you do P.E. or gym indoors?

b. How do you feel about doing P.E. or gym indoors?

6a. How often do you do sports or games outside?

b. How do you feel about doing sports or games outside?

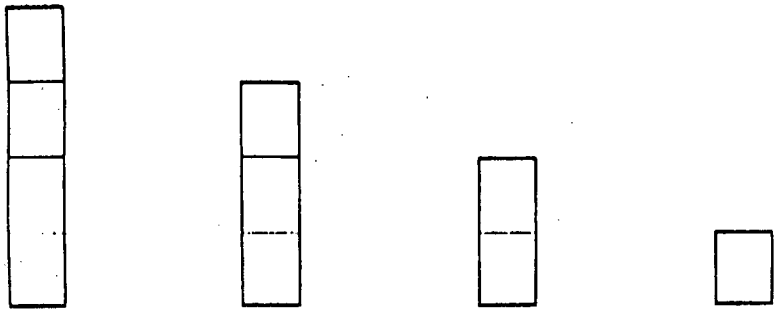
7a. How often do you go out when the weather is fine?

b. How do you feel about going out when it is fine?

8a. How often do you go out when the weather is cold?

b. How do you feel about going out when it is cold?

How often?



A lot or very often, or all of the time.

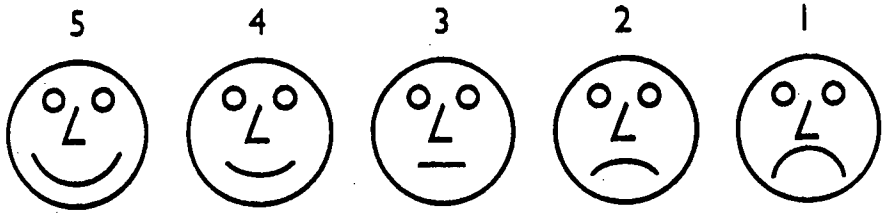
Sometimes, or some of the time.

Hardly ever or not very often.

Never or not at all.

213

How do you feel?



Great! or I really like it or I am very happy when I am doing this.

OK or I quite like it or I am fairly happy doing this.

I don't mind, I don't like or dislike it.

I don't really like this or it makes me a bit unhappy.

I hate this or it makes me very unhappy to do this.

On this page, if your answer is **1, (never)** to part **a** of any question, you should miss out part **b** of that question. The questions on this page are about your asthma **in the last two weeks.**

9a. How often have you been wheezy or tight-chested recently? ☐

b. How do you feel about getting wheezy or tight-chested? ☐

10a. How much have you coughed recently? ☐

b. How do you feel about coughing? ☐

11a. How often have you had asthma attacks recently? ☐

b. How do you feel about having asthma attacks? ☐

12a. How often have you woken at night with asthma recently? ☐

b. How do you feel about waking at night with asthma? ☐

13a. How often have you missed school because of asthma recently? ☐

b. How do you feel about missing school because of asthma? ☐

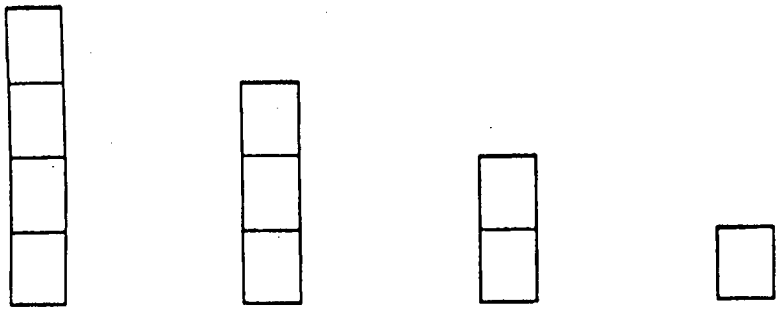
14a. How often do animals make you cough or wheeze? ☐

b. How do you feel about having to avoid animals? ☐

15a. How often does running make you cough or wheeze? ☐

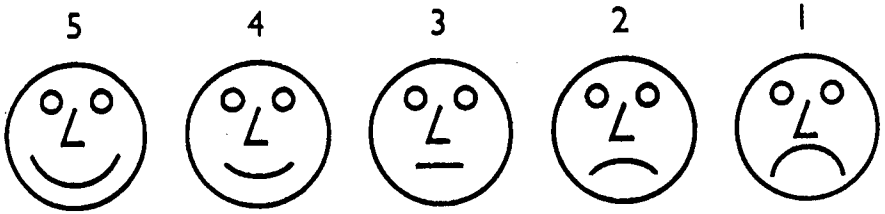
b. How do you feel about getting asthma when you run? ☐

How often?



214

How do you feel?



16. How do you feel about making new friends?
17. How do you feel about having to carry your inhaler?
18. How do you feel about having to avoid things that make you cough or wheeze?
19. How do you feel when parents or teachers fuss over you?
20. How do you feel about telling other people that you have asthma?
21. How do you feel about people around you smoking?
22. How do you feel about having a cigarette yourself?
23. How do you feel about finding that you have forgotten your inhaler?
24. How do you feel about having asthma?

25. How often have you had headaches recently?
26. How often have you had stomach aches recently?
27. How often have you missed school because you were not well recently?
28. How often do you get coughs and colds?

For Office Use On

29. How bad do you think your asthma is? (tick one box)

Not too bad ☐

Quite bad ☐

Very bad ☐ ☐

30. How well do you think that your medicine is working at the moment? (tick one box)

Very well ☐

Quite well ☐

Not at all ☐ ☐

31. Does anyone else in your close family have asthma? Please tell us what relation they are to you?

_____

_____

_____

_____

_____ ☐

Appendix 4 PAQLQ

PAEDIATRIC ASTHMA

QUALITY OF LIFE QUESTIONNAIRE

INTERVIEWER ADMINISTERED

McMASTER UNIVERSITY

HAMILTON, ONTARIO

CANADA

For further information:

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FEBRUARY 1995

PAEDIATRIC ASTHMA QUALITY OF LIFE QUESTIONNAIRE

THE PAEDIATRIC ASTHMA QUALITY OF LIFE QUESTIONNAIRE HAS BEEN TESTED AND VALIDATED USING THE WORDING AND FORMAT THAT FOLLOWS. IT IS IMPORTANT THAT INTERVIEWERS ADHERE TO THE EXACT WORDING WHEN ADDRESSING THE PATIENT (REGULAR TYPE) AND FOLLOW THE INSTRUCTIONS (ITALIC TYPE). DEVIATION FROM BOTH WORDING AND INSTRUCTIONS MAY IMPAIR THE RELIABILITY AND VALIDITY OF THE QUESTIONNAIRE.

I want you to tell me all the things you do in which you are bothered by your asthma.

CIRCLE THE NUMBER ON THE ANSWER SHEET LIST ADJACENT TO EACH ACTIVITY MENTIONED. IF AN ACTIVITY MENTIONED IS NOT ON THE LIST, WRITE IT IN, IN THE RESPONDENT'S OWN WORDS, IN THE SPACE PROVIDED.

Together, we are going to look at a list of things that you may have done during the last week. Because of your asthma, you may have found some of these activities difficult to do or not very much fun. Let's look at the list and you tell me in which activities you've been bothered by your asthma during the past week. If you haven't done something on the list or if it hasn't bothered you, just say "no".

READ ACTIVITIES, OMITTING THOSE WHICH RESPONDENT HAS IDENTIFIED SPONTANEOUSLY. PAUSE AFTER EACH ACTIVITY TO GIVE THE PATIENT A CHANCE TO REPLY. CROSS OUT THE ACTIVITIES WHICH THE PATIENT INDICATES ARE <u>NOT</u> TROUBLESOME USING A THICK DARK FELT PEN.

Can you think of any other activities in which you are bothered because of your asthma?

Of the activities listed, I want you to tell which ones bother you the most.

TURN THE ACTIVITY SHEET TO PATIENT. TOGETHER, READ THROUGH ALL THE IDENTIFIED ITEMS.

Which of these activities bothers you the most?

WRITE ACTIVITY ON BOTH THE QUESTIONNAIRE AND THE RESPONSE SHEET.

Of the remaining activities, which one bothers you the most?

RECORD RESPONDENT'S ANSWERS AND CONTINUE UNTIL 3 ACTIVITIES HAVE BEEN IDENTIFIED.

SHOW THE BLUE AND GREEN CARDS TO THE PATIENT AND EXPLAIN THE SCALES. RECORD THE PATIENT'S ANSWERS ON THE RESPONSE SHEET.

I now want you to tell me how much you were bothered by your asthma while doing these activities. I will tell you which card to use. Pick the number which best describes how much you were bothered by your asthma in doing each activity during the last week.

A 1. How much have you been bothered by your asthma in (ACTIVITY 1:_____) during the past week. [BLUE CARD]

A 2. How much have you been bothered by your asthma in (ACTIVITY 2:_____) during the past week. [BLUE CARD]

A 3. How much have you been bothered by your asthma in (ACTIVITY 3:_____) during the past week. [BLUE CARD]

S 4. How much did COUGHING bother yo[illegible] he past week? [BLUE CARD]

E 5. How often did your asthma make you feel FRUSTRATED during the past week? [GREEN CARD]

S 6. How often did your asthma make you feel TIRED during the past week? [GREEN CARD]

E 7. How often did you feel WORRIED, CONCERNED, OR TROUBLED because of your asthma during the past week? [GREEN CARD]

S 8. How much did ASTHMA ATTACKS bother you during the past week? [BLUE CARD]

E 9. How often did your asthma make you feel ANGRY during the past week? [GREEN CARD]

S 10. How much did WHEEZING bother you during the past week? [BLUE CARD]

E 11. How often did your asthma make you feel IRRITABLE during the past week? [GREEN CARD]

S 12. How much did TIGHTNESS IN YOUR CHEST bother you during the past week? [BLUE CARD]

E 13. How often did you feel DIFFERENT OR LEFT OUT because of your asthma during the past week? [GREEN CARD]

S 14. How much did SHORTNESS OF BREATH bother you during the past week? [BLUE CARD]

E 15. How often did you feel FRUSTRATED BECAUSE YOU COULDN'T KEEP UP WITH OTHERS during the past week? [GREEN CARD]

S 16. How often did your asthma WAKE YOU UP DURING THE NIGHT during the past week? [GREEN CARD]

E 17. How often did you feel UNCOMFORTABLE because of your asthma during the past week? [GREEN CARD]

S 18. How often did you feel OUT OF BREATH during the past week? [GREEN CARD]

A 19. How often did you feel YOU COULDN'T KEEP UP WITH OTHERS because of your asthma during the past week? [GREEN CARD]

S 20. How often did you have trouble SLEEPING AT NIGHT, because of your asthma, during the past week? [GREEN CARD]

E 21. How often did you feel FRIGHTENED BY AN ASTHMA ATTACK during the past week? [GREEN CARD]

A 22. Think about all the activities that you did in the past week. How much were you bothered by your asthma doing these activities? [BLUE CARD]

S 23. How often did you have difficulty taking a DEEP BREATH in the past week? [GREEN CARD]

RESPONSE SHEET

NAME:_____ NUMBER:_____

DATES OF COMPLETION (D/M/Y)

1st:_____/_____/_____ 2nd:_____/_____/_____

3rd:_____/_____/_____ 4th:_____/_____/_____

ITEM	RESPONSES 1st	2nd	3rd	4th
1. Activity 1_____	___	___	___	___
2. Activity 2_____	___	___	___	___
3. Activity 3_____	___	___	___	___
4. Cough	___	___	___	___
5. Frustrated	___	___	___	___
6. Tired	___	___	___	___
7. Worried/Concerned/Troubled	___	___	___	___
8. Asthma attacks	___	___	___	___
9. Angry	___	___	___	___
10. Wheezing	___	___	___	___
11. Irritable	___	___	___	___
12. Tightness in chest	___	___	___	___
13. Feeling different or left out	___	___	___	___
14. Shortness of breath	___	___	___	___

ITEM	RESPONSES 1st	2nd	3rd	4th
15. Frustrated can't keep up with others	___	___	___	___
16. Wake up during the night	___	___	___	___
17. Uncomfortable	___	___	___	___
18. Out of breath	___	___	___	___
19. Can't keep up with others	___	___	___	___
20. Trouble sleeping at night	___	___	___	___
21. Frightened by asthma attack	___	___	___	___
22. Bothered in activities overall	___	___	___	___
23. Deep breath	___	___	___	___

ACTIVITY SHEET

1. Ball Hockey
2. Baseball
3. Basketball
4. Dancing (ballet/jazz)
5. Football
6. Playing at Recess
7. Playing with Pets
8. Playing with Friends
9. Riding a Bicycle
10. Running
11. Skipping Rope
12. Shopping
13. Sleeping
14. Soccer
15. Swimming
16. Volleyball
17. Walking
18. Walking Uphill
19. Walking Upstairs
20. Laughing
21. Studying
22. Doing Household Chores
23. Singing
24. Doing Crafts or Hobbies
25. Shouting
26. Gymnastics
27. Rollerblading/Rollerskating
28. Skateboarding
29. Track and Field
30. Tobogganing
31. Skiing
32. Ice Skating
33. Climbing
34. Getting up in the Morning
35. Talking

ACTIVITIES IDENTIFIED BY SUBJECT

1)_____ 5)_____

2)_____ 6)_____

3)_____ 7)_____

4)_____ 8)_____

Appendix 5 QOLiF

Patient Specific Quality of Life Questionnaire

QOLif

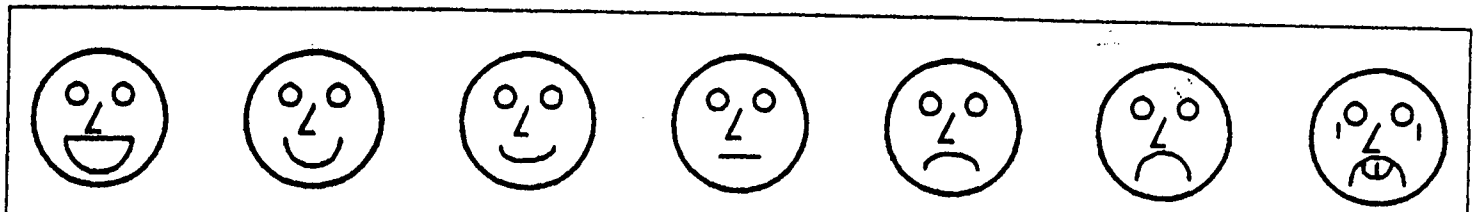
Patient Evaluation Form

226

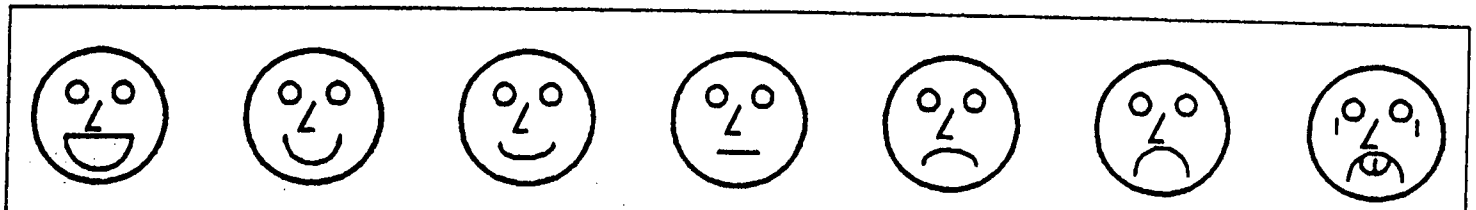
PATIENT ID	
DATE (M/D/Y)	
VISIT	1 2

1. For each physical activity listed below, how much have you been bothered by asthma during the past week?

[227]



Not bothered	Hardly bothered at all	Bothered a bit	Somewhat bothered	Quite bothered	Very bothered	Extremely bothered
☐	☐	☐	☐	☐	☐	☐



Not bothered	Hardly bothered at all	Bothered a bit	Somewhat bothered	Quite bothered	Very bothered	Extremely bothered
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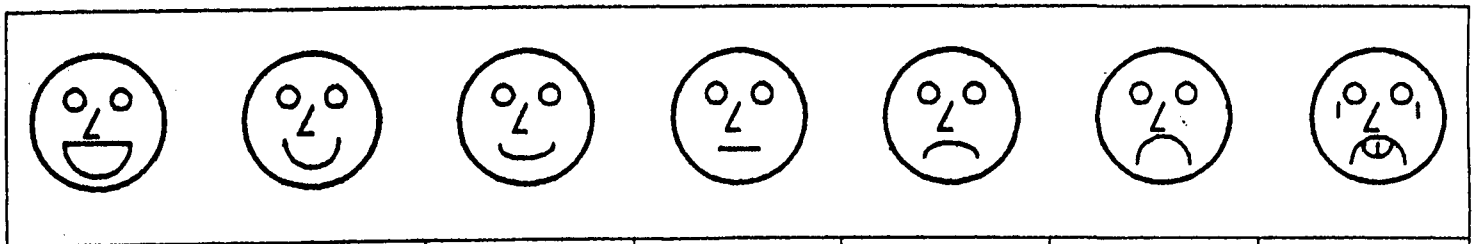
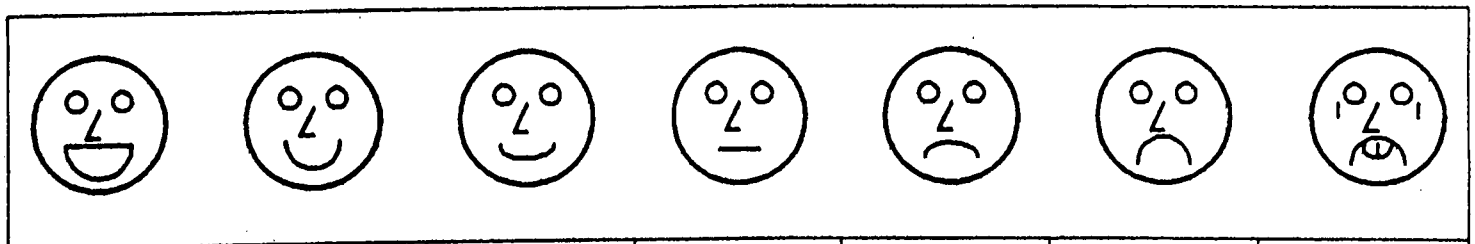
2. For each role listed below, how much has asthma bothered you in each role during the past week?

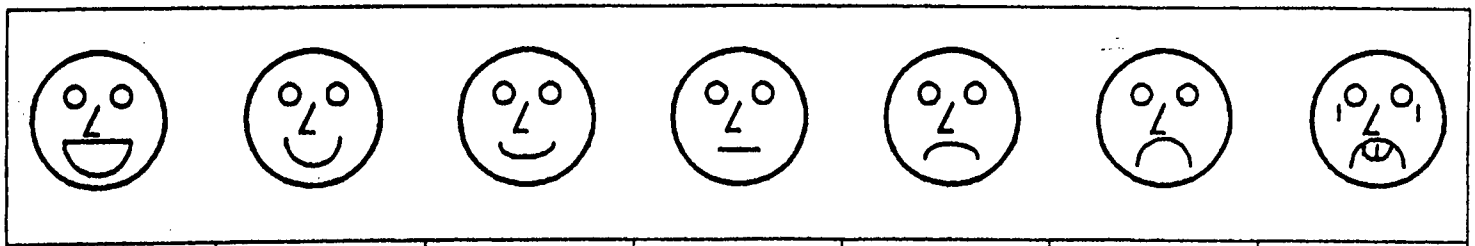


	Not bothered	Hardly bothered at all	Bothered a bit	Somewhat bothered	Quite bothered	Very bothered	Extremely bothered
228	☐	☐	☐	☐	☐	☐	☐



	Not bothered	Hardly bothered at all	Bothered a bit	Somewhat bothered	Quite bothered	Very bothered	Extremely bothered
	☐	☐	☐	☐	☐	☐	☐

3. For each social function listed below, how much has your asthma bothered you in each social function during the past week?



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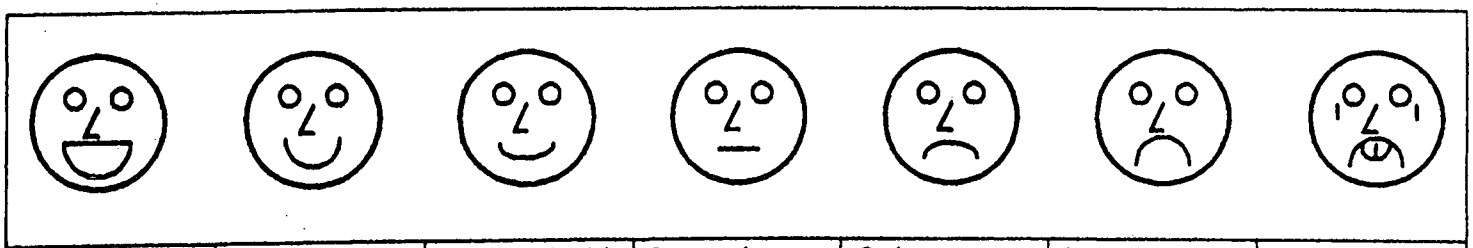

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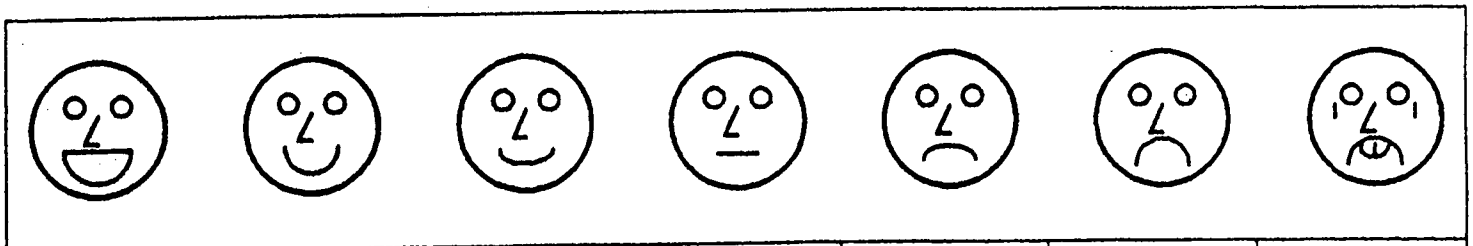

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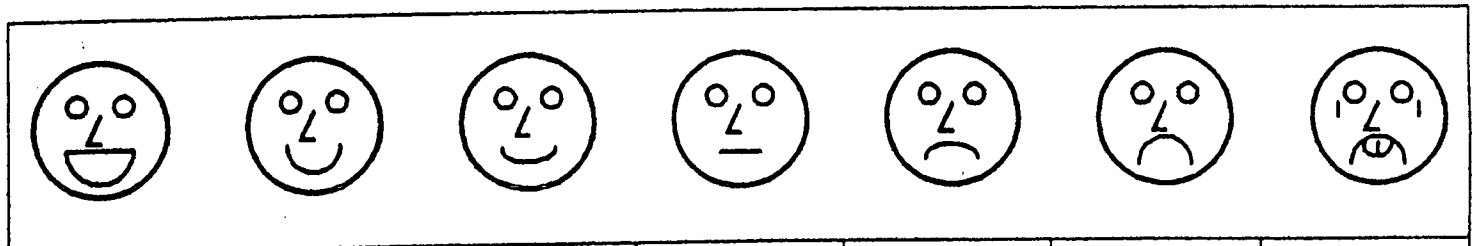
☐	☐	☐	☐	☐	☐	☐



Not bothered	Hardly bothered at all	Bothered a bit	Somewhat bothered	Quite bothered	Very bothered	Extremely bothered
☐	☐	☐	☐	☐	☐	☐

Patient Specific Quality of Life Questionnaire

QOLif

Evaluation Form For Parent/Guardian

PARENT/GUARDIAN	
NAME OF CHILD	
DATE (M/D/Y)	
VISIT	1 2

1. For each physical activity listed below, how much has your child been bothered by his or her asthma during the past week?

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

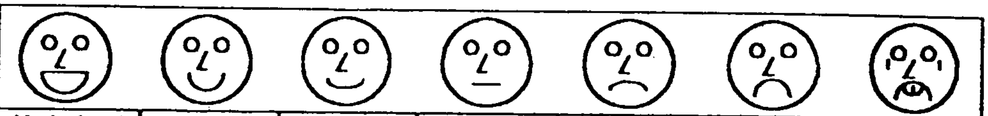
	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

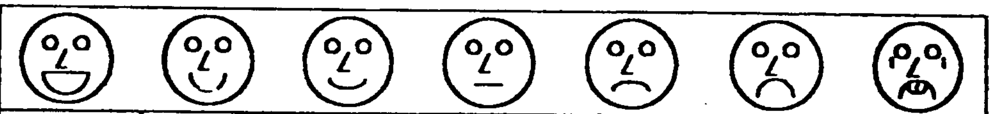
	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

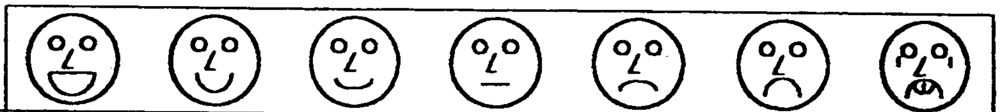


	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered



	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered



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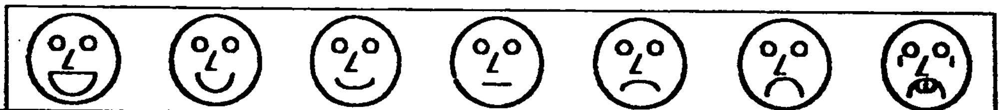

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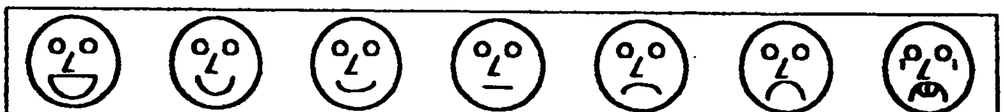

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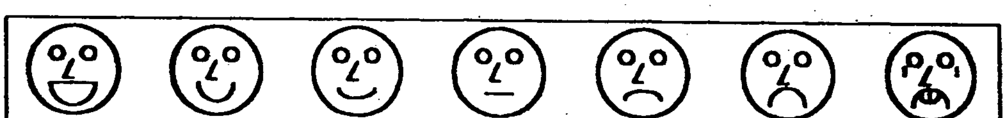
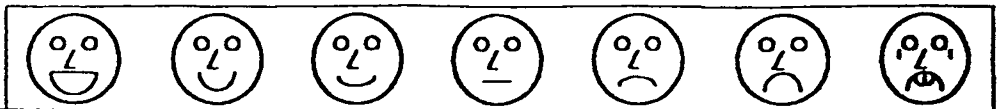
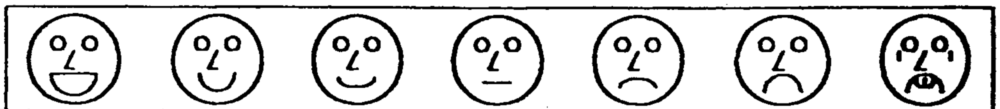


	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered



	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered



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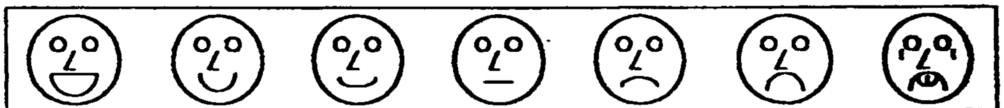

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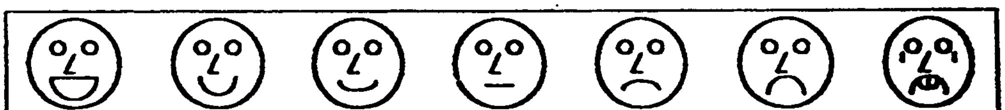

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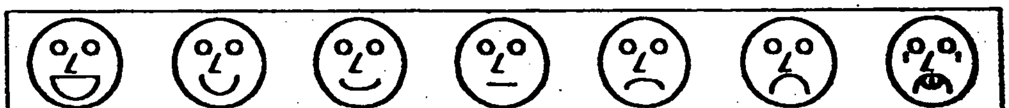
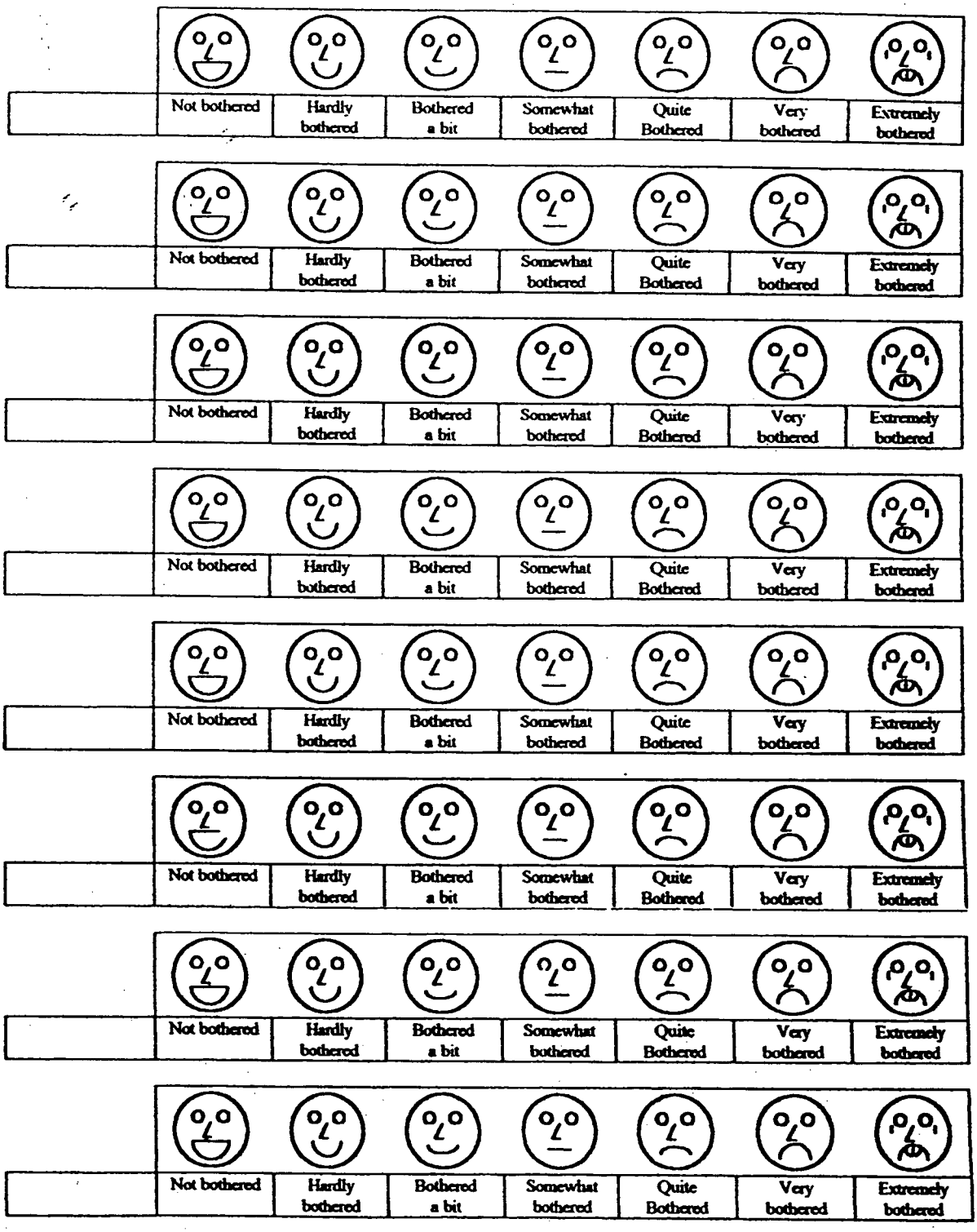


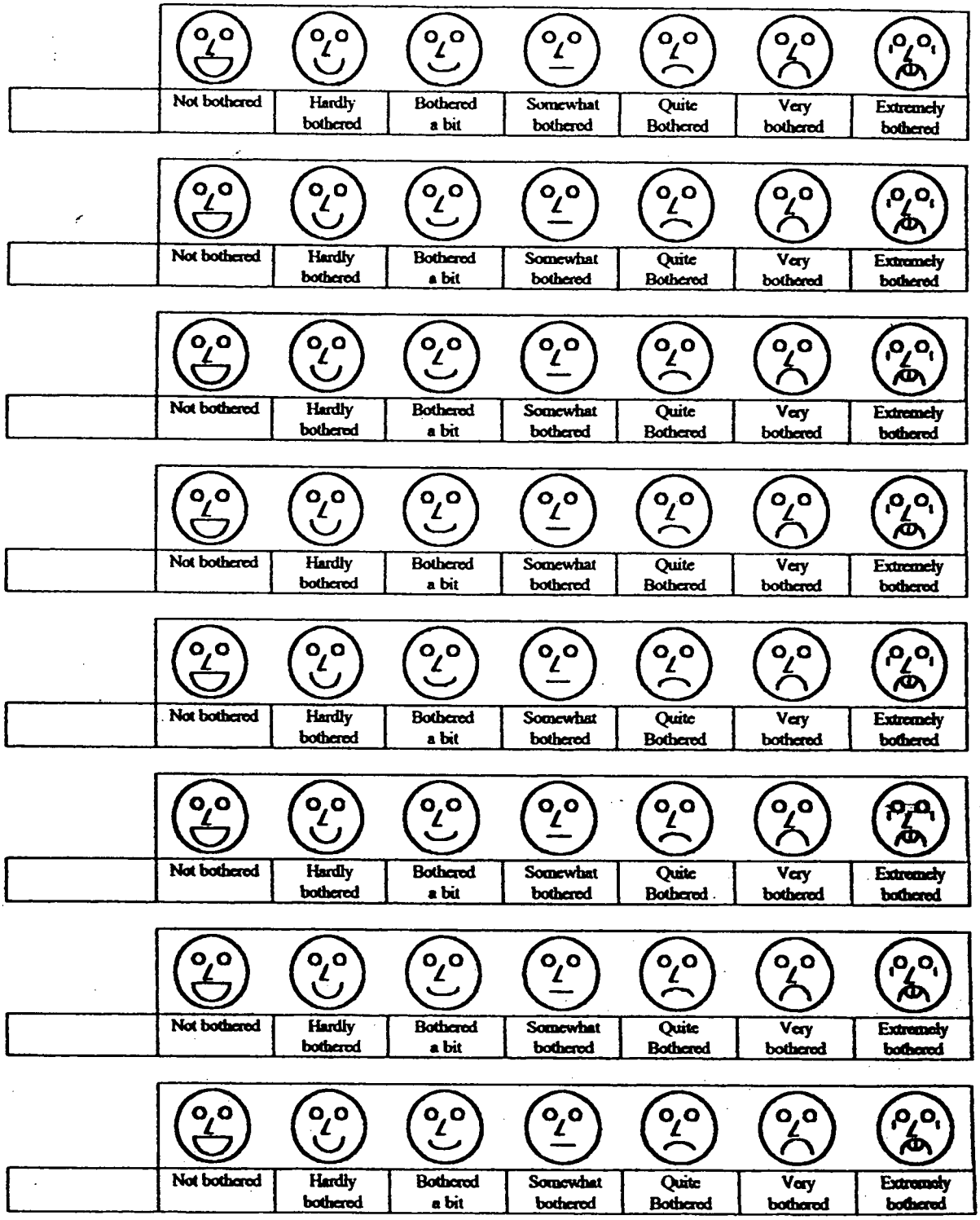
	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

	Not bothered	Hardly bothered	Bothered a bit	Somewhat bothered	Quite Bothered	Very bothered	Extremely bothered

2. For each role listed below, how much has asthma bothered your child in each role during the past week?



3. For each social function listed below, how much has your child been bothered by his or her asthma during the past week?



Patient Specific Quality of Life Questionnaire

QOLif

Preference Assessment (Physical, Role Function, Social Function)

Instructions to

Parents/Guardians

CHILD ID	
PARENT	
DATE (M/D/Y)	
VISIT	1 2

1a. Mark an "X" in each box next to each physical activity that your child likes to do:

Physical Activities	
Arts And Crafts	**Sports**
Bake Cook Color Draw Knit Model Building Paint Pottery Sew Write	Aerobics Ball Hockey Basketball Bowling Canoeing Cycling Fish Football Gymnastics Hike Hockey Lift Weights Run Skate Skipping Rope Soccer Softball Snooker Stepmaster™ Skiing Skip Swim Tennis Tobogganing Volleyball
Music And Performance	**Play And Leisure**
Clarinet Dance Drums Guitar Karaoke Piano Saxaphone Sing Violin	Computers Drive Internet Play with Pets Play at Recess Read Shopping Sleep Smoke Talk Television Toys Video Games Walking

b. List any additional activities that your child likes to do:

2. From the physical activities in question 1, which are your child's 3 favourite activities?

3. From the physical activities in question 1, which are your child's 3 least favourite activities?

4a. Mark an "X" in each box next to each role that your child does.

Roles	
Babysit	School
Chores	Study
Church	Take care of pet
Dishes	Work
Religion	Vacuum

b. List any additional roles that your child does:

5a. Mark an "X" in each box next to each social function that your child is in:

Social Functions	
Camping	Friends
Circus	Movies
Clubs	Parties
Dances	Travel
Dinner	Visit Relatives

b. List any additional social functions that your child is in:

Appendix 6 Consent Form

STUDY PROCEDURES

This study will consist of questionnaires and interviews. The questionnaires and interviews will occur once during your child's stay in the hospital and again approximately one month after hospital discharge. You and your child may be asked questions about previous medication, about your child's health, and about his or her health related quality of life status. Additional information may be obtained from your child's health and/or medication record. Moreover, your child may perform a simple breathing test called Peak Expiratory Flow Rate Monitoring, a routine procedure performed in asthmatic patients that requires less than two minutes to complete. The amount of time to complete both interviews and questionnaires will be approximately forty minutes for the first session and 20 minutes for the second.

SIDE EFFECTS AND DISADVANTAGES

Your child's participation in this study will not increase his or her risk of known side effects or cause your child to be in any disadvantage compared to other asthmatic children in the hospital.

BENEFITS

However, while your child is participating in this study, study investigators and a committee of health professionals will examine your child's health record for any problems related to the medication that he or she may have taken in the past, while prescribed in the hospital, or will be taking home. This will help ensure that your child is treated with the best medication for his condition. Also, the study assessment tests will be provided free of charge while your child is actively participating in the study. Finally, your child's participation may be help future patients by providing vital information about potentially preventable medication related problems that cause asthma attacks and provide data to help measure the health related quality of life status of asthmatic children.

You are making a decision whether or not to allow your child to participate. Your signature indicates that you have read the information provided above and have decided to allow your child to participate. You will be provided with a copy of this form.

SIGNATURE OF PATIENT _____ DATE _____

PRINT NAME OF PATIENT _____

SIGNATURE OF PARENT/GUARDIAN _____ DATE _____

PRINT NAME OF PARENT/GUARDIAN _____

RELATIONSHIP TO PATIENT _____

SIGNATURE OF WITNESS _____ DATE _____

PRINT NAME OF WITNESS _____

SIGNATURE OF INVESTIGATOR _____ DATE _____

PRINT NAME OF INVESTIGATOR _____

Appendix 7 Data Collection Form

DRUG RELATED HOSPITAL ADMISSIONS

Patient ID:

Medication History

Medication/Physician	SIG	Actual SIG	Start	Stop
In Community				
Frequency of Ventolin Use				
In Hospital				
Discharge				

HOSPITAL ADMISSIONS/DOCTORS VISITS

Transfer From: _____ **Admitted To:** _____ **Hospital:**_____

Ward Admission Date: __/____/9__ **Diagnosis:**_____
Discharge Date: __/____/9__ **Diagnosis:**_____

Doctor's Visits
Checkups To GP/Year: _____
Urgent Visits (6 Months): _____
Annual Visits Specialist: _____
Urgent Visits (6 Months): _____

Previous Hospitalizations
No. Previous Hospitalizations: _____
No. of Admissions (Last 6 months): _____
Days Hospitalized (Last 6 months): _____
No. of ER Visits In Last 6 Months: _____

Comments:

- Where was the child transferred from?
- Which hospital ward has the child been admitted to?
- Which hospital is the present admission?
- When was the patient admitted to the ward?
- What was the admission diagnosis?
- When was the patient discharged?
- What is the discharge diagnosis?

- How many times per year does your child see the family doctor for regular checkups for his/her asthma?
- How many times per year in the last 6 months have you had to take your child to the child's doctor's office for urgent treatment of asthma or breathing problems? By urgent, I mean that you had to see the doctor within the next 24 hours.
- How many times per year do you take your child to see your specialist for regular check-ups of asthma?
- How many times in the last 6 months has your child had to go to the specialist for urgent treatment of asthma or breathing problems?

- How many times has your child been admitted to hospital for asthma?
- How many times in the last 6 months has your child been admitted for asthma?
- How many days in total has your child been hospitalized for asthma in the last 6 months?

How many times in the last 6 months has your child had to visit a hospital emergency room for urgent treatment of asthma or breathing problems?

HISTORY OF ASTHMA

Age Breathing Problems First Developed: _____
Age Asthma First Diagnosed: _____

Other Medical Conditions:

History of Present Illness:

Mechanical Ventilation: ☐ Y ☐ N
Premature: ☐ Y ☐ N
Months Breastfed: _____

Family Hx of Asthma/Allergy/Atopy:

Evidence of Infection:

1. **Has your child developed a cold/flu/infection in the last 2 weeks?**
2. **Have you noticed any unusual symptoms in the last 2 weeks?**
3. **Has your child had a runny nose, sore throat, fever, pain?**

Symptoms

Time of Day Symptoms Occur: ☐Morning ☐Afternoon ☐Evening ☐Night ☐No Pattern

Pattern of Symptoms: ☐Daily ☐ Occasionally

Season Symptoms Are Worse: ☐Summer ☐ Fall ☐Winter ☐Spring ☐No Pattern

Over the last 4 weeks, how often has he/she experienced the following symptoms:

Over the Last 4 Weeks:	2X or more/day	Every Day	3-6X/ week	<2X/ week	Only at episodes	Not at all
Chest Tightness						
Coughing						
Coughing Up Phlegm						
Diarrhea/vomiting						
Fast Heart Beat						
Headache/migraines						
Heartburn						
Itchy skin/rash/watery eyes						
Night time awakenings						
Night time mouth breathing						
Shaky hands/tremor						
Shortness of breath						
Stuffy/runny nose						
Wheezing						

Triggers

Allergies	
Food Allergies	
Skin	
Known Triggers	

Smokers	Y/N	In the House	PPD
Mother	☐	☐	____
Father	☐	☐	____
Patient	☐	☐	____

Smoking:

Total No. Smokers: ____

	Yes	No
Cat	☐	☐
Dog	☐	☐

What do you think has triggered your child's asthma recently?
Does your child have any allergies to any medication?
Does your child have any food allergies?
Does your child suffer from any eczema, rashes, etc?
Are you aware of any triggers in the home or outside that can set off your child's asthma?
Does the mother smoke?
Does the father smoke?
Does the patient smoke?
Does anyone smoke in the house?
How many packs per day does each one smoke?
How many people in the family smoke?
Where do they smoke?
Has there been an increase, decrease, or no change in the amount of smoking that the family members do?

Asthma Management Plan

Asthma Effect On QOL

Days of School Missed In the Last Year: _____

Role (School)	
Physical Functioning	
Sleep	
Child's Mood	
Social Functioning	

- How many days of school has your child missed in the last year?
- Is your child worried about his asthma? Does he have some friends?
- Would any of these physical activities make your child's asthma worse?
  - Vigorous activities (such as running)
  - Moderate activities (cycling or jumping)
  - Climbing several flights of stairs
  - Walking
  - Temper tantrums
  - Laughing/crying hard
- How would you describe the quality of your child's sleep in the last 4 weeks?
- How would you describe your child's mood in the last 4 weeks?

Compliance

Does your child ever forget to take prescription medication?	YES ☐	NO ☐
Is your child able to take medication at the same time each day?	YES ☐	NO ☐
When your child feels better, does your child stop taking any medication?	YES ☐	NO ☐
If your child feels worse while taking medication, does your child sometimes stop taking it?	YES ☐	NO ☐

PARENTS' OCCUPATIONS

PEFR ON ADMISSION

PEFR IN COMMUNITY

Appendix 8 Chronic Symptoms of Asthma Before Hospital Admission (n=54)

The following table shows whether each patient had a previous diagnosis of asthma or not, and whether or not each patient had chronic symptoms of asthma before hospital admission. For each case where chronic symptoms of asthma was present, the details of the chronic symptoms are described in the last column. The chronic symptoms have been transcribed from the physicians' notes of each patient's hospital health record and from responses of parents of children during the interviews.

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
1	Y	Y	37	Asthma acts up about every three months.
3	Y	Y		He has frequent episodes of shortness of breath and coughing associated with colds during the cold weather and exercise. He often has difficulty breathing, in response to cold drinks, exercise, playing a lot, cold weather. He also coughs a lot in such
4	Y	Y	NA	However, before this, "had not had any symptoms." Patient admits he wakes up during the night because of asthma some of the time during the last week. He experiences asthma symptoms after exercising.
5	Y	Y	NA	Longstanding history of poorly controlled asthma
6	Y	Y	NA	Patient feels asthma is not under control
7	Y	Y	NA	NA
8	Y	Y	1	No symptoms prior to this episode.
10	Y	Y		Every time she does any type of exercise she would wheeze and cough. This occurred quite frequently, too frequently to count. Every time she got a cold, her asthma would also become worse. So she takes the influenza vaccination every year.

Appendix 8 (cont...) **Chronic Symptoms of Asthma Before Hospital Admission (n=54)**

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
11	Y	Y	1	Patient's asthma attacks seem to come on very quickly without much warning at all. Once attack comes it is hard to thwart it.
12	Y	Y	NA	Unwell, distressed, speaks in short sentences, very fidgety.
13	Y	Y	NA	Runny nose and cough for the past two weeks
15	Y	Y	2	Chest tightness, coughing, diarrhea, night-time awakenings, mouth breathing, and shortness of breath only at episodes.
16	Y	Y	8	Has been well until 24hours ago, but requires salbutamol 15-17X per week. shortness of breath and stuffy/runny nose only at episodes.
17	Y	Y	NA	Symptoms come and go. Last few years appears that condition is getting better since attacks less frequent.
18	Y	Y	NA	Questionable history of asthma. Patient has used inhalers in the past.
19	Y	Y	10	From time of last admission in March patient has been stable until five days ago when sore throat began, together with shortness of breath/cough which began two days ago. He denies chronic cough

Appendix 8 (cont...) **Chronic Symptoms of Asthma Before Hospital Admission (n=54)**

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
21	Y	Y	NA	Previously healthy boy until two days ago, when cough with yellow/green sputum began
22	Y	Y	15	Chest tightness, coughing, diarrhea, vomiting, shaky hands, shortness of breath occur only at episodes, which occur about ten times ear year.
23	Y	Y	NA	Normally does not have any symptoms at all.
24	Y	Y	NA	Wheezes early in the AM every day. Wheezes if she goes jogging and during heavy exercise.
25	Y	Y	NA	Long history of nocturnal cough and wheezing with URTI's but never received any medication for this.
26	Y	Y	0	Has has not recently had symptoms in the last couple of months. Previous episodes of colds/flu were no problem.
27	Y	Y	NA	She usually does not have any symptoms.
28	Y	Y	NA	NA
29	Y	Y	NA	NA
30	Y	Y	NA	For 2 years, he has had no symptoms. Completely asymptomatic until 2 days ago when he discovered he had a runny nose and all of a sudden started to cough and wheeze.

Appendix 8 (cont...) **Chronic Symptoms of Asthma Before Hospital Admission (n=54)**

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
31	Y	Y	NA	She gets A's and B's except for PE, which she gets a C because of her asthma.
32	Y	Y	20	Severely asthmatic since age 1. Child reports chest tightness every day. shortness of breath 1-2 X / week. Parents report child usually has no symptoms.
33	Y	Y	NA	Before this cold (URTI) she did not have any symptoms. Did not wake up at night at all. Did not wheeze during sports. Gets a cold about three times per year.
34	Y	Y	NA	For at least two years, she has not had any asthma symptoms.
35	Y	Y	NA	Usually three episodes/year which get treated with bronchodilators and antibiotics. No symptoms between flare-ups. Patient developed a cough and runny nose 2 days before admission.
36	Y	Y	20	NA
37	Y	Y	NA	When she has a flare up she begins to get a runny nose, cough which worsens at night, fatigue
38	Y	Y	12	Was doing well until yesterday when he started to cough and wheeze overnight; couldn't sleep so mother gave 20 mg prednisone, salbutamol nebules q4h. The attacks are twice weekly requiring salbutamol nebulizer. Child wakes up at night 3-6X/week because of asthma.

Appendix 8 (cont...) **Chronic Symptoms of Asthma Before Hospital Admission (n=54)**

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
39	Y	Y	NA	Lungs get wheezy on humid days. Patient experiences symptoms on and off. Patient well until night prior to admission.
40	Y	Y	20	Coughing at night and during physical activity gets shortness of breath. Normally coughs two times per day, shortness of breath, stuffy nose, and wheezing more than twice daily.
41	Y	Y	14	Experiences symptoms mainly from winter to spring during which time he usually has four to six attacks.
42	Y	Y	NA	Known mild asthmatic.
43	Y	Y	NA	Long history of cough and respiratory distress with URTI's-approx. 10-12/ year
44	Y	Y	NA	Diagnosed just 10 months ago
45	Y	Y	NA	Ongoing cough-since he was a baby
46	Y	Y	NA	Symptoms are usually worse in winter. Gets a cold about once every three weeks. Always gives salbutamol when child gets a cold. Symptoms only appear if child gets a cold. Otherwise no symptoms.
47	Y	Y	NA	Has not had any symptoms in the last year.
48	Y	Y	1	Two months after discharge, he is still not able to do all the activities that he would like. For example, his mother does not let him do the church activities because she is afraid that he would catch a cold which would trigger his asthma.
50	N	N	NA	First episode of asthma.
51	N	N	NA	First episode of asthma.
52	N	N	NA	First episode of asthma.

Appendix 8 (cont...) **Chronic Symptoms of Asthma Before Hospital Admission (n=54)**

Patient	Chronic Symptoms Before This Episode	Previous Diagnosis of Asthma	School Days Missed in the Previous 12 Months	Details of Chronic Symptoms
53	N	N	NA	First episode of shortness of breath and cough ever.
54	N	N	NA	First episode of asthma.
55	N	N	NA	Previously healthy boy. Lately, has coughing about once every two to three days.
56	Y	Y	NA	NA
57	NA	NA	NA	NA
60	Y	N	NA	Previously well. He has had the occasional past wheezing and cough for the last year and one half, ever since he started smoking. He has also had some exercise induced cough and wheezing. However, otherwise he has not had any real suggestion of asthma. He has had on and off mild wheezing with upper respiratory tract infections, about two attacks in the last 18-24 months. Nothing was sufficient enough to cause him to come to the hospital, otherwise the remainder of his medical history was negative.
61	Y	Y	NA	NA

Appendix 9 Demographic Data of the Study Population (n=54)

Each patient's age, gender, ethnic origin, and municipality or city of residence is shown in each row.

Patient	Age (Years)	Gender	Ethnicity	Residence
1	10.1	Male	Caucasian	Vancouver
3	5.8	Male	Chinese	Vancouver
4	8.9	Male	Chinese	Vancouver
5	12.9	Male	Chinese	Burnaby
6	12.7	Male	Caucasian	Vancouver
7	5.6	Male	Chinese	Vancouver
8	12.9	Male	Vietnamese	Vancouver
10	12.6	Female	East Indian	Burnaby
11	6.1	Male	Filipino	Vancouver
12	9.2	Male	African	Burnaby
13	6.7	Female	Japanese	Vancouver
15	6.5	Male	Caucasian	Vancouver
16	10.8	Male	Chinese	Vancouver
17	8.3	Female	Chinese	Vancouver
18	9.0	Male	Filipino	Vancouver
19	16.6	Male	Chinese	Vancouver
21	5.7	Male	Chinese	Vancouver
22	5.3	Female	Caucasian	Vancouver
23	5.1	Male	Caucasian	Brackendale
24	16.9	Female	Vietnamese	Vancouver
25	9.5	Female	Chinese	Vancouver
26	7.3	Female	Caucasian	Vancouver
27	8.0	Male	Caucasian	Calgary
28	6.8	Male	Caucasian	Vancouver
29	7.6	Female	Vietnamese	Vancouver

Appendix 9 (cont...) **Demographic Data of the Study Population (n=54)**

Patient	Age (Years)	Gender	Ethnicity	Residence
30	10.8	Male	East Indian	Vancouver
31	11.4	Female	Chinese	Vancouver
32	10.7	Male	Caucasian	Coquitlam
33	9.6	Female	Caucasian	South Delta
34	11.6	Female	First Nation	Vancouver
35	5.9	Male	Chinese	Vancouver
36	9.0	Female	First Nation	Vancouver
37	5.0	Female	Cambodian	Vancouver
38	5.6	Male	Cambodian	Vancouver
39	6.2	Male	Chinese	Vancouver
40	7.0	Female	Chinese	Vancouver
41	14.6	Male	Chinese	Vancouver
42	5.6	Male	Caucasian	Richmond
43	6.4	Male	Caucasian	Delta
44	6.8	Female	East Indian	Vancouver
45	9.4	Male	East Indian	Surrey
46	5.1	Female	Philipino	Richmond
47	9.4	Male	Chinese	Burnaby
48	5.5	Male	Caucasian	Richmond
50	4.8	Male	Philipino	Vancouver
51	6.0	Male	Chinese	Vancouver
52	6.3	Female	Sri Lankan	Vancouver
53	5.0	Male	Caucasian	Vancouver
54	6.1	Male	Philipino	Vancouver
55	11.7	Male	Vietnamese	Vancouver
56	6.4	Female	Caucasian	Vancouver
57	8.6	Male	Caucasian	Surrey
60	15.6	Male	Chinese	Vancouver
61	10.8	Male	Kenyan	Vancouver

Appendix 10 Physical Characteristics of Patients (N=54)

Each Patient's height (cm), height (percentile), weight (kg) and weight (percentile) is shown in each row.

Patient	Height (cm)	Height (Percentile)	Weight (kg)	Weight (Percentile)
1	97	93	41.0	85
3	111	25	18.0	25
4	126	50	25.0	75
5	163	NA	58.6	NA
6	139	5	32.8	10
7	109	50	16.1	10
8	147	10	34.7	5
10	NA	NA	62.2	NA
11	117.5	50	22.4	75
12	135	75	78.8	95
13	116	25	18.4	25
15	NA	25	21.3	25
16	147	75	35.9	50
17	104	50	19.0	10
18	136	75	39.4	95
19	170	NA	52.5	NA
21	115	75	18.3	25
22	112	NA	20.0	60
23	NA	NA	NA	NA
24	NA	NA	NA	NA
25	127	25	22.5	5
26	130	NA	27.5	NA
27	NA	NA	23.3	NA
28	NA	25	28.3	90
29	NA	NA	NA	NA

Appendix 10 (cont...) **Physical Characteristics of Patients (N=54)**

Patient	Height (cm)	Height (Percentile)	Weight (kg)	Weight (Percentile)
30	149	NA	31.0	NA
31	NA	NA	36.2	37
32	125	NA	29.3	NA
33	NA	80	33.9	75
34	150	NA	39.0	NA
35	116	98	24.9	75
36	130	23	27.4	45
37	103	25	17.3	25
38	107	25	17.7	25
39	111	25	20.0	10
40	50.5	50	24.9	79
41	163	30	58.3	60
42	115.7	NA	22.0	NA
43	122	90	20.5	40
44	123	50	28.2	95
45	146	95	42.2	95
46	103	10	13.3	5
47	NA	NA	25.5	NA
48	103	3	13.2	3
50	112.5	50	25.2	95
51	112	NA	17.9	NA
52	120	75	22.6	60
53	117	95	25.8	50
54	115	35	19.4	25
55	137	5	31.9	10
56	NA	NA	NA	NA
57	NA	NA	NA	NA
60	173	NA	77.3	NA
61	146	90	51.9	105

Appendix 11 Clinical Respiratory System Data at Time of Hospital Admission and Changes in Peak Expiratory Flow Rate of Patients

Each patient's respiratory rate (breaths per second) and heart rate (beats per minute) is shown in each row. In all cases where data were available, the PEFR improved on discharge.

Patient	HR (beats /min)	RR (breaths per minute)	Oxygen Saturation Room Air (%)	PEFR (mL/min)	PEFR (percent predicted)	PEFR (mL/min)	PEFR (percent predicted)
	On Admission					On Discharge	
1	116	28	94	NA	NA	260	95
2	70	24	98	NA	NA	300	100
3	150	36	94	NA	NA	NA	NA
4	128	28	96	120	50	210	95
5	138	18	90	220	70	350	100
6	90	20	93	140	50	220	90
7	120	32	92	NA	NA	NA	NA
8	112	26	93	250	74	300	88
9	130	32	90	NA	NA	NA	NA
10	120	24	98	160	50	300	NA
11	160	40	92	100	50	150	75
12	124	28	92	NA	NA	NA	NA
13	140	36	93	100	NA	160	NA
14	130	24	90	110	NA	NA	NA
15	106	32	86	NA	NA	NA	NA
16	138	36	86	260	79	340	100
17	135	28	97	180	NA	NA	NA
18	130	25	97	200	73	NA	NA
19	110	27	94	400	90	450	100
20	136	24	95	NA	NA	NA	NA
21	130	40	94	NA	NA	NA	NA
22	166	42	88	NA	NA	NA	NA
23	NA	NA	NA	NA	NA	NA	NA
24	NA	NA	NA	NA	NA	NA	NA
25	136	40	96	150	NA	220	NA
26	153	28	89	200	NA	250	NA
27	130	22	94	NA	NA	NA	NA
28	120	28	95	NA	NA	NA	NA
29	NA	NA	NA	140	NA	200	90

Appendix 11 (cont...) Clinical Respiratory System Data at Time of Hospital Admission and Changes in Peak Expiratory Flow Rate of Patients

Patient	HR (beats /min)	RR (breaths per minute)	Oxygen Saturation Room Air (%)	PEFR (mL/min)	PEFR (percent predicted)	PEFR (mL/min)	PEFR (percent predicted)
	On Admission					On Discharge	
30	80	20	97	200	NA	335	NA
31	170	36	94	200	NA	NA	NA
32	108	28	90	NA	NA	NA	NA
33	132	24	94	NA	NA	NA	NA
34	68	30	95	NA	NA	55	NA
35	140	40	96	135	70	NA	NA
36	128	36	93	150	75	NA	NA
37	166	52	94	NA	NA	110	NA
38	140	28	96	NA	NA	NA	NA
39	140	24	96	NA	NA	NA	NA
40	NA	32	96	NA	NA	220	100
41	NA	32	93	150	30	390	80
42	166	28	92	NA	NA	NA	NA
43	140	26	95	100	NA	120	NA
44	120	28	96	130	55	160	70
45	151	40	86	120	50	200	65
46	126	36	94	NA	NA	NA	NA
47	180	38	91	100	NA	NA	NA
48	160	28	95	150	NA	NA	NA
49	152	40	94	NA	NA	NA	NA
50	130	48	94	NA	NA	NA	NA
51	130	28	98	NA	NA	NA	NA
52	140	30	92	NA	NA	NA	NA
53	145	40	90	NA	NA	NA	NA
54	138	40	87	NA	NA	NA	NA
55	149	24	95	195	75	270	100
56	NA	NA	NA	NA	NA	NA	NA
57	NA	NA	NA	NA	NA	NA	NA
58	140	32	98	NA	NA	NA	NA
60	48	49	49	157	60	168	65
61	131	30	94	33	13.2	91	45

Appendix 12 Estimation of Severity of Acute Exacerbations of Asthma in Children[32]

Sign/Symptom	Mild	Moderate	Severe
PEFR	70-90% predicted or personal best	50-70% predicted or personal best	<50% predicted or personal best
Respiratory rate, resting or sleeping	Normal to 30% increase above the mean	30 – 50% increase above the mean	Increase over 50% above the mean
Alertness	Normal	Normal	May be decreased
Dyspnea	Absent or mild; speaks in complete sentences	Moderate; speaks in phrases or partial sentences; infant's cry softer and shorter, infant has difficulty suckling and feeding	Severe; speaks only in single words or short phrases; infant's cry softer and shorter, infant stops suckling and feeding.
Pulsus paradoxus	< 10 mm Hg	10 – 20 mm Hg	20-40 mm Hg
Accessory muscle use	No intercostal to mild retractions	Moderate intercostal retraction with tracheosternal retractions; use of sternocleidomastoid muscles, chest hyperinflation	Severe intercostal retractions wit nasal flaring during inspriation; chest hyperinflation
Color	Good	Pale	Possibly cyanotic
Auscultation	End expiratory wheeze only	Wheeze during entire expriation and inspiration	Breath sounds becoming audible
Oxygen saturation	>95%	90-95%	< 90%
PCO_2	<35	<40	>40

Appendix 13 Acute Symptoms of Asthma on Hospital Admission of Patients (n=54)

The following table shows the number of days each patient experienced the acute symptoms of the asthma exacerbation prior to hospital admission, the acute symptoms on admission, and the number of days each patient was treated in the hospital. The acute symptoms have been transcribed from the "physicians' notes" of each patient's hospital health record.

Patient	Number of Days Patient was Symptomatic Prior to Hospitalization	Acute Symptoms of Asthma On Hospital Admission	Length of Hospital Stay (Days)
1	1	Shortness of breath, bilateral wheeze, cough unresponsive to salbutamol in the emergency room.	2
3	2	Shortness of breath, rhinorrhea, congested cough	2
4	2	Worsening dry cough, shortness of breath, fine exp. and inspiratory wheezes	NA
5	2	24 hour history of shortness of breath, chest tightness, and right-sided chest pain.	4
6	NA	Decreased air entry to both lungs, bilateral wheeze	4
7	2	Increased shortness of breath, cough, wheezing, lethargy, nasal flaring, bilateral breath sounds, intercostal and subcostal indrawing.	2
8	3	Very wheezy, using accessory muscles to breathe, had expiratory wheeze. Increased coughing, gasping for air.	3
9	NA	Shortness of breath, scattered wheezes, decreased air entry to the right base.	2
10	NA	Increasing chest tightness, shortness of breath,cough.	3
11	NA	Respiratory distress (tachypneic and nasal flare), wheeze, crackles	3
12	3	cold dry cough, severe shortness of breath and wheezing.	3
13	14	Poor air entry to bases, crackles throughout and expiratory wheeze	4
14	2	Worsening respiratory distress, wheeze	1

Appendix 13 (cont...) **Estimation of Severity of Acute Exacerbations of Asthma in Children**

Patient	Number of Days Patient was Symptomatic Prior to Hospitalization	Acute Symptoms of Asthma On Hospital Admission	Length of Hospital Stay (Days)
15	NA	Harsh congested cough.	NA
16	1	Difficulty breathing, bilateral wheeze.	6
17	1	Episodic wheezes, mild nasal flare, mild tracheal tug, dry cough	3
18	2	Moderate respiratory distress- inspiratory crackles, expiratory wheeze, shallow breaths	1
19	5	Cough, dyspnea and bilateral wheeze, moderate secretions	2
20	7	On examination, subcostal indrawing, mild intercostal indrawing, slightly decreased air entry, crackles in the left lower lobe.	
21	2	Moderate respiratory distress with cough and wheeze, intercostal indrawing	2
22	NA	Moderate respiratory distress, slight nasal flaring, slight erythematous rash on face, tracheal tug, subcostal/intercostal indrawing, decreased air entry to bases bilaterally; right > left.	1
23	5	Cough, audible wheeze	NA
24	2	NA	NA
25	1	Moderate respiratory distress:harsh breath sounds, intrecostal indrawing, use of accessory muscles, very tight chest, bilateral wheezes	3
26	2	Decreased appetite, shortness of breath, dyspnea, vomiting.	NA
27	NA	Shortness of breath, vomiting, wheezy chest on right side.	2
28	14	NA	2
29	1	Difficulty breathing	3
30	3	Cough, wheeze, moist cough, not productive,	5

Appendix 13 (cont...) **Estimation of Severity of Acute Exacerbations of Asthma in Children**

Patient	Number of Days Patient was Symptomatic Prior to Hospitalization	Acute Symptoms of Asthma On Hospital Admission	Length of Hospital Stay (Days)
31	1	Tired, accessory muscle use, chest very tight, decreased AE to bases, decreased breath sounds.	4
32	3	Decreased level of consciousness, grey colour to skin, unable to speak. Vomiting, wheezing.	2
33	2	NA	3
34	NA	Unable to speak, as "too tight."	NA
35	2	Tight indrawing, tracheal tug, using accessory muscles, diffuse wheezing.	2
36	NA	Moderate respiratory distress-intercostal and suprasternal indrawing, marked expiratory wheezes	3
37	3	Nasal flaring, suprasternal and subcostal indrawing, bilateral wheeze	4
38	1	Clean air entry bilateral but full of rhonchi and with prolonged expiration.	2
39	NA	Wheeze, congested cough, crackles, trachial tug	2
40	3	mild respiratory distress, poor air entry and inspiratory and expiratory wheezes	2
41	4	Decreased air entry to both bases, chest tightness, cough	3
42	NA	Sneezing for 24 hours, shortness of breath, dyspnea.	3
43	3	Decreased air entry with bilateral wheeze-moderate respiratory distress	3
44	NA	Decreased breath sounds bilateral with expiratory wheeze, minimal tracheal tug	2
45	14	Severe respiratory distress, wheezes to both lungs	6
46	NA	Moderate subcostal indrawing, decreased air entry to both bases, coarse crackles and wheezes bilateral	5

Appendix 13 (cont...) **Estimation of Severity of Acute Exacerbations of Asthma in Children**

Patient	Number of Days Patient was Symptomatic Prior to Hospitalization	Acute Symptoms of Asthma On Hospital Admission	Length of Hospital Stay (Days)
47	4	Fever, increased respiratory distress and cough.	3
48	1	worsening cough, wheeze, shortness of breath	4
49	1	bilateral wheeze with prolonged expiratory phase, coarse rhonchi bilateral, air entry decreased to bases	2
50	1	Diffuse wheezing, marked respiratory distress	2
51	1	Shortness of breath, cough to the point patient could not talk.	2
52	NA	Wheezing, trachial tug, shortness of breath and noisy breathing since lunch at school with harsh cough. Worse tonight,	2
53	NA	Shortness of breath, slight intercostal indrawing and bilateral wheezes	2
54	2	Moderate respiratory distress-coarse cough with tachypnea, wheezing	1
55	NA	Dry paroxysmal cough, shortness of breath, mild fever, use of accessory muscles	4

Appendix 14 Chronic Medications and Medications For Current Episode of Patients Evaluated For DRHA (N=44)

Patient	Chronic Medications	Medications For Current Episode
1	Salbutamol Liquid PRN, Pulmicort 1 puff BID	Salbutamol, 3 puffs with no improvement, Ibuprofen
3	Alupent, Tussiaminnic Cough Syrup, Puffer Not Used	No Medications Given
4	Bricanyl PRN (Not Used)	Bricanyl At Sign of Symptoms
5	Salbutamol MDI 2 Puffs TID, Pulmicort 2X/week	Salbutamol Q30 min
6	No Medications Used	Salbutamol MDI 100 mcg PRN, Becloforte 250 mcg BID
7	No Medications Used	Salbutamol Mask 4 Times
8	No Medications Used	Flovent 1 Puff QID, salbutamol inhaler 1 Puff QID
10	Salbutamol PRN, Pulmicort BID Not Used	Salbutamol Q1H
11	Alupent PRN	Salbutamol PRN, Beclovent PRN
12	Salbutamol Nebule TID- Not Used, Pulmicort TID	Salbutamol NEB Increased Use
13	Salbutamol MDI 2 Puffs Q6H PRN Aerochamber, Becloforte MDI 2 Puffs BID Aerochamber, Also has nebulizer, not used.	Salbutamol and Becloforte
15	Salbutamol MDI PRN, Beclovent 2 Puffs QID X 10 Days PRN Aerochamber	Increased Salbutamol Use, Benylin 2 teaspoonfuls
16	Salbutamol MDI - 1 MDI per month, Pulmicort Inhaler Usually BID - Rarely Used, Nebulizer – Not Used	Benylin, Increased salbutamol Use, Pulmicort 1 puff
17	Salbutamol PRN MDI	Salbutamol MDI PRN
18	No Medications Used	Dimetapp PO
19	Salbutamol MDI PRN (Used 1-2 times per month)	Salbutamol MDI
21	No Medications Used	No Medications Used
22	No Medications Used	Salbutamol MDI (Used 2 Doses Before Hospital Admission)

Appendix 14(cont...) **Chronic Medications and Medications For Current Episode of Patients Evaluated For DRHA (N=44)**

23	Salbutamol Nebule BID – Actual Use NA, Pulmicort Nebule BID – Actual Use NA	Salbutamol Nebule Up to QID, Pulmicort Nebule BID
24	Salbutamol 1 Puff QD AM	Salbutamol 1 Puff QD AM
25	No Medications Used	No Medications Used
26	No Medications Used	No Medications Used
27	No Medications Used	No Medications Used
28	No Medications Used	Budesonide Nebule TID, Salbutamol MDI PRN Cold, Salbutamol Nebule, Beclomethasone 5 mg BID
29	Alupent, Salbutamol Nebulizer, Pulmicort Nebulizer	Alupent, Salbutamol Nebulizer, Pulmicort Nebulizer
30	No Medications Used	Amoxil, Salbutamol Neb 1 dose, Salbutamol Inhaler 1 dose
31	No Medications Used	Salbutamol MDI 2 puffs
32	5 mg betamethasone alternate days, Salbutamol nebules 2 mg/mL BID, Pulmicort 0.5 mg Nebules not used.	Salbutamol MDI (Used 4-5 puffs)
33	No Medications Used	Salbutamol MDI (Used 2 Puffs Q3H)
34	No Medications Used	Salbutamol MDI 5-7 Puffs, Beclovent MDI 5-7 Puffs, Prednisone 40 mg, (All Medications Were Expired), No Medications Were Used
35	No Medications Used	Benylin and Tylenol
36	Intal Sporadically, Salbutamol Sporadically	No Medications Used
37	Tylenol PRN	No Medications Used
38	Pulmicort BID, Salbutamol PRN 2X/week	20 mg Prednisone, Salbutamol Nebule Q4H All Day and Night
39	Salbutamol MDI PRN	Pulmicort MDI 2 Puffs BID X 5 days
40	Salbutamol MDI 5/7 QID, Pulmicort 200 mcg 2 puffs BID	Salbutamol MDI 5/7 QID, Pulmicort 200 mcg 2 puffs BID
41	No Medications Used	Salbutamol 5X, Alupent 2 mg/mL
42	Beclovent Via Aerochamber Not Used, Salbutamol MDI Via Aerochamber	Beclovent Via Aerochamber Not Used, Salbutamol MDI Via Aerochamber Not Used

Appendix 14(cont...) **Chronic Medications and Medications For Current Episode of Patients Evaluated For DRHA (N=44)**

43	No Medications Used	Salbutamol MDI (Used 1 puff TID for 3 days), Beclovent MDI (Used 1 puff TID for 3 days)
44	No Medications Used	No Medications Used
45	Salbutamol 4X Per Year, Pulmicort Not Used	Salbutamol nebules
46	No Medications Used	Salbutamol MDI 4 puffs, Pulmicort MDI 4 Puffs, Ceclor 2 Doses
47	No Medications Used	Beclofort MDI 2 puffs BID, Salbutamol MDI 2 puffs TID
48	Salbutamol MDI 1-2 P uffs QID PRN, Beclovent 2 Puffs 2-4 X daily (Not Used)	Beclovent 2 puffs BID for 1 day, then 1 puff daily for 7 days.

Appendix 15 Results of Evaluation of DRHA

The results of the expert panel's evaluation of the presence of an adverse drug reaction, presence of therapeutic failure, degree of significance of symptoms to hospital admission, and degree that each admission was avoidable.

Patient	Presence of ADR	Presence of TF	Significance of Symptoms to Hospital Admission	Avoidable Admission
1	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
3	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
4	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
5	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
6	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
7	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
8	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
10	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
11	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
12	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
13	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
15	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
16	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
17	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
18	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable

Appendix 15 (cont...) **Results of Evaluation of DRHA**

Patient	Presence of ADR	Presence of TF	Significance of Symptoms to Hospital Admission	Avoidable Admission
19	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
21	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
22	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
23	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
24	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
25	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
26	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
27	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
28	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
29	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
30	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
31	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
32	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
33	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
34	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
35	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable

Appendix 15 (cont...) **Results of Evaluation of DRHA**

Patient	Presence of ADR	Presence of TF	Significance of Symptoms to Hospital Admission	Avoidable Admission
36	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
37	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
38	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
39	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
40	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
41	Unlikely/Unevaluable	Definite	Dominant	Definitely Avoidable
42	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated
43	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated
44	Unlikely/Unevaluable	Possible	Partly Contributing	Not Evaluated
45	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated
46	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated
47	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated
48	Unlikely/Unevaluable	Possible	Dominant	Not Evaluated

Appendix 16 Asthma Management Before Hospital Admission

The following table shows the actions taken by parents and/or the child at the first sign of asthma symptoms related to the hospital admission.

Patient	Actions Taken At First Sign of Asthma Symptoms
1	Mother increased salbutamol, used a humidifier, and limited physical activities of the patient.
2	Required salbutamol every two hours and mother started on oral steroids
3	Orciprenaline sulfate and over-the-counter cough medication.
4	He was doing well when he had a cough and cold symptoms for the previous two days prior to admission. The cough had increased on the day of the hospital admission and the father gave inhaled turbutaline to the child without much improvement.
5	Salbutamol increased to five to six times per day; one puff of budesonide given.
6	NA
7	36 hours before admission, symptoms began. Inhaled salbutamol and inhaled beclomethasone were given.
8	One day before admission, began taking inhaled salbutamol and inhaled beclomethasone four times daily without significant improvement.
9	No appropriate asthma management therapy was initiated.
10	Used salbutamol by metered-dose inhaler every one hour.
11	Used orciprenaline sulfate at home.
12	Increased use of salbutamol.
13	Gave 1 dose of salbutamol after ninedays of "cough" and wheeze symptoms.
14	Did not implement any treatment.
15	Increased frequency of salbutamol dose. Given Benylin cough medication.
16	Lack of an appropriate asthma management plan.
17	No medications were administered at home.
18	Acute asthma symptoms treated with bropheniramine--phenylepherine.
19	Sporadic use of salbutamol.
20	Two puffs of salbutamol and two puffs of budesonide given.

Appendix 16 (cont...) Asthma Management Before Hospital Admission

Patient	Actions Taken At First Sign of Asthma Symptoms
21	Asthma managed at home with bropheniramine--phenylepherine.
22	Salbutamol X3 and budesonide X1 via nebuliizer with no improvement.
23	Symptoms of a cold started five days before admission. Was sneezing, had diarrhea, but had no fever, and no vomiting. Two doses of salbutamol were given. One dose at 4 pm and one dose at 10 pm. Cough worsened, and increased in frequency.
24	No asthma management plan was used.
25	Did not treat acute symptoms at home.
26	No treatment was available.
27	No treatment was available.
28	Began salbutamol and budesonide nebules 3X/day about 2 weeks ago after symptoms started.
29	NA
30	Gave salbutamol only once after two days of symptoms.
31	No asthma treatment plan was used.
32	Increased frequency of salbutamol use.
33	NA
34	Three days ago she started getting the symptoms. Parents gave her salbutamol, inhaled beclomethasone inhalers yesterday. Last night she also got oral steroids. They that it was important to give her medication with the wheezing symptoms but think that maybe they react
35	No treatment was started.
36	No treatment was started.
37	No treatments were given.
38	Mother gave 20 mg prednisone PO and salbutamol Q4H all day.
39	Inhaled beclomethasone 2 puffs BID
40	NA

Appendix 16 (cont...) Asthma Management Before Hospital Admission

Patient	Actions Taken At First Sign of Asthma Symptoms
41	Orciprenaline sulfate 5X the day before admission. Did not use his salbutamol inhaler.
42	Was given salbutamol and inhaled beclomethasone.
43	NA
44	No asthma treatment was started.
45	No appropriate acute asthma treatment was given.
46	Mom gives salbutamol TID and pulm TID when she has an URTI (via neb)
47	Father started patient on inhaled beclomethasone (400 ug BID) and salbutamol TID when symptoms began to appear about 4 days ago.
48	NA
49	No previous knowledge about asthma.
50	NA
51	First episode of asthma.
52	NA
53	NA
54	NA
55	NA

Appendix 17 Classification of Asthma Severity

Patient	Chronic Severity
1	MILD-PERSISTENT
3	MILD-INTERMITTENT
4	MILD-PERSISTENT
5	MODERATE-PERSISTENT
6	MILD-PERSISTENT
7	MILD-INTERMITTENT
8	MILD-INTERMITTENT
10	MODERATE-PERSISTENT
11	MILD-INTERMITTENT
12	MILD-PERSISTENT
13	MILD-PERSISTENT
15	MILD-INTERMITTENT
16	MODERATE-PERSISTENT
17	MILD-INTERMITTENT
18	NON-DETERMINABLE
19	MILD-PERSISTENT
21	MILD-INTERMITTENT
22	MILD-PERSISTENT
23	MILD-PERSISTENT
24	MODERATE-PERSISTENT
25	MILD-PERSISTENT

Appendix 19 (cont...) **Classification of Asthma Severity**

Patient	Chronic Severity
26	NON-DETERMINABLE
27	MILD-INTERMITTENT
28	NON-DETERMINABLE
29	MILD-PERSISTENT
30	MILD-INTERMITTENT
31	MILD-PERSISTENT
32	MODERATE-PERSISTENT
33	MILD-INTERMITTENT
34	MILD-INTERMITTENT
35	MILD-INTERMITTENT
36	MODERATE-PERSISTENT
37	NON-DETERMINABLE
38	MODERATE-PERSISTENT
39	MILD-INTERMITTENT
40	MILD-PERSISTENT
41	MILD-PERSISTENT
42	MILD-PERSISTENT
43	NON-DETERMINABLE
44	MILD-INTERMITTENT
45	MILD-PERSISTENT
46	MILD-INTERMITTENT
47	NON-DETERMINABLE
48	MILD-PERSISTENT

Appendix 18 Inhaled Steroids Use and Oral Steroid Use Before Hospital Admission of Patients

The presence or absence of inhaled steroid use and oral steroid use is shown in each row.

Patient	Did the patient take any inhaled steroids for the acute exacerbation?	Did the patient take any oral steroids for the acute exacerbation?
1	NO	NO
3	NO	NO
4	YES	NO
5	NO	NO
6	YES	NO
7	NO	NO
8	YES	NO
10	NO	NO
11	YES	NO
12	NO	NO
13	YES	NO
15	NO	NO
16	YES	NO
17	NO	NO
18	NO	NO
19	NO	NO
21	NO	NO
22	NO	NO
23	NO	NO
24	NO	NO
25	NO	NO
26	NO	NO
27	NO	NO
28	YES	YES
29	YES	NO
30	NO	NO
31	NO	NO
32	NO	NO

Appendix 18 (cont...) **Inhaled Steroids Use and Oral Steroid Use Before Hospital Admission of Patients**

Patient	Did the patient take any inhaled steroids for the acute exacerbation?	Did the patient take any oral steroids for the acute exacerbation?
33	NO	NO
34	YES	YES (medication expired 2 years ago)
35	NO	NO
36	NO	NO
37	NO	NO
38	NO	YES
39	YES	NO
40	YES	NO
41	NO	NO
42	YES	NO
43	YES	NO
44	NO	NO
45	NO	NO
46	YES	NO
47	YES	NO
48	YES	NO

Appendix 19 Compliance With Medications Before Hospital Admission

Patient	Compliance	Details of Non-compliance
1	Non-compliant	Budesonide started one year ago on twice daily dosing and he misses the occasional dose. Child forgets to take medication sometimes. Does not always take the medication at the same time each day. If he feels better, he would stop taking medication on his own.
3	Non-compliant	Has had difficulty using the puffer so did not use it at all.
4	Non-compliant	Had been prescribed terbutaline sulphate one year ago. This was the only medication he had been prescribed (no other meds). However, previous to this episode, he had not used it.
5	Non-compliant	Was on one puff of budesonide twice daily, but he reported taking it about twice weekly even though he requires salbutamol three to four puffs daily.
6	Not enough data	Puffer technique was poor.
7	Compliant	Not applicable.
8	Non-compliant	Dr. had prescribed Flovent 50ug four times daily on a regular basis, but he did not take it regularly.
10	Non-compliant	She did not use her budesonide. Mom frustrated with frequency of medication use and seeking a traditional medicine through a "naturalpath."
11	Non-compliant	Medication was just given in bursts. Either the medication was running out or he was not given it.
12	Non-compliant	Patient was non-compliant. Does not increase dose of budesonide as instructed, only increases dose of salbutamol.
13	Non-compliant	Did not administer the preventative medication.
15	Not enough data	Not applicable.
16	Non-compliant	Salbutamol had been used about 15 to 17 times per week. Rare use of budesonide MDI.
17	Non-compliant	No medications were given by parents before going to ER at BCCH.
18	Not enough data	Not applicable.
19	Not enough data	Not applicable.

Appendix 19 (cont...) **Compliance With Medications Before Hospital Admission**

Patient	Compliance	Details of Non-compliance
21	No previous asthma medications	Not applicable.
22	Not enough data	Not applicable.
23	Compliant	Not applicable.
24	Non-compliant	Non-compliant with nedocromil sodium inhaler therapy ever since the patient moved to Vancouver.
25	No previous asthma medications	Not applicable.
26	No previous asthma medications	Not applicable.
27	Not enough data	Not applicable.
28	Non-compliant	Poor compliance according to family physician.
29	Not enough data	Not applicable.
30	Not enough data	Not applicable
31	Non-compliant	Patient's reported use of medication is not consistent. Parents do not appear to be very involved in her management. They do not come to visit her.
32	Non-compliant	Child reports that the parents can't afford the corticosteroid medications. That is why they only have the salbutamol at home.
33	Not enough data.	Not applicable.
34	Non-compliant	Corticosteroids taken were expired 2 years ago.
35	No previous asthma medications	Not applicable.
36	Non-compliant.	Did not take inhaled corticosteroids regularly.
37	No previous asthma medications	Not applicable.
38	Non-compliant	Mother sometimes forgets to give the medication.
39	Compliant	Not applicable.
40	Non-compliant	Poor technique with budesonide inhaler.
41	Non-compliant	Did not use his salbutamol puffer. Inappropriate chronic asthma management. Does not use his spacer.
42	Non-compliant	Did not use inhaled corticosteroids as directed.
43	Non-compliant	Upon diagnosis two weeks ago, patient was given salbutamol and beclomethasone dipropionate inhalers but only used them on and off.
44	Non-compliant	Did not take medications as directed.

Appendix 19 (cont...) **Compliance With Medications Before Hospital Admission**

Patient	Compliance	Details of Non-compliance
45	Non-compliant	Salbutamol used four times per year during acute attacks and budesonide is not used.
46	Compliant	Not applicable.
47	Non-compliant	Previous medications were salbutamol and beclomethasone dipropionate as needed, but had not been taking them since last year.
48	Non-compliant	Mother is not compliant with medication because she is afraid of the side effects.