

**HEALTH QUALITY OF LIFE MEASUREMENTS AND THEIR RELATIONSHIP TO  
ASTHMA SEVERITY IN CHILDREN**

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## **ABSTRACT**

*Background:* Asthma exacerbations are a leading cause of school absenteeism and time lost from work, affecting the quality of life (QOL) of children with asthma and their caregivers.

*Objective:* The objective of this study is to determine the relationship between measures of asthma severity and the QOL of children with asthma and their caregivers living in rural Saskatchewan.

*Methods:* Data for this research was previously collected in 2005-2007 using a case-control study design. Children were recruited for the case control study following a cross-sectional school based survey of children aged 6-18 year. Cases with physician-diagnosed asthma (n=77) were then selected to examine associations between asthma severity and QOL, with respiratory information collected from a home visit, clinic visit and two-week home monitoring of diurnal peak flow variability (DPV). During the clinic visit, children underwent spirometry and completed the Pediatric Asthma QOL Questionnaire (PAQLQ). During the home visit, parents completed the Child Health Questionnaire (CHQ-PF50) and the Pediatric Asthma Caregiver QOL Questionnaire (PACQLQ) and were given instructions on how to complete the two-week diurnal peak flow home monitoring. Higher mean scores on measures of QOL questionnaires indicated better QOL. Asthma severity was measured by Forced Vital Capacity (FVC), Forced Expiratory Volume in one Second (FEV<sub>1</sub>), and mean DPV. Linear regression was used to assess the association between the three QOL measures and measures of asthma severity (mean diurnal peak flow variability and percent predicted lung function adjusting for smoking, parental education and asthma medication use in the last 12 months).

*Results:* The lowest mean score on the PAQLQ completed by the children was being bothered by physical activity (mean = 5.8, standard deviation = 1.19) whereas the lowest mean score on the PACQLQ completed by parents was feeling helpless or frightened (mean = 6.1, standard deviation = 1.28). No significant relationships were found between QOL scales. When the PACQLQ and the PAQLQ were stratified by age groups, parents reported higher mean scores for children in the 13-17 age group ( $p = 0.01$ ) on the total score of the PACQLQ and activity and emotional subscales ( $p = 0.003$  and 0.03, respectively). No significant correlations were found between spirometry measurements and the three QOL measures. Significant negative correlations were found between mean DPV and the mean PAQLQ Total Score. In a post hoc analysis, examining minimum morning peak flow expressed as percent recent best and QOL, significant positive correlations were found between the minimum morning peak flow measurements and the mean PAQLQ Total Score and Activity subscale.

*Conclusions:* While findings from this study suggest that the CHQ-PF50 could be used to assess emotional aspects of QOL in children with asthma, overall, it may not be a useful tool in assessing the QOL of children with asthma. Peak flow may be a better measure of asthma severity than spirometry when assessing QOL for children with asthma and their parents.

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## **LIST OF ABBREVIATIONS**

### Abbreviations

CHQ-PF50	Child Health Questionnaire Parent Form 50
CHQ-PF50 PSS	Child Health Questionnaire Psychosocial Summary Score
CHQ-PF50 PHS	Child Health Questionnaire Physical Summary Score
DPV	Diurnal peak flow variability
FEF <sub>25-75</sub>	Forced expiratory flow between 25 and 75% of forced vital capacity
FEV <sub>1</sub>	Forced expiratory volume in 1 second
FVC	Forced vital capacity
PACQLQ	Pediatric asthma caregiver quality of life questionnaire
PAQLQ	Pediatric asthma quality of life questionnaire
PEFR	Peak expiratory flow rate
QOL	Quality of life
GINA	Global Initiative for Asthma Guidelines
NAEPP	National Asthma Education and Prevention Program
NHLBI	National Heart Lung and Blood Institute
ASI	Asthma Severity Index
AAQOL	Adolescent Asthma Quality of Life Questionnaire
ITG-CASF	Integrated Therapeutics Group Child Asthma Short Form

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## **CHAPTER ONE**

### Introduction and Literature Review

#### *Introduction*

The prevalence of childhood asthma in Saskatchewan has been estimated at 16%-22% of children ages 6-12 years, higher than the previously reported rate of 10%-12% (Rennie, Lawson, Cockcroft, Senthilselvan, & McDuffie, 2004). According to findings from the International Study of Asthma and Allergies in Childhood (ISAAC) asthma symptom prevalence is more likely increased rather than decreased with a wide variation by geographical location (Asher, Montefort, Bjorksten, Lai, Strachan et al., 2006).

Childhood asthma is consistently reported as the number one reason for school absenteeism (Alvim, Picin, Camargos, Colosimo, Lasmar et al., 2009; Shendell, Alexander, Sanders, Jewett, & Yang, 2010). A study by Butz, Pharm, Lewis, Lewis, Hill et al., (2005) found that 31% of children with asthma missed one or more weeks in the past six months of school because of their asthma. In a 2009 review of respiratory health of Saskatchewan children, Reisman reported that respiratory illness was the number one cause of hospitalizations for Saskatchewan babies and children.

Pediatric asthma frequently manifests itself in acute exacerbations causing increased shortness of breath, increased lung secretions, smooth muscle contraction and inflammation (Fink, 2001). In 2008-2009, asthma exacerbations requiring emergency room visits by children accounted for over 300,000 visits or hospital admissions across Canada (Canadian Institute for Health Information, 2009). As a result of frequent exacerbations, the quality of life (QOL) of the child and family can be impaired. In a study by Subbarao, Mundhane & Sears (2009), examining 1254 children with asthma, poorly controlled asthma was shown to

be associated with unscheduled physician visits, hospitalizations, more days missed from work or school, limitations of daily activities, impaired QOL, peak expiratory flow variation greater than 10-15%, and forced expiratory volume at one second (FEV<sub>1</sub>) less than 90% personal best. Asthma exacerbations require periodic medical attention and may pose a distinct disadvantage for children living in rural areas where accessibility to health services can be a challenge. In a cross-sectional study of 2457 children with and without asthma, Rennie & Dosman, (1999) found that while most rural children with asthma lived close to medical care or health care for their asthma, children with less control of their asthma (more symptoms and episodes of asthma in the past year) were more likely to live further than 30 km from their medical care.

Measures of QOL are thought to indicate how much illness interferes with an individual's daily life and how much burden is placed on the individual and their family. QOL and one's adaptation are associated with social, emotional and physical functioning (Levi & Drotar, 1998). Previous QOL research in asthma has primarily focused on QOL for adults (Juniper, O'Byrne, Guyatt, Ferrie & King, 1999; Moy, Israel, Weiss, Juniper, Dube et al., 2001; Kanter, Seigel, Snyder, Pelletier, Buchner et al., 2002; Schatz, Mosen, Kosinski, Vollmer, Magid et al., 2007). Much of the research in the QOL in children with asthma has relied on the parent's, with limited information from the child (Asher, Keil, Anderson, Beasley, Crane et al., 1995; Guyatt, Juniper, Griffith, Feeny, & Ferrie, 1997; Juniper, Guyatt, Feeny, Ferrie, Griffith et al., 1996(a); Rutishauser, Sawyer, & Bowes 1998; Waters & Maher, 2007). Parent and child reports of QOL in relation to the child's asthma can differ (Erickson, Muzenberger, Plante, Kirking, Hurwitz & Vanuya, 2002; Guyatt et al., 1997). As well, studies have also shown that while children tend to rate their severity as mild to

moderate, caregivers tend to rate the child's asthma as moderate to severe (Brunner, Grundland, Young, Blanchette, & Stain, 2003; Guyatt et al., 1997; Ungar, Mirabelli, Cousins, & Boydell, 2006; Williams & Williams, 2003). These observations suggest that there may be a difference in parent and child perceptions, of QOL, and should be compared against other indicators of severity.

It is well known that as asthma severity increases, the child's QOL can decrease (Chan, Mangione-Smith, Burwinkle, Rosen, & Varni, 2005; Flapper, Koopman, Napel, & Van der Schans, 2006; Van de Ven, Engels, Sawyer, Otten, & Van Dec Eijnden, 2007; Warschburger, Busch, Bauer, Kiosz, Statchow, et al., 2004). However, accuracy of the findings for children's QOL may be questioned. Of the research conducted assessing asthma severity and QOL, nearly half of the studies utilize the parent's perceived QOL as a proxy for the child's perception of their own QOL.

Presently, there is limited study of the use of objective measures to assess the relationship between asthma severity and QOL in children. Two potential objective methods of measuring of asthma severity are spirometry and peak flow. Spirometry allows measurements of lung volumes and airflow by exhaling forcibly into a spirometer. Juniper, Guyatt, Feeny, Ferrie, Griffith et al., (1996)(b) found a correlation between better QOL and better lung function measured during 3 follow-up visits with pediatric clinic patients. Children with better lung function (FVC) had higher QOL scores on the PAQLQ compared to children with severe asthma (Juniper et al., 1996)(b). However, in a study by Brouwer, Roorda & Brand (2006) there was no correlation between average 3 month FEV<sub>1</sub> and PAQLQ scores with children who were taught to perform daily spirometry at home. Only one study has been conducted where FEV<sub>1</sub> was reported to be associated with QOL in

children (Zandieh, Moin & Movahedi, 2006). This study found a strong association ( $p < 0.001$ ) between measured FEV<sub>1</sub> and impairment of the child's QOL but not for FEV<sub>1</sub> percent predicted.

#### *Purpose of the Study*

The purpose of this study is to identify the relationship between QOL measures of rural children with asthma from the perspectives of the child and the parent. Furthermore, this study will help to identify if poorer QOL scores are associated with asthma severity in children. This will be accomplished by assessing the level of agreement between three instruments of QOL measurement and two objective measures of asthma severity.

#### *Relevance and Significance*

There is limited study of the association between asthma severity and QOL measures for children with asthma. Measures of the QOL by children with asthma and their parents correlate poorly in studies of younger urban children. Less is known about these associations in rural children, where QOL may be different from urban children. As well, there is limited study comparing asthma-specific measures of QOL to generic measures of QOL in children. The information obtained from this study will help to fill the gap in rural literature of the QOL of children with asthma from both the parent and child's perspective. The comparison of different measurement tools to assess QOL could assist health care professionals and researchers in identifying the best methods of assessing QOL for children with severe asthma. This information would be useful for healthcare professionals as part of evidence-based, informed practice.

## *Literature Review*

For the purpose of the literature review on QOL and asthma in children a search of the databases Cumulative Index to Nursing and Allied Health (CINAHL), MEDLINE with Full Text and Education Resources Information Center (ERIC OvidSP) was conducted using numerous combinations of the following key words: *asthma, quality of life, asthma severity, asthma exacerbation, Pediatric Asthma Quality of Life Questionnaire, PAQLQ, Pediatric Asthma Caregiver Quality of Life Questionnaire, PACQLQ, Child Health Questionnaire, CHQ, diurnal peak flow variation, lung function, spirometry, rural and asthma burden*. Searches were restricted to children and no searches were limited by year of publication. There were 89 articles retrieved and reviewed related to QOL tools, asthma severity measures and childhood asthma.

### *Pathophysiology of Asthma*

Asthma is a chronic inflammatory disorder of the airways characterized by intermittent paroxysmal or persistent symptoms such as dyspnea, chest tightness, wheezing, sputum production and cough associated with variable airflow limitation and variable degree of airway hyper-responsiveness to endogenous or exogenous stimuli (Boulet, Bai, Becker, Berube, Beveridge et al., 2001). Inflammation of the airway and its resulting effect on airway structure are considered the main mechanisms leading to the development of asthma symptoms (Lougheed, Lemiere, Dell, Ducharme, FitzGerald, et al., 2010).

Asthma exacerbations are characterized by any combination of the following physical symptoms: breathlessness preventing a child from talking in sentences or eating properly, persistent cough, wheezing or whistling noise on auscultation, mucus production, nasal flaring, marked use of sternocleidomastoid muscles, respiratory rate greater than two

standard deviations above the normal for age, markedly decreased air entry and excessive anxiety, prolonged expiratory phase, restlessness, or lethargy resulting from air hunger (Kovesi, Schuh, Spier, Berube, Carr et al., 2009). As well, these symptoms may often occur during the night interrupting sleep for both the child and caregiver.

As pediatric airways are smaller to begin with, airflow is more easily decreased and restricted during an asthma exacerbation. The chronic lung inflammation caused by frequent exacerbations and insufficient therapeutic interventions can result in pathologic changes to the lung leading to thickening of the airway wall (remodeling), and degradation of the airway epithelium making the airway more irritable (Becker, Lemiere, Berube, Boulet, Ducharme et al., 2005; Fink, 2001).

#### *Burden of Asthma*

There are three types of burden that can be associated with chronic asthma in children: those associated with the health care system, the family caregivers, and with the individual. Burden to the health care system is measured in terms of cost. In Ontario, (1996) the annual cost to the health care system of a child with asthma has been assessed to be \$1,922 to \$2,386 per child. These costs for asthma account for the largest portion of physical care expenditures for children at approximately 244 million dollars per year (To, Dell, Dick, & Cicutto, 2008). In addition, children with asthma have been shown to have three times more hospitalizations than a general population of children, (To et al., 2008). The direct economic societal cost also corresponds with the severity of asthma. Studies indicate that expenditures of patients with severe asthma are almost twice that of patients with moderate asthma (Krahn, Berka, & Langlois, 1996; Serra-Batilles, Plaza, Morejon, Comella, & Brugues, 1998). The financial burden associated with asthma, is not static, but rather an

evolving burden to the health care system over time; severe asthma requires long-term management increasing the burden to the health care system.

Caregivers of children with asthma have been shown to have higher rates of emotional distress, uncertainty and fears related to the illness due to the demands associated with caring for a chronically ill child (Kieckhefer & Ratcliffe, 2000; Frankel & Wamboldt, 1998; Everhart, Fiese & Smyth, 2008). In a qualitative study, Kieckhefer & Ratcliffe (2000) reported that caregivers of children with asthma reported sleepless nights and greater anxiety about their child. This lack of sleep appeared to increase the stress of living with asthma and affected family dynamics. The burden of actively managing this chronic condition can drain physical, emotional and financial resources of the family and affect the child's ability to deal with other life challenges (Frankel & Wamboldt, 1998, Halterman, Yoos, Conn, Callahan, Montes, Neely & Szilagyi, 2004). As well, caregivers of children with asthma also report the fear of their child dying from asthma, (Handelman, Rich, Bridgemohan & Scheider, 2004) further compounding the psychological stressors associated with QOL in pediatric asthma management. The above challenges could be magnified in rural populations with limited access to health care resources (Walker, Winkelstein, Land, Lewis-Boyer, Quartey et al., 2008).

Caregiver absenteeism from work is another concern associated with the management of childhood asthma. It has economic consequences for the family, including loss of wage and productivity. Research indicates approximately one third of caregivers of children with asthma will require time absent from work due to asthma-related illness and 13.3% will require more than five days absent per year (Laforest, Yin, Sazonoz, Pacheco, Dickson, et al., 2004).

The personal burden to the child with asthma is an important consideration. Childhood asthma ranks first among medical disorders that significantly limit children from attending school (Alvim et al., 2009; Msall, Avery & Tremont, 2003; Millard, Johnson, Hilton & Hart, 2009; Shendell, et al., 2010). Research indicates children with asthma average a 12.6-36.0% increase in missed days of school compared to non-asthmatic classmates (Austin, Selvaraj, Godden, & Russell, 2005; Fillmore, Jones, & Blankson, 1997). These issues should not be overlooked owing to the potential long-term consequences in terms of children's academic performance (Laforest, et al., 2004). Children with asthma have been shown to report higher rates of depression and other behavioural disorders compared to non-asthmatic children (Blackman & Gurka, 2007; Vila Burwinkle, Seid, Katz & Jacob, 2003).

In a study conducted by Neder, Nery & Silva (1999) children with asthma showed less tolerance to exercise because of shortness of breath and restriction of activities secondary to medical advice or family influence. Basaran, Guler-Uysal, Ergen, Seydaoglu, Bingol-Karakoc, et al., (2006) also found a positive correlation between children participating in a home exercise program and improved reported QOL scores on the PAQLQ (PAQLQ total score 6.23 with exercise vs. 5.31 without exercise). Children who reported wheezing symptoms in the last 12 months were also limited in their school activities and unable to participate in physical education (Austin, et al., 2005; Glazebrook, McPherson, Macdonald, Swift, Ramsay, et al., 2006). Glazebrook et al., (2006) also reported that two thirds of children with asthma stated that asthma stopped them from doing sports and limited their activity.

Fear of asthma symptoms may also cause children with asthma to avoid physical activities and social situations they might otherwise enjoy. This fear has been shown to be greater when asthma is not adequately controlled, further contributing to the isolation of the disease process and potentially hindering interpersonal relationships (Blackman & Gurka, 2007; Schmier, Chan & Leidy, 1998; Walker, et al., 2008).

In summary, three types of burden have been shown to be associated with childhood asthma: burden or cost to the health care system; personal burden to the family caregivers; and individual burden to the child with asthma. Pediatric asthma accounts for Canada's largest portion of physical care expenditures in children to the health care system. Caregivers of children with asthma report higher rates of emotional distress, uncertainty and fears related to the illness due to the demands associated with caring for a chronically ill child. Children with asthma are more likely to have missed days of school and psychological impairments such as fear of asthma symptoms and increased rates of depression compared to children who do not have asthma.

### *Asthma Severity*

According to Horner, Keickhefer & Fouladi, (2006) asthma severity is a term used for both intermittent asthma exacerbations and chronic asthma as reflected in the patterns of symptom frequency and functional impairment. There are a variety of national and international recommended guidelines for the diagnosis and management of asthma that also include assessment of asthma severity. In Canada, the Canadian Pediatric Asthma Consensus Guidelines define poor control as daytime symptoms (wheezing, cough, dyspnea, chest tightness and sputum production) greater than 4 days a week, night-time symptoms greater than 1 night a week, the need for  $\beta_2$ -agonist medication more than 4 doses per week, a FEV<sub>1</sub>

less than 90% of personal best and PEF diurnal variation of greater than 10-15% (Lougheed, Lemiere, Ducharme, Licskai, Dell, et al., 2012).

Internationally, the World Health Organization recommends considering four components in assessing asthma severity: level of control (current control or impairment, symptoms, and functional limitations over the previous two weeks, and exacerbations over the previous 6-12 months); level of current treatment prescribed (inhalation technique and compliance with treatment); responsiveness to treatment and risk (Bousquet, Mantzouranis, Cruz, Ait-Khaled, Baena-Cagnani, et al., 2010). The two objective measures that are frequently used to assess asthma management clinically or asthma outcomes in research are spirometry and peak flow variability (Clough, 1996, Lougheed, et al., 2012).

There is little agreement amongst researchers as to what is the best method of assessing asthma severity in children. Spirometry is considered the gold standard measurement in clinical studies to objectively assess asthma severity. In particular, forced expiratory volume in the first second ( $FEV_1$ ) is the most often used index to measure airway obstruction associated with disease severity (Miller, Hankinson, Brusasco, Burgos, Casaburi et al., 2006). Previous research has shown spirometry to be underutilized in clinical settings due to time and resource constraints (O'Dowd, Fife, Tenhave & Panettiere, 2003). Few studies (Brouwer et al., 2006; Moy et al., 2001; Raat, Beuving, Jongste, Grol, Juniper et al., 2005; Zandieh et al., 2006) used spirometry ( $FEV_1$ ,  $FVC$ ,  $FEV_1/FVC$  ratio,  $FEF_{25-75}$ ) in assessing asthma severity) as an objective measurement of asthma severity when comparing to QOL.

Asthma severity requires the documentation of ongoing lung function (Bousquet, et al., 2010). Measurement of spirometry is recommended when available. This is usually

performed during clinic visits, where acceptable maneuvers are obtained by trained technicians. Ideally, if spirometry is to be useful in assessing severity, one time measurement, may underestimate the degree of asthma severity within a study population. In the study of by Brouwer et al., (2006) home spirometry was used with good success (91.5 % compliance) but showed poor concordance with other measures of asthma severity (PEF and asthma severity scores). The World Health Organization recommends the use of peak expiratory flow monitoring as a means of assessing asthma severity in a cost-effective manner (Bousquet, et al., 2010).

A variety of measures have been used to assess asthma severity including self-reported psychometric scales in questionnaires such as the Asthma Control Questionnaire (ACQ), (Juniper, et al., 1999); the Asthma Severity Index (ASI), (Sawyer, Spurrier & Whaites, 2000; Sawyer, Spurrier, Whaites, Kennedy, Martin & Baghurst, 2001), and the Functional Severity of Asthma Scale (FSAS), (Everhart, Fiese & Smyth, 2008). Several national guidelines of asthma symptoms have been used in studies to classify asthma severity, in research reports, including; the Dutch Medical Guidelines (Flapper et al., 2006), the German Asthma Guidelines, (Warschburger et al., 2004), the Global Initiative for Asthma (GINA) Guidelines (Goldbeck, Koffman, Lecheler, Thiessen & Fegert, 2007), the National Asthma Education and Prevention Program (NAEPP), (Kwok, Walsh-Kelly, Gorelick, Grabowski & Kelly, 2006), and the National Heart, Lung and Blood Institute (NHLBI) Guidelines (Chan et al., 2005). Asthma severity can also be classified by parental report of child asthma symptoms (Annett, 2001; Erickson, et al., 2002; Horner et al., 2006; Montaldo, Buzzese, Moskaleva, Higgins-D'Alessandro & Webber, 2004; Sawyer et al., 2001; Williams, Sehgal, Falter, Dennis, Jones et al., 2000; Van De Ven et al., 2007), and by child

report of symptoms or by physician classification of asthma (Annett, Bender, Lapidus, DuHamel & Lincoln, 2001; Flapper et al., 2006; Mussaffi, Omer, Prais, Mei-Zahav, Weiss-Kasirer et al., 2007; Williams & Williams, 2003).

### *Spirometry*

Since its original introduction in 1846 by Hutchinson, spirometry stands as the most widely performed pulmonary function test (Hyatt, Schilder & Fry, 1958; Miller, Crapo, Hankinson, Brusasco, Burgos, et al., 2005). Spirometry allows for measurements of lung volumes and airflow in the diagnosis of asthma and management of asthma. The Canadian Pediatric Asthma Consensus Guidelines recommends the use of spirometry, where possible, to diagnose asthma and evaluate asthma control (Lougheed et al., 2012). Spirometry is not recommended for children under the age of three and children under the age of five or six may have difficulty performing reproducible results (Becker et al., 2005; Gorelick, Stevens, Schultz & Scribano, 2004.). It is dependent on subject effort and good coaching by a trained technician to obtain valid and reliable results.

Among the lung function assessments spirometry provides, is measurement of forced vital capacity (FVC), the total lung capacity expired during a forced expiratory maneuver; forced expiratory volume (FEV<sub>1</sub>), a measurement of the expired volume in the first second of a forced expiratory maneuver; the mean forced expiratory flow rate between 25% and 75% of FVC (FEF<sub>25-75</sub>), the average flow expired in the middle half of FVC that represents the status of medium and small airways; and forced vital capacity ratio (FEV<sub>1</sub>/FVC), a measurement of airflow obstruction (Miller et al., 2005). These measurements can be used to diagnose asthma and assess asthma severity. The assessment of lung function can be staged by percent-predicted values based on previously standardized lung function values adjusted for height,

weight, gender, age and ethnicity (Pellegrino, Viege, Brusasco, Crapo, Burgos, et al., 2005; Miller et al., 2005). A reduction in FEV<sub>1</sub> and FEV<sub>1</sub>/FVC can be seen in the earlier stages of obstructive lung disease such as asthma (Ruppel, 2004). The FEV<sub>1</sub>/FVC ratio can be used to calculate mean airflow obstruction, where a decreased ratio implies an obstructive lung disease such as asthma. This ratio is the most important measure for assessing obstruction and has been shown to predict morbidity and mortality even when the FEV<sub>1</sub> is high (Pellegrino, et al., 2005 & Mannino, Buist, Petty, Enright & Redd, 2003). Standardization of lung function has been developed by the American Thoracic Society (2005) and should be followed in all lung function testing (Miller et al., 2005).

*Peak flow variability.*

Peak expiratory flow rate (PEFR) variability is a measure that is useful in the diagnosis and ongoing management of asthma (Clough, 1996) and can be used as a measure of asthma severity over time. It provides an easily executed method of serial lung function monitoring in study populations and aids in the assessment of asthma severity (Ruppel, 2004). Expiratory air flow (peak flow) is measured in Litres per minute (L/min). The test is completed by blowing forcefully into a hand held portable peak flow meter at intervals of at least twice daily, prior to administration of a bronchodilator medication if prescribed. The results are recorded over a specific period of time and variability in readings are then calculated (Thiadens, de Block, Dekker, Huysman, Houwelingen, et al., 1998). PEFR variability has been found to correlate fairly well with FEV<sub>1</sub> and FEF<sub>25-75</sub> with correlations ranging from 0.59-0.73 (Eid, Yandell, Howell, Eddy, & Sheikh, 2000, Slieker, van der Ent, 2003).

In summary, a variety of methods have been used to assess asthma severity in children. Most frequently measures such as questionnaires, scales and national consensus guidelines regarding symptoms and medication use for asthma management have been used. Objective measures such as spirometry and peak flow variability have been used infrequently although these measures often form part of the national guidelines for measuring control of asthma. Spirometry, (specifically FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>) garners a reproducible standard to objectively measure asthma severity, particularly if conducted over time. However, it can be costly in research as it requires technical support to administer the test each time. A less costly alternative may be the use of a hand held peak flow monitor, which can be used at home and recorded over time.

### *Quality of Life*

Quality of life is an important measure of the child's subjective experience with their disease. It is defined by Schipper, Clinhc & Powell (1990) as representing the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient. It is conceptualized as being comprised of patient functioning across several domains including social interactions, psychological well-being, physical status and economic factors (Schipper, et al., 1990). The assessment of patient QOL assists in decisions regarding their treatment, planning and medication usage. In the same way that the determinants of QOL are specific to the individual child, the importance attached to those determinants will be influenced by the child's expectations and aspirations as well as their own belief system (Carr & Higginson, 2001).

Measurement of the child's adaptation to the chronic disease of asthma is important, because it acknowledges and validates the impairments that the child and their parents

themselves consider important (Schmier, et al., 1998). Research to date suggests asthma affects all domains of QOL, with its largest influence in physical health and emotional functioning.

*Studies Examining Agreement Between Parent and Child Reports of QOL.*

Traditionally, in both clinical and research work, the assumption that parents can answer for children has gone unchallenged. Children have been seen as unreliable respondents who lack the linguistic and cognitive skills required to understand and respond to questionnaires (Eiser & Morse, 2001). However, it has been well documented that parents' perceptions and the child's perceived QOL often differ.

Twelve studies were located that examined both parental and child perceptions of QOL. The major findings from these studies are outlined in Table 1.1. While the majority of studies specifically examined QOL in asthma patients, two studies were related either to muscular dystrophy (Brunner et al., 2003) or pediatric cancer (Sweeting & West, 1998). The major findings of the review were that few studies showed good agreement between parent and child's perceptions of their own QOL whereas most studies indicated variation in agreement that was dependent on the age of the child, severity of illness, or the nature of the QOL under assessment.

Table 1.1 Studies examining parental vs. child report of QOL

Study & Location	Age of Child(Sample Size)	Questionnaire	Asthma Specific	Findings
Annett et al., 2001 United States	7-12 yrs (339 parent-child pairs)	PACQLQ (parent)	Yes	Caregivers total QOL scores compared to child total QOL scores 6.34 vs. 5.88
		PAQLQ (child)	Yes	
Braun-Fahrlander et al., 1998 Switzerland	13-15 yrs (1374 parent-child pairs)	ISAAC questionnaire	Yes	Absolute agreement between adolescent and parent report of symptoms (0.83-0.98)
Brunner et al., 2003 Canada	8-18 yrs (80 parents) (55 children)	CHAQ MSKD specific  ASK	No	No significant relationship between parent and child agreement ( $r = 0.25$ , $p = 0.09$ , $ICC = 0.24$ )
Butz et al., 2005 United States	6-12 yrs (221 parent-child pairs)	PACQLQ (parent)  PAQLQ (child)	Yes Yes	No significant relationship between parent and child QOL scores.
Erickson et al., 2002 United States	9-17 yrs (99 parent-child pairs)	PACQLQ (parent)  PAQLQ (child)	Yes Yes	Children rated asthma severity as mild to moderate. Caregivers rated child's asthma severity as moderate to severe.
Guyatt et al., 1997 Canada	age groups: 7-10, 11-17 (52 parent-child pairs)	PAQLQ  Global Rating of Change Questionnaire	Yes	Differences between parent and child scores were greater in the 7-10 age group

Lindgren et al., 2005 Sweden	13-14 yrs (294 parent-child pairs)	Questionnaire made by research team asthma symptoms, nocturnal symptoms and asthma medication use	yes	Agreement between parental and adolescent questionnaires was good
Renzoni et al., 1999 Italy	13-14 yrs (21068 parent-child pairs)	Questionnaire from ISAAC modules	Yes	Agreement between parental and child reported asthma symptoms ranged from 47.4-73.3%
Ungar et al., 2006 Canada	8-15 yrs (16 parent-child pairs)	PAQLQ (child) PedsQL™ QOL Inventory	Yes Yes	Qualitative study found good agreement between child and parent on concrete items.
Sweeting & West, 1998 United Kingdom	Age 11 (2586 parent-child pairs)	General Health Survey Generic		Parental/child agreement was 54.1% for reports of poor health and 83.4% for reports of moderate health. CI 95%
Williams et al., 2000 United States	5-12 yrs (240 parent-child pairs)	PAQLQ (child) PACQLQ (parent)	Yes Yes	Caregivers QOL scores correlated with QOL scores among children with asthma ( $r = 0.64$ , $p<0.001$ )
Williams & Williams, 2003 Sweden	7-17 yrs (42 parent-child pairs)	PACQLQ (parent) PAQLQ (child)	Yes Yes	Caregivers total QOL scores compared to child total QOL scores 6.6 vs. 5.8

PAQLQ = Pediatric Asthma QOL Questionnaire; PACQLQ = Pediatric Asthma Caregiver QOL Questionnaire; ISAAC = International Study of Asthma and Allergy in Children; CHAQ = Childhood Health Assessment Questionnaire; MSKD = Chronic Musculoskeletal Disorders; ASK = Activities Scale for Kids; QOL = Quality of Life

There is mixed reporting of agreement of QOL perceptions between children and their parents. Parental perceptions for this population may provide limited information into the adolescent's QOL (Kieckhefer & Ratcliffe, 2000). Several studies, including a systematic review (Everhart & Fiese, 2009) concluded that parental perceptions of QOL may not be sufficient in accounting for the subjective nature of the child's QOL measurement. These studies recommend the children's perception of their own QOL must be considered in assessing QOL (Butz et al., 2005; Drotar, 2004; Eiser & Morse, 2001; Frankel & Wamboldt, 1998; Kieckhefer & Ratcliffe, 2000; Petrou, 2003, Osman & Silverman, 1996).

Several studies reviewed in Table 1.1 found disagreement between child reported QOL and parent's perceived QOL for their child (Brunner et al., 2003; Butz et al., 2005; Guyatt et al., 1997; Renzoni, Forastiere & Biggeri, 1999; Sweeting et al., 1998 & Ungar et al., 2006). In a Canadian study, Guyatt (1997) completed a two-month cohort studying exploring children and their parents' assessment of the child's asthma. For this study, children and their caregivers attended a clinic for an interview at enrolment and after weeks 1, 5 and 9. At the 5 and 9-week follow-up visits the parents completed the Global Rating of Change Questionnaire while the child completed the PAQLQ. Children and parents were interviewed separately and completed the questionnaires independently. The Global Rating of Change Questionnaire relates to changes in the child's asthma scoring responses on a 15-point Likert scale. The findings from this study show important differences between parental and child perceptions in 7 to 10 year old children and 11 to 17 year old children. In younger children, age 7-10, changes in both physiological measures and asthma control were more closely related to the parents rather

than to the child's global rating of change [ $r = 0.21$ (child) vs.  $r = 0.48$ (parent) for FEV<sub>1</sub>, ( $r = 0.67$ (child) vs.  $r = 0.24$ (parent) for PAQLQ Symptom Domain scores)]. The reverse was true in the older children, age 11-17, the correlation of global ratings of change in the symptoms with changes in physiological measures and asthma control were higher in the children than the parents [ $r = 0.04$  (child) vs.  $r = 0.09$  (parent) for FEV<sub>1</sub>,  $r = 0.74$  (child) vs.  $r = 0.43$  (parent for PAQLQ Symptoms Domain scores)]. Overall, in adolescents with asthma, self-reported respiratory symptoms were better correlated than parental reports with measures of respiratory function and QOL.

Renzoni et al. (1999) examined epidemiological and clinical information on respiratory and allergic disorders in adolescents with a history of asthma or allergy using 10 centers across Italy for a study population of 21,068 children. Adolescents and their parents independently completed a questionnaire from the ISAAC modules regarding respiratory symptoms, housing, schooling, lifestyle and other possible risk or confounding factors for asthma and allergic disease. Agreement between self-reported and parent-completed asthma symptoms ranged from the lowest (47.4%) for wheeze to (73.3%) for dyspnea.

A Canadian study highlighted the differences of agreement of QOL perceptions between children and their parents. Brunner et al., (2003) investigated health state preference measurements in children with chronic musculoskeletal disorders (MSKD). 80 parents of children with MSKD along with 55 of the children who were age 8 or older were surveyed using the Childhood Health Assessment Questionnaire (CHAQ) and the Activities Scale for Kids (ASK). The CHAQ is a physical functional index sensitive to change in children with MSKD consisting of 8 domains. The ASK is a self-administered

questionnaire that assesses a child's physical function on the basis of the performance of the child during the week prior to the assessment. This study did not find a strong relationship between the CHAQ utilities of the parents and their children ( $r = 0.25$ ,  $p=0.09$ ,  $ICC = 0.24$ ).

Two studies included in Table 1.1 also examined the discrepancy between child reported QOL and parent's perceived QOL for their child primarily focusing on the emotional aspects of QOL. One study from the United Kingdom found parental and child agreement for symptoms of general health in the last 12 months was 54.1% for reports of poor health and 83.4% for reports of moderate health with a confidence interval of 95% (Sweeting et al., 1998). This exploratory longitudinal school based study examined self-reports by children and report by their parents on behalf of their children to general health, current conditions and recent symptoms. The final sample of 2586 children and their parents were randomly selected from the 137 primary schools surveyed. Each pair completed a General Household Survey, which included identical questions regarding the child's health over the last 12 months and whether the child had a longstanding illness. The survey also included symptom evaluation in two categories physical, (stomach ache or sickness, cold or flu, headache, aching back, legs or arms, rashes or skin problems, felt dizzy or faint, asthma or wheezing chest) or malaise (nervous, worried or anxious, irritable or bad tempered, difficulty getting to sleep, been sad, unhappy or low). Parent-child agreement was highest for conditions that are common, visible and diagnosed and greatest disagreement occurred in respect of conditions related to the child's emotional state.

In another Canadian study using a qualitative approach, children completed two asthma specific QOL questionnaires the PAQLQ and Peds QL™ QOL Inventory (Unger et al., 2006). In addition, the parents and children both completed an interview to learn about the context and individual perceptions that influence health-related QOL among children with asthma. Researchers found good agreement between child and parent for items that were concrete, observable and unambiguous, with poor agreement on items where a judgment was required.

Two studies from the USA examined parental and child agreement on their QOL. In the study by Annett, Bender, DuHamel & Lapidus (2003) parents completed the PACQLQ assessing caregiver QOL while the children completed the PAQLQ assessing their own QOL. A total of 339 pairs of children with asthma and their parents completed the 12-month study, which found parents who reported higher scores on the parental distress component of the PACQLQ scored their child's QOL lower. In addition a significant correspondence between parent and child reports of QOL in the older child age cohort was observed. This correlation was particularly strong with the factor that measures parental feelings of distress about the child's asthma symptoms ( $p<0.001$ - 0.01,  $r = 0.15-0.43$ ).

In the second American study reviewed, Erickson et al., (2002) also found that the QOL scores differed between parents and children. Scores in this study on the PAQLQ ranged from the lowest for the Activity Domain (4.51) to the highest score for the Emotional Domain (5.22). Parents' scores on the PACQLQ for the domains and Total Score ranged from the Activity Domain being the lowest (4.78), to the Emotional Domain being the highest (4.9). In addition, Erickson et al., (2002) also had participants

rate their perceptions of the child's asthma severity and found that more children rated their asthma severity in the mild to moderate category (60%), while more parents rated the children in the moderate to severe category (78%).

Two studies that showed good agreement in the QOL of parents and their children with asthma focused on the comparison of asthma QOL scores between adolescents with asthma and their parents. One study from Switzerland examined factors influencing agreement between adolescents with a diagnosis of asthma and their parents (Braun-Fahrlander, Gassner & Grize, 1998). There were 1374 pairs of adolescents with asthma and their parents living in ten different communities in Switzerland who participated in the study. The adolescents completed the ISAAC questionnaire including questions regarding asthma and wheeze. Parents completed a questionnaire created by the researchers also including asthma symptoms and wheeze. The absolute agreement between adolescent and parent report of symptoms was quite high (0.83-0.98) although chance-adjusted agreement was considerably lower (kappa coefficients of reported symptoms between 0.22 and 0.51).

In the study from Sweden, 294 adolescents with asthma and their parents were randomly selected to compare agreement between parental and self-completed questionnaires about asthma (Lindgren, Perzanowski & Ronmark, 2005). The questionnaires used were developed by the research team and included questions regarding asthma symptoms, use of asthma medication and nocturnal symptoms. The study found the agreement between the parents' and teenagers' responses to the asthma questionnaire were good (kappa-values between 95.5% and 0.78 to 98.9% and 0.93).

There was one study located that assessed asthma and QOL in Canadian rural children. Guyatt et al., (1997) completed a two-month cohort studying exploring children and their parents' assessment of the child's asthma in rural and urban centers in Ontario, Canada. Children and their caregivers attended a clinic for an interview at enrolment and after 1, 5, and 9 weeks. At the 5 and 9-week follow-up visits parents completed the Global Rating of Change Questionnaire (GRCQ) while the child completed the PAQLQ. The findings from this study show important differences between parental and child perceptions in 7 to 10 year old children and 11 to 17 year old children. In the younger children, changes in both physiological measures and asthma control were more closely related to the children's rating of the asthma symptoms, where the reverse was seen in the older children. The children aged 11 to 17 scored higher on all domains of the PAQLQ ( $r = 0.67-0.74$ ) than the parents did on the PACQLQ ( $r = 0.39-0.43$ ). Researchers did not report on the potential differences in QOL between the urban and rural settings.

In summary, there is an inconsistent relationship between parental and child report of QOL. There is an increase in discrepancy between the parental and report of QOL as disease severity increased. There were also some studies, which demonstrated good agreement between parents and children perceptions of the child's QOL. Children tended to rate their asthma severity as mild to moderate, while caregivers tended to rate the children asthma severity in the moderate to severe category. The child's rating of their asthma severity was largely influenced by limitations to their activity, while parents rating of their child's asthma severity was mostly influenced by the impact or burden the child's asthma had on the parent's QOL. Overall, the agreement between child and parent report of QOL was better for domains of physical functioning and less for social

and emotional domains. Several researchers concluded that relying on only parental informant may result in incomplete QOL assessment to the extent that the child's subjective experience and perceptions of QOL may be overlooked. Differences in perceptions of QOL between children and their caregivers are similar in other childhood disease processes. Brunner et al., (2003) found no agreement between child and parents perceptions of QOL in children with muscular dystrophy while Sweeting & West (1998) found less agreement between perceptions as the health of the child with pediatric cancer worsened.

#### *Quality of Life and Asthma Severity*

Nineteen studies were reviewed measuring child QOL in relation to asthma severity (see Table 1.2). Most studies reported QOL from the perspective of the child (Annett et al., 2001; Brouwer et al., 2006; Chan et al., 2005; Erickson et al., 2002; Goldbeck et al., 2007; Horner et al., 2006; Juniper et al., 1996(a); Montaldo et al., 2004; Poachanukoon et al., 2006; Van de Ven et al., 2007; Vila et al., 2003; Warschburger et al., 2004) while three studies used the parents as informants for the child's QOL (Chan et al., 2005; Gorelick et al., 2004; Kwok et al., 2006) and six studies collected both parent and child reports of QOL (Brouwer et al., 2006; Flapper et al., 2006; Guyatt et al., 1997; Sawyer et al., 2001; Williams et al., 2000; Zandieh et al., 2006). The majority of studies used asthma specific QOL questionnaires, two studies used a generic QOL questionnaire and two studies used both a generic and asthma specific QOL questionnaire.

Table 1.2 Studies examining the relationship between QOL and asthma severity.

Author, Year (Location)	Age of Child (Sample Size)	Measurement of Asthma Severity	QOL Measurement/ Questionnaire (Asthma/generic specific)	Informant	Findings
Annett et al., 2001 (United States)	5-12 yrs (339)	Parent report of child symptoms rated by physician or CAMP Coordinator	PAQLQ/ Asthma specific	Child	Activity Limitation Domain ( $t = -2.04$ ; $p = 0.04$ )
Brouwer et al., 2006 (Netherlands)	6-16 yrs (26)	Asthma Severity Index (ASI)	PAQLQ Asthma specific PACQLQ Asthma specific	Child Parent	No significant correlation between mean FEV <sub>1</sub> variation and ASI or QOL
Chan et al., 2005 (United States)	2-18 yrs (463)	NHLBI Guidelines based on parent report of daytime and night time symptoms	PedsQL 4.0 SF-15 Generic  PedsQL 3.0 SF-22 Asthma specific	Parent if child <12 Adolescent	Association with: Mild persistent and mod/severe persistent asthma ( $p < 0.05$ ) Same results for PedsQL3.0 SF-22
Erickson et al., 2002 (United States)	9-17 yrs (99)	NHLBI Guidelines based on parent and child report of medication use	PAQLQ Asthma specific	Child	No significant correlation

	Flapper et al., 2006 (Netherlands)	8-16 yrs (289)	Dutch Medical Guidelines based on frequency of asthma symptoms and response to medication. Classified by paediatrician.	PAQLQ Asthma specific	Child	PAQLQ, (p = 0.019)
				TACQOL Asthma specific	Parent	TACQOL 5 Domains: (p = 0.001 - 0.078)
	Goldbeck et al., 2007 (Germany)	7-18 yrs (81)	Classification of asthma severity by physician based on GINA guidelines, asthma medication use, symptoms and response to medication	Ulm Inventory for Children Generic	Child	t = <1.00; n.s.
	Gorelick et al., 2004 (United States)	2-17 yrs (121)	NHLBI guidelines moderate or severe by physician based on parent report of daytime and night time symptoms	ITG-CASF Asthma specific	Parent	Significant correlation between child QOL and asthma severity ( $r = 0.45$ ; 95% CI)
26	Guyatt et al., 1997 (Canada)	Age groups: 7-10, 11-17 (52) parent-child pairs	ATS guidelines based on symptoms	PAQLQ Asthma specific	Child	No significant relationship
	Horner et al., 2006 (United States)	6-12 yrs (94)	Parent report: <i>How Bad is Asthma (HBA)</i> Scale and <i>Severity of Chronic Asthma (SCA)</i> Scale	PAQLQ Asthma specific	Child	HBA: $r = 0.07-0.19$ ( $p < 0.05$ ); SCA: $r = 0.35-0.49$ ( $p = 0.01$ )
	Juniper et al., 1996 (a) (Canada)	7-17 yrs (52)	ATS guidelines based on symptoms, FEV <sub>1</sub> and PEFR	PAQLQ Asthma specific	Child	No significant correlation between FEV1 % predicted and PAQLQ. Moderate correlations found with PEFR and PAQLQ ( $r = 0.31-0.43$ ).

Kwok et al., 2006 (United States)	0-18 yrs (750)	NAEPP severity classification (additive 4-item score) based on parent report of activity limitation, daytime and night time symptoms	ITG-CASF Asthma specific	Parent	$f = 82.1$ ( $p < 0.001$ ); $r^2 = 0.25$
Montalto et al., 2004 (United States)	8-16 yrs (238)	Parent report of symptoms	KINDL Generic	Child	No significant correlation ( $F_{(20,4256)} = 1.13$ ; $P > 0.05$ )
Poachanukoon et al., 2006 (Thailand)	7-17 yrs (51)	Classified by parent report of symptoms according to the GINA guidelines. Three categories: mild intermittent, mild persistent or moderate persistent.	PAQLQ Asthma specific	Child	Poor correlations between Domain scores on the PAQLQ and $FEV_1$ % predicted ( $r = 0.01-0.03$ ) Significant correlations with PEFR morning value and PAQLQ Domains scores ( $p < 0.05$ , $r = 0.32-0.47$ ) and PEFR evening value and PAQLQ Domain scores ( $p < 0.05$ , $r = 0.32-0.47$ )
Sawyer et al., 2001 (Australia)	8-13 yrs (236)	Parental report of frequency and intensity of asthma symptoms based on the ASI, High service utilizers (HSU); Functionally limited (FL); and HSU/FL	CHQ- CF-87 Generic CHQ-PF-50 Generic PAQLQ Asthma specific	Child Parent Child	CF-87: $p < 0.01$ for physical and mental health domains; PF-50: $p < 0.01$ for physical and mental health domains; PAQLQ: $p < 0.001$ with overall score
Van de Ven et al., 2007 (Netherlands)	12-16 yrs (553)	Child report of symptoms (never, sometime, a lot)	AAQOL Asthma specific	Adolescent	Asthma severity was negatively related to QOL. [ $r = -0.38$ ( $p < 0.001$ )]

Vila et al., 2003 (France)	12-19 yrs (100)	NHLBI Guidelines based on clinical symptoms and medication use	PAQLQ Asthma specific	Adolescent	Not significant.
Warschburger et al., 2004 (Germany)	8-16 yrs (318)	German Asthma Guidelines based on medication use and symptoms	PAQLQ Asthma specific	Child	With ↑ disease severity, QC = 12.41, p<0.001; $r^2 = 0.117$ )
Williams et al., 2000 (United States)	5-12 yrs (240)	Parent report of symptoms including wheezing and nocturnal symptoms in prior 4 month period	PAQLQ Asthma specific  PACQLQ Asthma Specific	Child  Parent	PAQLQ ( $r = -0.39$ ; $p < 0.001$ )  PACQLQ ( $r = -0.47$ ; $p < 0.001$ )
Zandieh et al., 2006 (Iran)	7-17 yrs (113)	FEV <sub>1</sub> GINA Guidelines	PACQLQ  PAQLQ Asthma Specific	Parent  Child	No significant relationship between QOL scales and FEV <sub>1</sub> ; Lower QOL scores seen for males. PACQLQ: Inverse association ( $p < 0.001$ ) ; PAQLQ: Inverse association ( $p < 0.05$ )

AAQOL = Adolescent Asthma QOL Questionnaire; ASI = Asthma Severity Index; GINA = Global Initiative for Asthma

Guidelines; ITG-CASF = Integrated Therapeutics Group Child Asthma Short Form; NAEPP = National Asthma Education and Prevention Program Asthma Severity Classification; NHLBI = National Heart Lung and Blood Institute; PACQLQ = Pediatric Asthma Caregiver QOL Questionnaire; PAQLQ = Pediatric Asthma QOL Questionnaire; QOL = Quality of Life; TACQOL = Total Assessment of Child QOL Questionnaire

More than half of the studies found a significant association between QOL and asthma severity (Annett et al., 2001; Chan et al., 2005; Flapper et al., 2006; Gorelick et al., 2004; Horner et al., 2006; Juniper et al., 1996(a); Kwok et al., 2006; Poachanukoon et al., 2006; Sawyer et al., 2001; Van de Ven et al., 2007; Warschburger et al., 2004; Williams et al., 2000; Zandieh et al., 2006). The nineteen studies were completed in a variety of geographical locations including Australia, France, Germany, Iran, Netherlands, Thailand and the United States. Two studies were completed in Canada and all studies with the exception of one were completed with urban areas.

Of the studies reviewed a variety of criteria were utilized to determine asthma severity. Of the nineteen research studies reviewed only four assessed the relationship between asthma severity and child QOL using objective measurement of severity; pulmonary function testing or PEFR (Brouwer et al., 2006; Juniper et al., 1996(a); Poachanukoon et al., 2006; Zandieh et al., 2006). In half of the studies reviewed, asthma severity was defined according to parental report of child asthma symptoms.

In a study from the United States asthma severity was defined based on the National Heart Lung and Blood Institute (NHLBI) guidelines, classifying children with asthma into four categories: mild intermittent, mild persistent, moderate or severe (Chan et al., 2005) This study evaluated asthma severity and QOL using two short form versions of the PedQL; PedsQL<sup>TM</sup> 4.0 SF 15 and the PedsQL<sup>TM</sup> 3.0 SF22 (Varni, Burwinkle, Seid, Katz, & Jacobs, 2003). The PedsQL<sup>TM</sup> 4.0 SF 15 is composed of 15 items from the original instrument, which measures generic QOL across five domains: Physical Health, Psychological Health, Emotional Functioning, Social Functioning and School Functioning (Varni et al., 2003). The PedsQL<sup>TM</sup> 3.0 SF22 Asthma Module is composed of 4 scales: Asthma symptoms, Treatment Problems, Worry

and Communication. Asthma symptoms are assessed in all four of the scales (Varni et al., 2003). For this study, adolescents provided all the information for both QOL questionnaires. However, for children age 2-11 parental proxy report of QOL was used. This study found that as scores on both the asthma-specific and generic QOL scales increased (indicative of better QOL), asthma severity decreased. In addition, both measures of QOL, asthma-specific and generic, were able to discriminate across different levels of asthma severity ( $p = 0.01-0.05$ ).

The NHLBI guidelines (National Institute of Health, 1997) were used to classify asthma severity in a study conducted by Vila et al., (2003) in France. This study assessed the relationship between emotional and behavioural problems and QOL in children with asthma. QOL was assessed by child completion of the PAQLQ and parental completion of the PACQLQ. This study did not find asthma severity scores to be significantly related to QOL scores on the PAQLQ or the PACQLQ.

In a study conducted in the Netherlands, severity of asthma was graded by a paediatrician unfamiliar to the case based on the Dutch Guidelines. Frequency of asthma symptoms and the child's response to medication were used as indicators of asthma severity (Flapper et al., 2006). This study examined the psychometric properties of the Total Assessment of Children's QOL (TACQOL) while comparing the questionnaire to the PAQLQ. The TACQOL questionnaire, an asthma specific questionnaire, evaluates the presence and appraisal of problems related to symptoms, activities, medication use and doctor's visits. It also evaluates the occurrence of negative emotions in relation to having asthma. The appraisal of symptoms is completed in five domains Complaints, Situations, Treatments, Medication Use, and eEotions (Vogel, Verrips, & Verloove-Vanhorick, 1998). This study found a significant correlation between QOL scores on

the TACQOL and the PAQLQ. The study also determined both QOL questionnaires were able to significantly discriminate between mild, moderate and severe groups.

Several of the studies defined asthma severity according to national or regional asthma guidelines. Goldbeck et al., (2007) determined asthma severity by a physician according to the Global Initiative for Asthma Guidelines (GINA) guidelines, which classifies children into severity groups based on the frequency of asthma symptoms, types of asthma medications and response to asthma medication. This study examined the impact of asthma severity and emotional/behavioural problems on QOL of children and adolescents with asthma living in Germany. Children completed the generic Ulm Inventory for Children, a multi-dimensional instrument for assessing health-related QOL of children and adolescents with chronic conditions. The inventory consists of 27 items, which can be summarized into five dimensions: physical well-being, psychological well-being, disease and therapy related illness, family relations and perception of general QOL (Goldbeck & Storck, 2003). This study did not find a significant association between asthma severity and child QOL. Warschburger et al., (2004) determined asthma severity using the German Asthma Guidelines to classify children as mild intermittent, mild persistent, moderate or severe based on parental report of medication usage. Asthmatic children and adolescents ages 8-16 were assessed for psychological wellbeing in a multicenter clinical trial. This study found a significant association between asthma severity and child QOL. As asthma severity increased, QOL decreased in both the total score ( $F= 12.41$ ;  $p<0.001$ ) and the sub-domains ( $F= 5.85$ ;  $p<0.001$ ). In addition, children and adolescents with mild intermittent asthma reported a significantly higher QOL score than children with moderate or severe asthma (mean total QOL score 4.3 vs. 3.4;  $p<0.01$ , post hoc tests).

More studies classified asthma severity using parental and/or child report of asthma symptoms. One American study classified asthma severity classification using information regarding previous asthma treatments, asthma symptoms and asthma medication history (Annett et al., 2001). The study population was a double-masked, randomized, placebo controlled group of children aged 5-12 with mild to moderate asthma. This study reported no significant differences among QOL scores between children with mild and moderate asthma on the Emotional Functioning, Symptoms or Total scores on the PAQLQ. However, children with moderate asthma reported lower scores on the Activity Limitation Domain than those with mild asthma (5.71 vs. 5.44, p = 0.04). In another American study asthma severity was determined by both child and parent report of whether the child's asthma was mild, moderate or severe (Erickson et al., 2002). The study was a cross-sectional design to describe disease-specific QOL of pediatric patients with physician-diagnosed asthma and their caregivers. The study used a disease specific QOL questionnaire, the PAQLQ, for the children and the PACQLQ, for the parents. The study found, parents rated the child's asthma more often in the moderate to severe range whereas the child rated their own asthma as mild to moderate. However, neither child nor parent report of asthma severity was a predictor of child QOL. As well no significant relationship was reported comparing QOL and asthma severity.

Similarly, asthma severity was based on parental survey response to questions including frequency of asthma symptoms in the last 12 months, use of asthma medications, limitations in children's activities, emergency room visits and hospitalizations (Montalto et al., 2004). Following consent from the parents and children completed the KINDL<sup>R</sup>, a generic QOL survey. This questionnaire is made up of four scales that assess the child's physical state, social relationships, functional capacity in everyday life and psychological well-being (Ravens-

Sieberer, & Bullinger, 1998). This study found children with high health care utilization, a measure of asthma severity, scored similar or lower than children with mild asthma and children without asthma on overall QOL. There was no association between scores found on the QOL scale and having current asthma or no asthma.

Williams et al., (2000) determined asthma severity from parental report of asthma symptoms in a group of American children. The asthma severity scores were not categorized based on severity but rather used as a continuous variable and were calculated from the parent responses to questions about their child's wheezing frequency, nocturnal and early morning symptoms and speaking during an asthma attack as well as the impact of the disease on their child's physical activity and breathing during the prior 4-month period. Higher asthma severity scores indicated more severe disease. The study used asthma specific questionnaires for both the child with asthma (PAQLQ) and the parent (PACQLQ). The study found that higher scores reported on the modified PAQLQ were significantly correlated with lower asthma severity scores. Higher QOL scores among caregivers also correlated with higher QOL scores among children ( $r = 0.64$ ,  $p<0.001$ ).

Sawyer et al., (2000) assessed the relationship between QOL and asthma severity in Australian children using parental report of the frequency and intensity of asthma symptoms on the Asthma Severity Index (ASI) (Sawyer et al., 2000). The ASI is a 6-item questionnaire designed to assess the severity of children's asthma in a population survey (Rosier, Bishop, Nolan, Robertson, Carlin & Phelan, 1994). On the basis of the frequency and intensity of asthma symptoms reported on the questionnaire, cut-off scores were employed to categorize children into groups experiencing mild, moderate or severe asthma symptoms (Rosier et al., 1994). The association between QOL and asthma severity was examined in a cross-sectional study using the

CHQ-PF50, completed by the parent, and the PAQLQ, completed by the child. Children with moderate or severe asthma had lower scores on the PAQLQ and CHQ-PF50 as compared to children with mild asthma ( $p < 0.05$ ). Parents of children with moderate or severe asthma reported lower scores on the CHQ-PF50 as compared to parents of children with mild asthma, ( $p < 0.05$ ).

The NAEPP guidelines were used in a study conducted in the United States to determine asthma severity. Severity was based on parent report of activity limitations, daytime symptoms and night-time symptoms over a two-week time period (Kwok et al., 2006). QOL was measured using an asthma-specific QOL questionnaire, the Integrated Therapeutics Group Child Asthma Short Form (ITG-CASF). This 10-item QOL questionnaire includes asthma symptoms and health-related QOL items (Bukstein, McGrath, Buchner, Landgraf & Goss, 2000). The study found asthma QOL scores decreased with increasing asthma severity ( $p < 0.001$ ,  $r = 0.24-0.26$ ).

A study in the Netherlands determined asthma severity by child report of how often they suffered from specific asthma symptoms (Van de Ven et al., 2007). Responses to each item were averaged to determine a severity score with higher scores indicating more severe asthma. This study utilized a cross-sectional design with an asthma-specific questionnaire, the Adolescent Asthma QOL Questionnaire (AAQOL). This instrument is specifically designed for adolescents and consists of six dimensions: symptoms, medication, physical activity, emotions, social interactions and positive effects (Rutishauser, Sawyer, Bond, Coffey, & Bowes, 2001). The study found that asthma severity was negatively associated with asthma-specific QOL in adolescents in asthma ( $p < 0.001$ ).

Horner et al., (2006) determined asthma severity using the Severity of Chronic Asthma Scale (SCA). The SCA is a parent-completed questionnaire regarding frequency of asthma

symptoms, nocturnal asthma symptoms and limitations to the child's activity in a one-month recall period (Horner et al., 2006). Parents answered three questions regarding frequency of daytime asthma symptoms, frequency of night-time symptoms with disturbances due to asthma and days limited by asthma. The study also used the *How Bad is Asthma* questionnaire. This is 4-item tool that is designed to yield a continuous score reflecting asthma severity which can be used to categorize individuals' asthma severity into mild, moderate or severe based on their scores. The PAQLQ was administered to measure QOL. Scores on the SCA and the PAQLQ were significantly correlated  $p<0.01$  ( $r = 0.35-0.49$ ).

One study using objective measures of asthma severity was conducted in Iran (Zandieh et al., 2006). This 18-month single cohort study assessed the impact of asthma on the lives of children and their caregivers. Asthma severity was determined by completion of spirometry and application of the Global Initiative for Asthma (GINA) guidelines. Each child completed the PAQLQ to assess QOL, while the parent of the child with asthma completed the PACQLQ to assess caregiver QOL. Impairment of the child's QOL was not associated with  $\text{FEV}_1$  percent predicted. Caregiver's QOL was associated with asthma severity as measured by the GINA Guidelines ( $p < 0.001$ ).

Poachanukoon et al., (2006) also used the GINA guidelines to define asthma severity, classifying asthma into three categories: mild intermittent asthma, mild persistent asthma or moderate persistent asthma. This validation study also compared QOL scores on the PAQLQ to  $\text{FEV}_1$  percent predicted values and PEFR morning and evening values. Poor correlations were found between domain scores on the PAQLQ and  $\text{FEV}_1$  percent predicted values ( $r = 0.01-0.03$ ). Significant correlations were found with the PEFR morning value ( $p<0.05$ ,  $r = 0.31-0.42$ , respectively) and the PEFR evening value ( $p<0.05$ ,  $r = 0.32-0.47$ , respectively).

In summary most of the studies determined asthma severity using parental and or child recall of asthma symptoms or national/international asthma guidelines to classify asthma severity. There was limited study of asthma severity using lung function measures including FEV<sub>1</sub> percent predicted or PEFR. Of the studies reviewed there was no association between FEV<sub>1</sub> from spirometry and children's QOL was poor. Better associations were found between PEFR and children's quality of life as measured by the PAQLQ.

#### *Quality of Life and Asthma in Rural Populations*

Limited study has been completed examining the QOL of rural children and their caregivers and asthma severity. Of the studies completed one was conducted in Canada (Guyatt et al., 1997), several in the United States (Arif, 2008, Butz et al., 2005; Horner et al., 2006; and one from Jordan (Al-Kour & Khader, 2008 & 2009).

Al-Kour and Khader (2008) recruited 200 children, age 7-17, with asthma and their parents from rural and urban areas of Jordan. The parents completed the PACQLQ and the children with asthma completed the PAQLQ. Mothers living in towns were approximately twice more likely to achieve a better QOL score than mothers living in the city in the Emotional Function domain (OR 2.09, CI 1.03 - 4.24, p = 0.04). The study also noted that the age of the child and severity of asthma, were the most important factors associated with the QOL of the parents. Parents of children with asthma over the age of 12 reported better QOL (odds ratio 1.09-1.43; CI 95%) compared to parents of children with asthma under the age of 12 years. The study also reported that children living in town were 1.4 times more likely to achieve a better outcome with their asthma than children living in the city on the Symptom domain (OR 1.4, CI 0.57-2.4, p = 0.001). These findings may be explained by the fact that children living in towns reported less impairment in their QOL than children living in the city.

Two studies examining QOL and asthma severity in rural populations were reported for children living in Texas. Arif, (2008) examined the presence of night-time asthma symptoms and impaired QOL in 406 children with asthma living in rural Texas. QOL was assessed using the parent completed CHQ-PF50. There were 13.5% of children who reported night-time asthma symptoms. Parents of children with asthma experiencing night-time asthma symptoms reported lower QOL scores on the CHQ-PF50 compared to all others ( $p = 0.05$ ). Children with asthma, ages 6-12 ( $n = 94$ ) and their parents participated in an assessment of QOL in a study conducted by Horner et al., (2006). All participants were from a rural population in central Texas. In this study children's QOL scores on the PAQLQ were associated with asthma severity as measured on the Severity of Chronic Asthma Scale.

In another U.S. study of 221 rural children ages 6 to 12 and their parents, Butz et al., (2005) evaluated the effectiveness of an asthma educational intervention in improving asthma knowledge, self-efficacy and QOL. The parents completed the PACQLQ and the child completed the PAQLQ. Parents provided information of the child's day and night time symptoms of cough, wheeze, and shortness of breath or chest tightness in the past 6 months. Asthma severity was then classified by a physician into one of three categories: mild intermittent, mild persistent or moderate/severe persistent. Over half of the children reported daytime symptoms of cough, wheeze, and shortness of breath at least 4 times or more a week. This study found there were no statistically significant differences between parental QOL scores reported on the PACQLQ and child QOL reported on the PAQLQ. Findings from this study also indicate that parents in the intervention group scored significantly higher on the asthma knowledge care and on the PACQLQ post intervention ( $p = 0.0004$ ).

### *Summary of Literature Review*

1. Asthma is a chronic inflammatory lung disease which produces symptoms such as dyspnea, chest tightness, wheezing, sputum production and cough. It also manifests in acute exacerbations characterized by dyspnea, mucus production, use of accessory muscles, increased respiratory rate, and prolonged expiratory phase which can lead to anxiety and lethargy.
2. Research has shown that there are personal, caregiver/family and societal costs to chronic asthma in children. Caregiver of children with asthma experience higher rates of emotional distress and children with asthma are more likely to be absent from school and have physical activity limitations.
3. Parental perceptions of QOL are often different from the child's perception of QOL. This discrepancy is increased as disease severity increases. Higher disagreement was found between parental and child perceptions of QOL when comparing younger children to adolescents.
4. A variety of methods have been used to assess asthma severity including asthma severity scales, national and international guidelines and physician, child or parent ratings of symptoms and lung function. Asthma severity was most often based on patient and /or caregiver recall of symptoms rather than by objectively measured lung function as recommended in national consensus guidelines. More than half the studies using national guidelines or symptom reports found a significant association between QOL and asthma severity. Of those studies using more objective measures of asthma severity, no associations were found with FEV<sub>1</sub> percent predicted and QOL. In two studies decreased PEFR was associated with poorer QOL in children with asthma.
4. The two most common asthma specific QOL measurements are the PAQLQ and the PACQLQ. The CHQ-PF50 has been used less often to assess QOL of parents of children with

asthma. Both the PAQLQ and PACQLQ show good construct validity ( $r = 0.30$ - $0.60$ ) and good internal consistency reliability ( $r = -0.28$  to  $-0.56$ ) when tested in research studies. The CHQ-PF50 also demonstrates good construct validity (0.62 to 0.92) and internal consistency reliability ( $r = 0.37$  to  $0.84$ ) when tested against appropriate dimensions of other validated instruments.

6. Children tend to rate their asthma severity as mild to moderate, while caregivers tend to rate the child's asthma severity in the moderate to severe category. However, overall there is agreement that as asthma severity worsens the QOL of the child decreases.

7. There is limited reported research examining the association between caregiver's scores on the PACQLQ and measures of asthma severity in children with asthma.

8. Limited study could be found assessing pediatric QOL in asthma using pulmonary function testing or PEFR as objective measures of asthma severity. Poor correlations were found between QOL and FEV<sub>1</sub> percent predicted while moderate correlations have been found using PEFR and QOL.

9. Limited study has been completed examining quality of life of children living in rural areas. One study has shown that certain parameters of quality of life for children with asthma may differ between rural and urban populations and that QOL may be better for rural children although asthma severity may be worse. There is limited study of the relationship between QOL and asthma severity of children and their parents living in rural Canada.

## **CHAPTER TWO**

### *Theoretical Framework*

The conceptual model used for this research study is the Systems Theory Model developed by Wright & Leahey (2009) within the Calgary Family Assessment and Intervention Model. This model can be used to outline key factors influencing QOL for both the child with asthma and their parent(s).

The Systems Theory Model within the Calgary Family Assessment and Intervention Model consists of five key concepts. The five key concepts are;

1. A family system is part of a larger Suprasystem and is composed of many subsystems.
2. The family as a whole is greater than the sum of its parts.
3. A change in one family member affects all family members.
4. The family is able to create balance and stability between change.
5. Family member's behaviours are best understood from a view of circular rather than linear causality (Wright & Leahey, 2009).

The Systems Theory has three major components; Individual System, Family System and Supra System. This model will be used to examine how it can function to explain and provide direction for QOL in the management of asthma in children. It may also assist in the organization and management of pediatric asthma care.

### *Key Concepts and Pediatric Asthma Care*

*Concept One: A family system is part of a larger Suprasystem and is composed of many subsystems, some of which are physical, and some of which are psychological.* In this case asthma symptoms, asthma exacerbations, hospital and emergency room visits, missed days at school or work are could be considered reflective of the physical subsystems and fear of asthma

exacerbations or symptoms and parental beliefs regarding treatment are reflective of the psychological subsystems. The components of both the physical and psychological subsystems contribute to QOL for the child with asthma and their caregiver.

Concept Two: *The family as a whole is greater than the sum of its parts*, highlights the importance of assessing all parts of the family to provide an understanding and evaluation of QOL. Illness in the child with asthma, affects all family members and this impact can disrupt the family unit, particularly if asthma is severe. The diagnosis and subsequent care generally means a collective family approach to health as they deal with exacerbations and managing symptoms that can impact the overall plans for the family unit. The use of both the PAQLQ to assess the child's perception of their QOL and the PACQLQ to assess the parent's QOL provides a comprehensive measurement of QOL for the family unit (Juniper et al., 1996a; Juniper et al., 1996b).

Concept Three: *A change in one family member affects all family members*. This concept is particularly useful for families influenced by the impact or burden of the asthma disease process. Previous research has reported when parents' QOL is decreased they rate the perceived QOL of the child lower than if the parents QOL was not impacted even though the child does not report decreased QOL (Sweeting & West, 1998; Braun-Fahrlander et al., 1998; Renzoni et al., 1999). This concept is reinforced through the use of three measures of QOL, the PAQLQ measuring the child's perceived QOL (Juniper et al., 1996a), the PACQLQ, measuring the parents perceived QOL (Juniper et al., 1996b), and the CHQ-PF50 assessing the parents' perception of the child with asthma's QOL (Landgraf & Abetz., 1998) rather than only one measure of QOL. A study by Al-Kour & Khader, (2009) compared parental QOL for parents of children of asthma. This study found mothers were less likely to have a high QOL in the

Emotional Function domain ( $p = 0.001$ ) than fathers. While 11% of fathers reported the need to change their plans very often because of the child's asthma during the preceding week, 19% of mothers need to change their plans. In addition, 16% of mothers and 9% of fathers reported being awakened often during the night because of their child's asthma. Night-time symptoms were reported as the number one symptom influencing parental QOL by both mothers and fathers.

*Concept Four: A family is able to create balance and stability between change.* Here the family finds homeostasis. This may be constructive or destructive depending on coping strategies acquired to adapt to the management of the chronic illness of asthma. In a study completed by Al-Kour & Khader, (2009) assessing QOL of caregivers for children with asthma, researchers found 43% of mothers and 37% of fathers reported the child's disease changed their marriage relationship towards less emotional, affectionateless and loving. This finding is consistent with the findings of other authors who reported psychological burden, financial burden and marital stress have been associated with caring for a child with asthma (Al-Kour & Khader, 2009; Annett et al., 2003; Juniper et al., 1996(b); Frankel & Wamboldt, 1998).

*Concept five: A family members' behaviours are best understood from a view of circular rather than linear causality.* This illustrates there is not a direct cause and effect relationship, the effect influences other changes.

#### *Systems Theory and Pediatric Asthma Care*

Within the Individual System are components that are exclusive to the child with asthma. These include history of hospitalizations, previous asthma exacerbation and the coping skills developed, the child's developmental stage, knowledge of asthma and its management, how long the child has been diagnosed with asthma, current asthma health including level of inflammation,

stage and severity of the disease, FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub> and PEFR (Juniper et al., 1996a; Osman & Silverman, 1996; Butz et al., 2005).

The family system encompasses the families coping style, available external supports, who they call as a health resource when an exacerbation occurs, level of education of the family members and socio economic status. This is important to pediatric asthma patients living in rural communities as access to health care may be further in distance and health care resources may be limited compared to urban populations.

Finally, the Suprasystem consists of the neighbourhoods, organizations and communities available to the child with asthma and their parents. These may include the child's school, healthcare resources such as hospitals and family physician, asthma educator and extended family. Educational resources such as Certified Respiratory Educators specializing in assisting families and patients in improving their asthma management skills (Lung Association of Saskatchewan, 2013) may be health care resources available to pediatric asthma patients that could utilize in Saskatchewan.

The Systems Theory highlights the multidimensional aspect of QOL. The five concepts within this theory illustrate the diverse and individualized nature of QOL for the child with asthma and their parent(s). It considers the burden of asthma, the ability of the child and family to adapt to fluctuations in the disease process, coping strategies the family has integrated into their lifestyle among many physical and psychological variables, which influence the QOL for the child with asthma and their parent(s). As QOL is a very individualized concept the three major components of the Systems Theory reinforce the variety of domains influencing the perceived QOL for the child with asthma and their parent(s). It also reflects the multidimensional approach to chronic disease management of pediatric asthma; family,

accessibility to health care resources, educational level and resources all contribute to whether or not the child's asthma is effectively managed.

### *Research Questions and Rationale*

Based on the review of the literature, the following research questions were proposed:

1. Is there a correlation between QOL scores measured on the PAQLQ in children with asthma and QOL scores of their caregivers measured on the PACQLQ?

*Rationale:* Previous research identifies that parents and children are often in disagreement about the QOL related to asthma (Brunner et al., 2003; Butz et al., 2005; Erickson et al., 2002; Renzoni et al., 1999 & Sweeting & West, 1998). Studies have shown however, that parental scores on the PACQLQ correlate well on the PAQLQ scores of older children and adolescents but not with those of younger children (Lindgren et al., 2005; Braun-Fahrlander et al., 1998; Guyatt et al., 1997). At present there is limited study of asthma specific measures of QOL of parents and children in rural settings.

2. Is there a correlation between QOL as measured on a generic QOL assessment tool, the CHQ-PF50, and QOL measured on asthma specific QOL assessment tools, the PAQLQ and the PACQLQ, in children with asthma and their caregivers?

*Rationale:* Research suggests that a significant association between children's QOL and asthma severity was more likely to be found with asthma specific measures of QOL than with generic measures of QOL (Everhart et al., 2009; Annett et al., 2001).

3. Is there an association between QOL measurements (PACQLQ, PAQLQ and CHQ-PF50) and asthma severity as measured by percent predicted lung function ( $FEV_1$ , FVC,  $FEV_1/FVC$  ratio,  $FEF_{25-75}$ ) or by the mean diurnal peak flow variability during a two-week home monitoring period?

*Rationale:* There is limited reported research examining the association between caregiver's scores on the PACQLQ and objective measures of asthma severity in children with asthma

(Juniper et al., 1996b; Williams et al., 2000). A variety of criteria were utilized to determine asthma severity including report of symptoms, physician classification, national and international guidelines, FEV<sub>1</sub> and PEFR. The PAQLQ has been primarily evaluated with reported symptoms and less often with more objective measures of asthma severity such as peak flow variability and pulmonary function testing.

## **CHAPTER THREE**

### **Methodology**

#### *Design*

The data to be used in this study was previously collected between 2005 and 2007 using a cross-sectional, case-controlled study design conducted in rural, Saskatchewan (Lawson, Dosman, Rennie, Beach & Newman, 2009). Children for the cross-sectional, case-controlled study design, were initially recruited from a cross-sectional study completed in the town of Humboldt in the winter of 2004. Questionnaires were sent home with children attending grades 1 to 12 in any of the four schools (3 elementary schools and 1 high school) in the community. The questionnaires were completed by a parent and returned to school where they were collected by the research team members. Cases and controls for the case-controlled study were selected based on the cross-sectional study. If a parent reported any history of asthma or wheeze for their child the child was selected as a potential case (Lawson, 2008).

The case-control study was expanded in 2006 to include children in Grades 1 to 12 attending other schools from the same school district as the Humboldt schools. The cross-sectional survey was repeated using an identical design and questionnaire. The several towns outside the rural municipality included Muenster, Annaheim, Bruno, Cudworth, St. Brieux, and Middle Lake. None of these towns had a population of more than 800 people. In order to assess whether the two study populations included were similar (Humboldt case-control and rural town case-control), comparisons were made between the original Humboldt populations and the additional population made up of the primarily rural area outside of Humboldt. The populations were similar when comparing age, sex, single parent home status, family history of asthma and allergy and personal history of allergic disease. However, there were statistically significant

differences between the populations when considering parents' education and farm exposure where those from the additional rural area were less likely to have a parent with more than a high school education and were more likely to be living on a farm (Lawson, et al., 2009).

Details of the case-control study have been previously published (Lawson, 2008, Lawson, Dosman, Rennie, Newman, Beach & Senthilselvan, 2009). The study incorporated two phases of testing for controls and three phases of testing for cases (Figure 1.1). Cases were selected for study based on their response to the following question, in the cross-sectional survey questionnaire: "Has a doctor ever said that this child had asthma?" (yes/no) and wheeze experienced in the last 12 months? (yes/no)

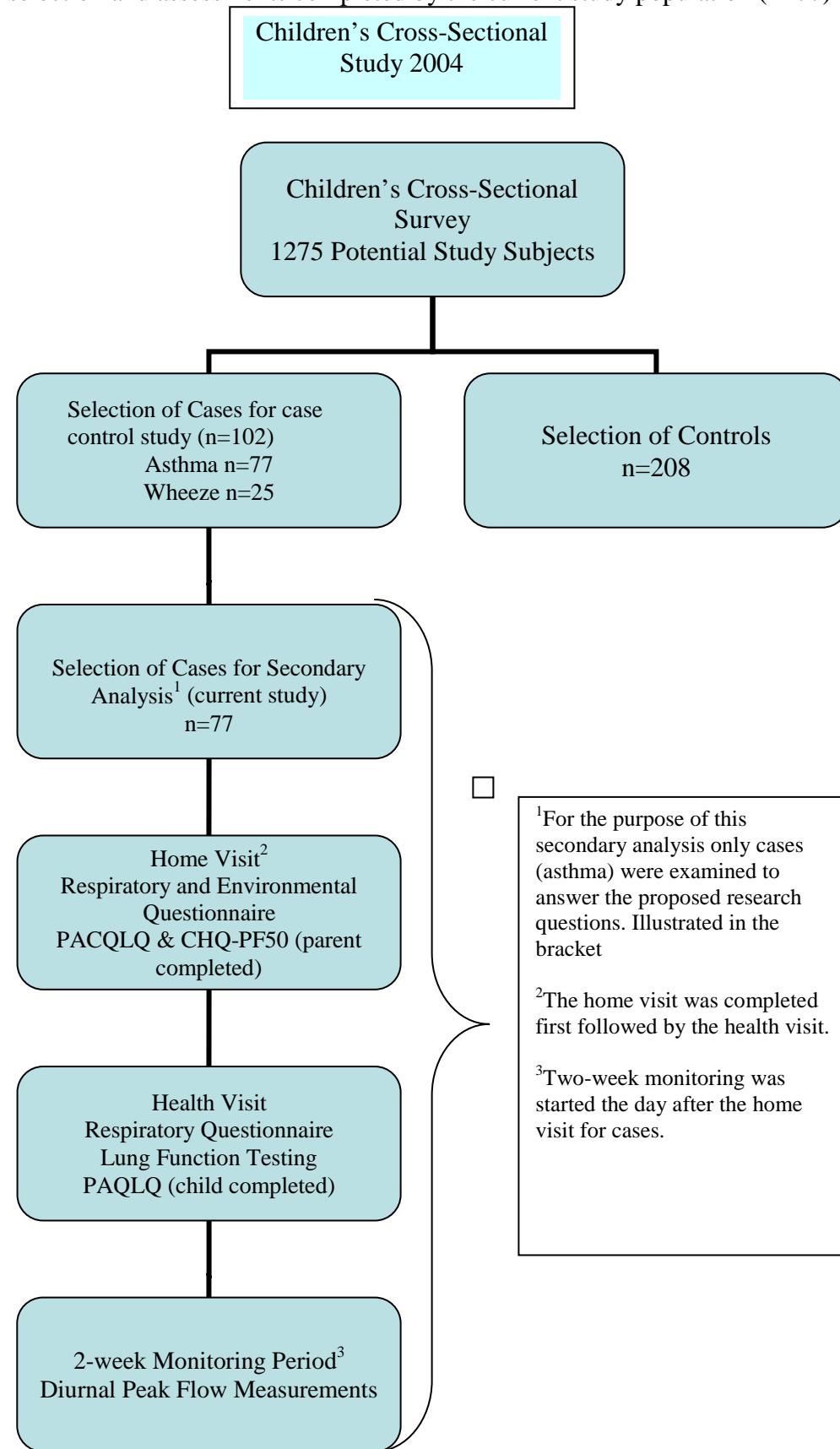
Controls were randomly selected and all cases (yes to either of the above questions) were initially selected to ensure sufficient statistical power for the case control study. Pre-selected cases and controls and their parents were approached to request their participation in this case control study. If they agreed to participate, the parents were administered a screening questionnaire (Appendix C) to confirm case or control status.

All cases and controls received a home visit followed by a clinic visit. Figure 3.1 identifies the assessments conducted during each visit. During the home visit parents completed an environmental survey and QOL questionnaires (PACQLQ, CHQ-PF50). Dust was collected by vacuum from the bed and floor of play areas of all participants using the ISAAC protocols (Weiland, Bjorksten, Brunekreef, Cookson, von Mutius, Strachan et al., 2004) and analyzed for endotoxin levels. Following the home visits, cases only were instructed on how to participate in the 2-week diurnal peak flow home monitoring activities. Each child and parent was instructed on how to use the peak flow monitoring provided by the study and how to complete the symptom diary. After the 2-week period, diaries and peak flow monitors were collected by the researcher.

During a clinic visit a respiratory questionnaire was completed by the parent and the child completed the PAQLQ and spirometry [(FVC), (FEV<sub>1</sub>), and FVC (FEF<sub>25-75</sub>), the FEV<sub>1</sub>/FVC ratio]. Following completion of spirometry, children completed the PAQLQ (Lawson et al., 2009).

The current secondary analysis is concerned only with cases of physician diagnosed asthma which is illustrated in Figure 3.1.

Figure 3.1 Study selection and assessments completed by the current study population (n=77)



*Study Location*

Humboldt, the site of the original study location, is located approximately 120 km east of Saskatoon, Saskatchewan. Details of the case-control study have been previously published (Lawson, et al., 2009, Lawson, Dosman, Rennie, Beach, Newman et al., 2011(a), Lawson, Dosman, Rennie, Beach, Newman et al., 2011(b)). The study location includes the town of Humboldt as well as the rural municipality of Humboldt and is primarily an agricultural based region. The total population of the town of Humboldt and the rural municipality at the time of the study was approximately 6072 (Census Canada, 2006). Humboldt has been the site of four previous cross-sectional studies (1977, 1983, 1993 and 2004) investigating respiratory health for adults and two cross-sectional studies of children's respiratory health (1994 and 2004) (Chen, Horne & Dosman, 1993; Chen, Rennie & Dosman, 1996; Chen, Schell, Rennie, Elston, Lockinger & Dosman, 2001; Chen, Rennie, Cormier & Dosman, 2005). The 2004 portion of the Humboldt study was a cross sectional survey that was distributed to parents of children grades 1-12. In 2005, the case-control portion of the study was extended beyond the original study of Humboldt township to include several towns in the rural municipality of Humboldt. The same cross sectional survey used in the Humboldt study was distributed to parents to locate children for the case control study (See Appendix A).

#### *Current Study Population*

The current secondary analysis is concerned with findings for only cases with physician diagnosed asthma and their caregivers (n=77). All parents completed the CHQ-PF50, with questions from all 14 domains. One participant did not complete a single question on the General Health domain resulting in a study population of 76. All children 77 completed the PAQLQ with questions from all three domains. All 77 parents completed the PACQLQ with no missing data.

### *Operational Definitions*

*Parental education level:* The highest education level attained by either the mother or father based on the following question for each of the mother and father. “What was the highest level of education completed by the child’s mother or father? Public school/Grade 12/Technical school/some university/University degree.” The variable was dichotomized as either high school or less, and more than high school.

*Case:* This includes cases based on the following definition: (a) any case with a positive report to physician-diagnosed asthma and who had experienced any of the following at least once in the past 12 months: physician visit for asthma, emergency room visit for asthma, intensive care visit for asthma, hospitalization for asthma, episodes of asthma, medication use for asthma, asthma symptoms, or missed school because of asthma. For this secondary analysis there were 77 cases with doctor diagnosed asthma in the past 12 months.

*Quality of life:* This was based on measurements of three QOL measurement tools. Two of these tools are asthma specific measurements of QOL (PAQLQ and PACQLQ) while one was a generic measurement of QOL (CHQ-PF50). One tool was completed by the child with asthma (PAQLQ) and the remaining two tools were completed by the parent (PACQLQ and CHQ-PF50).

*Asthma severity:* This was measured by pulmonary function testing (FEV<sub>1</sub>, FVC, FEF<sub>25-75</sub>, FEV<sub>1</sub>/FVC ratio) and PEFR.

*Parental Smoking:* This was based on either parent reporting smoking in the home the child with asthma primarily resides in.

### *Measures of QOL*

Health related QOL outcomes will be measured by three QOL scales, the PAQLQ, PACQLQ, and CHQ-PF50. Permission to use the PACQLQ and the PAQLQ was received from E. F. Juniper by the researcher of the case control study. Permission to use the CHQ-PF50 was received from J. Landgraf by the researcher of the case control study.

#### *PAQLQ*

The Pediatric Asthma QOL Questionnaire (PAQLQ), developed in 1992 is designed for assessing QOL in children with asthma age 7-17. The PAQLQ was adapted from the validated Asthma Quality of Life Question (AQLQ) for use in adults (Juniper, Guyatt, Ferrie & Griffith, 1993). The instrument contains 23 items within three domains, including Activity Limitation (five items), Symptoms (ten items) and Emotional Function (eight items) in which children rate their own functioning and produce a perceived QOL score. An example of a question in the Activity Limitation Domain is “How much have you been bothered by your asthma in PHYSICAL ACTIVITIES (such as running, swimming, sports, walking uphill/upstairs and bicycling) during the last week?” An example of a question in the Symptom Domain is “How much did COUGHING bother you in the past week?” An example of a question in the Emotional Function Domain is “How often did you feel WORRIED, CONCERNED OR TROUBLED because of your asthma during the past week?”

The instrument is available in both self-completion format and interviewer administered. For this study the interviewer format was used. The responses are on a 7-point Likert scale where 1 indicates maximum impairment and 7 indicates no impairment for the self-completion format. For the interview-administered version, children are given either a blue or green card, which the responses are listed. Verbal descriptors for the blue card follow each number, 1

represents extremely bothered, 2 represents very bothered, through to 7 representing not bothered. Verbal descriptors for the green card follow each number, 1 represents all of the time, 2 represents most of the time, through to 7 representing none of the time. A total score is derived from the mean of all responses. Higher scores represent no impairment for the child.

*Validation of the PAQLQ.*

The PAQLQ was originally developed in English for use in Canada and has been validated in English versions for Australia, New Zealand, the United Kingdom, and the United States (Juniper et al., 1996a; Juniper et al., 1996b). It has been translated and validated in French, Spanish, German, Dutch, Flemish, Italian, Norwegian, Danish, Swedish and Finish languages (Raat, et al., 2005; La Scala, Naslitz & Sole, 2005; Reichenberg & Broberg, 2000; Ricci, Dondi, Baldi, Bendandi, Giannette & Masi, 2009; Tauler, Vilagut, Grau, Gonzalez, Sanchez & Figueras, 2001).

The PAQLQ which was primarily designed for evaluative purposes with clinical trials, and has demonstrated good construct validity and responsiveness to change over time, [Juniper et al., 1996(a) ( $p = 0.001$ ); Juniper, Guyatt, Willan & Griffith, 1994 ( $p = 0.001$ ); Sanjuas, Alonso, Sanchis, Casan, Broquetas & Ferrie, 1995 ( $p = 0.01$ ); Tauler et al., 2001 ( $p = 0.01$ ); Raat et al., 2005 ( $p = 0.01$ ); Ricci et al., 2009 ( $p = 0.001$ ); La Scala et al., 2005 ( $p = < 0.001$ ); Reichenberg, & Broberg, 2000 ( $p = 0.001$ )]. The PAQLQ has also demonstrated good test-retest reliability ( $r = 0.30-0.60$ ) in research studies (Juniper et al., 1996(a); Juniper et al., 1994; Sanjuas et al., 1995; La Scala et al., 2005; Juniper, Guyatt, Feeny, Griffith & Ferrie, 1997; Juniper et al., 1996(b); Reichenberg & Broberg, 2000).

The PAQLQ has been validated with clinical asthma control outcomes, such as  $\beta_2$ -agonist use and morning peak flow rates (Juniper et al., 1996a) with a reported Cronbach's  $\alpha$  of

0.93 for overall QOL. The intra-class correlation coefficients for children age 7 to 10 years were 0.89 for overall QOL and 0.68, 0.83 and 0.87, respectively for the subscales of Emotional Function, Activity Limitation and Symptoms (Juniper et al., 1996b). The cross-sectional correlation between asthma QOL and asthma control for the three domains, Emotional Function, Activity Limitation and Symptoms were -0.37, -0.62 and -0.61 (Juniper et al., 1996b).

*Limitations of the PAQLQ.*

There is limited data for the PAQLQ with different age groups of children because of small sample sizes in some validation studies (Juniper, et al., 1996b; Williams & Williams, 2003). The single version PAQLQ covers the age range 7-17. Several research studies found the PAQLQ to lack age specificity with regard to psychological issues (Rutishauser et al., 2001; Williams & Williams, 2003). In addition, because the PAQLQ is applied to a pediatric population with diverse developmental levels it has been questioned by researchers whether the cognitive, social and emotional development are considered for all ages (Rutishauser et al., 2001; Williams & Williams, 2003). Four studies found the PAQLQ was difficult for children under the age of 8 to complete independently and required pictorial assistance from the interviewer (Everhart, et al., 2008; Reichenberg & Broberg, 2000; Rutishauser et al., 2001; Ricci et al., 2009). These studies also highlighted the difficulty for children under the age of 8 to comprehend the one-week recall period. Finally, several studies found the PAQLQ was unable to discriminate health-related QOL in children with good lung function and suggested a more sensitive instrument may be required to assess QOL for these cases (Ricci et al., 2009; Raat et al., 2005; Tauler et al., 2001).

### *PACQLQ*

The Pediatric Asthma Caregivers QOL Questionnaire (PACQLQ) also developed by Juniper, (1992) is an instrument designed to assess QOL of caregivers of children with asthma. The self-administered instrument contains 13 items within two domains: Activity Limitation (4 items), and Emotional Function (nine items). Parents rate their own functioning and produce a perceived QOL score. An example of a question on the Activity Limitation Domain is “Did your child’s asthma interfere with your job or work around the house”. An example of a question in the Emotional Function Domain is “Did you feel helpless or frightened when your child experienced cough, wheeze, or breathlessness”?

The PACQLQ is designed to measure the impact of the child’s asthma on the caregiver’s daily activities as well as fear and worry associated with caring for children with asthma. In addition, it measures areas of functional importance to the primary caregivers of children with asthma, including both physical and emotional impairments. Responses are scored on a 7-point Likert scale, where 1 represents severe impairment and seven represents no impairment. Descriptors for the PAQLQ follow each number, 1 represents very, very worried/concerned, 2 represents very worried/concerned, through to 7 representing not worried/concerned. All individual items are weighted equal, therefore the domain scores range from 1-7. A total score is derived from the mean of all responses, with a range of 13 to 91. Higher scores reflect a positive QOL for the caregiver.

### *Validation of PACQLQ.*

In a validation study of the PACQLQ conducted by Juniper et al., 1996(b), the intra-class correlation coefficients for the total PACQLQ score and the Emotional Function and Activity Limitation domains were 0.80 and 0.85. The cross sectional correlations between the caregiver

QOL and clinical asthma control for the two domains, Activity Limitation and Emotional Function subscales, were poor at 0.30 and 0.29 respectively (Juniper et al., 1996b). The PACQLQ has demonstrated responsiveness to change over time in a study by Rutishauser et al., (1998).

*Limitations of PACQLQ.*

The PACQLQ has been shown to lack age specificity with regard to psychological issues (Rutishauser et al., 1998). The inclusion of psychosocial items is particularly important for adolescents and children to assess QOL. QOL cannot necessarily be assessed in adolescents in the same manner as a younger child and psychosocial items should be age-appropriate by consideration of the impact maturation has on the activity (Rutishauser et al., 1998).

*CHQ-PF50*

The Child Health Questionnaire (CHQ-PF50) is a generic health related QOL tool developed by Landgraf, Abetz, Ware, (1996) for children age 5-18 years of age using traditional item scaling and psychometric methods. It can be used with healthy or ill pediatric populations. The CHQ-PF50 assesses the association between health of the child and QOL of the child and the association between health of the child and family, from the parents' perspective.

The instrument contains a broad spectrum of child and family-focused health questions, with 50 items within 14 domains/concepts including: Physical Functioning (six items), Role/Social Limitations-physical (two items), General Health Perceptions (six items), Bodily Pain/Discomfort (two items), Family Activities (six items), Roles/Social Limitations-Emotional/Behavioural (considered two domains) (three items), Self-Esteem (six items), Mental Health (five items), Behaviour (6 items), Parent Impact-time (3 items), Parent Impact-Emotion

(3 items), Family Cohesion (one item); Change in Health (one item) Landgraf, et al., (1996).

Each domain/concept is assessed on a Likert-type scale ranging from 1-4 to 1-7.

Parents complete the questionnaire by responding on a Likert-type scale (1-4), (1-5), (1-6) or (1-7) for each concept as identified above. Scores are then tabulated for each concept and a summative score is generated. Scores range from 0-100, with higher scores indicating better or more positive health status. Two summary scores are possible if the researcher divides the questionnaire to physical or psychosocial concepts, thus generating the Physical Summary Score (PHS) and the Psychological Summary Score (PSS). The CHQ-PF50 recognizes the different developmental stages of children and adolescents by providing a version for parent completion as well as a self -report for children age 10-17 years (Landgraf, et al., 1996).

For this study QOL for all study participants (n=77) was assessed using the CHQ-PF50. All parents completed the CHQ-PF50, with questions from all 14 domains. One participant did not complete a single question on the General Health domain resulting in a study population of 76. Two summary scores were calculated, Physical Summary Score (PHS) and Psychosocial Summary Score (PSS). These scores were calculated following the guidelines in the CHQ manual (Landgraf et al., 1996) using 10 of the CHQ-PF50 scales (Physical functioning, Role/Social Physical, General Health, Bodily Pain, Parent Impact-time, Parent Impact-Emotional, Role/Social-Emotional/Behaviour, Self-Esteem, Mental Health and Behaviour and omitting the CHQ scales Family Activities and Family Cohesion). In addition the CHQ-PF50 scales of Role-Emotional and Role-Behavioural were combined as a single scale and Change in Health and General Health were combined as a single scale. Calculation of the PHS score was completed using the CHQ-PF50 scales: Physical functioning, Role/Social Physical, General Health, and Bodily Pain. Calculation of the PSS score was completed using the CHQ-PF50

scales: Parent Impact-Time, Parent Impact-Emotional, Role/Social-Emotional/Behaviour, Self-esteem, Mental Health and Behaviour. Two CHQ-PF50 scales are not used in the calculation of either the PHS or PSS these are Family Activities and Family Cohesion.

*Validation of CHQ-PF50.*

The CHQ-PF50 was originally developed and validated for use in English in the United States (Landgraf et al., 1996; Landgraf & Abetz, 1998). It has since been validated for use in Canada, Australia, Sweden and New Zealand (Waters, Salmon & Wake, 2000(a); Waters, Salmon, Wake, Wright & Heskeath, 2000(b); Norby, Nordholm & Fasth, 2003). The CHQ-PF50 demonstrates good construct validity in research studies (0.62 to 0.92), (Norby, Nordholm, Anderson-Gare & Fasth, 2006; Rodary, Landgraf, Kalifa, Lerveger & Gentet, 2000). It has been cross-validated and found to be acceptable, using confirmatory factor analysis with an independent sample of generally healthy children, Physical Summary Score ( $r^2 = 0.15-0.63$ ) Psychosocial Summary Score ( $r^2 = 0.30-0.56$ ), (Hepner & Sechrest, 2002) and with the QOL in a Childs' Chronic Disease Questionnaire (QLCCDQ), (Farnik, Brozek, Pierzchala, Zejda, Skrzypek, et al., 2010).

*Limitations of CHQ-PF50.*

Although the CHQ-PF50 is a thoroughly validated measurement of QOL that covers a broad range of dimensions, a disease specific questionnaire in the same setting may reveal different results (Gorelick, Scribano, Stevens & Schultz, 2003). The CHQ-PF50 demonstrated a good ability to differentiate children with more and less severe asthma at a given point in time using more long-term measures of disease severity but was less responsive to small changes. These findings question the suitability of the generic questionnaire for measuring short-term changes in health related QOL for children with asthma (Asmussen, Olson, Grant, Fagan, &

Weiss, 1999; Gorelick, et al., 2003; Ware, Kemp, Buchner, Singer, Nolop & Gross, 1998; Merikallio, Mustalahti, Remes, Valovirta & Kaila, 2005).

#### *Measurements of Asthma Severity*

##### *Pulmonary Function*

Pulmonary function was assessed through spirometry using forced expiratory maneuvers using a dry-rolling seal spirometer (Sensorimedics model 922; Sensormedics Corporation, Anaheim, CA) to conduct testing. American Thoracic Society (ATS) guidelines for spirometry testing in children were followed (American Thoracic Society, 1995; American Thoracic Society, 1991; American Thoracic Society, 1987). Children completed the testing seated while using a nose clip and at least 3 and no more than 7 maneuvers were attempted. Prior to testing each day, calibration of the spirometer was performed using a three-Litre syringe. The spirometer was recalibrated at least once during the day of testing if there was an extended length of time of testing (greater than four hours) or if the room temperature changed by greater than or equal to two degrees. Pulmonary functions measures (FVC, FEV<sub>1</sub>, FEF<sub>25-75</sub>, FEV<sub>1</sub> / FVC ratio) were considered by using absolute values adjusted for age, sex, and height.

Height and weight were measured objectively as part of the pulmonary function testing. Height was measure against a wall using a fixed tape measure with subjects standing in socks on a smooth surface. Weight was measured using a calibrated spring scale with subjects in socks and dressed in normal indoor clothing. Temperature (°C), barometric pressure (mmHg) and relative humidity (%) were also collected at the time of pulmonary function testing (Traceable Model No. 61161-396, Friendswood, Texas).

Lung Function measures were considered by using absolute values adjusted for age, sex and height. In addition to this, descriptive values of lung function were considered using percent

predicted values based on predicted equations by Knudsen (Sensormedics, 1992). There was no adjustment for ethnic background in the analysis as the study population was almost exclusively Caucasian (97.7%).

#### *Diurnal Peak Flow Variability*

The variability in diurnal peak expiratory flow rate (PEFR) is determined through daily monitoring. In this study, the PEFR was measured at least twice daily over a period of two weeks by blowing into a portable hand held peak flow meter. The equipment used was an electronic PIKO peak flow monitor (Ferraris) that also recorded both PEFR and FEV<sub>1</sub>. The PIKO peak flow monitor stores 96 maneuvers. In order to allow for multiple users within families, a special mouthpiece and adaptor was provided for each child. During the two-week PEFR monitoring, an asthma symptom diary was also used. This was to be completed by each child, with parental guidance as necessary. Children were requested to carry out peak flow testing of five blows in a standing position. Testing occurred first thing after waking each morning and prior to going to bed each evening. Children were also requested to complete the testing prior to taking any asthma medications if possible. Testing included a minimum of three blows. If an error was recorded on the PIKO monitoring unit or if there was more than a 40L/min difference between any maneuver and the highest recorded maneuver, an additional maneuver was completed. Children were requested not to carry out more than five maneuvers in a given session. The two-week PEFR monitoring period was started the day after the home visit. Upon collection of the asthma symptom diary and peak flow monitor following the two-week monitoring, the information recorded by the PIKO monitoring unit was downloaded to a computer using specialized software (PIKONET Pro Software, Ferraris Respiratory). Children

were included if they had more than one day of PEFR recordings but greater than ninety percent of the children had more than one week of recorded values.

Daily Diurnal peak flow variation (DPV) was measured by:

Absolute DPV = [(maximum morning PEFR - maximum evening PEFR)/(maximum PEFR from the day)]

Mean diurnal peak flow variability over time was measured by the DPV value divided by the number of days of monitoring.

#### *Statistical Analysis*

Analysis was completed using SPSS version 20.0. Throughout the analysis, the level of statistical significance ( $\alpha$ ) was considered to be 0.05 or less.

#### *Statistical analysis for comparison of asthma specific QOL scales*

Spearman's rho correlation was performed to assess the relationship between the total score and the three domains of the PAQLQ (Symptoms, Activity Limitation and Emotional Function), the total score and the two domains of the PACQLQ (Activity Limitation and Emotional Function).

#### *Statistical Analysis for Comparison of Asthma Specific QOL Scales and the CHQ-PF50.*

Spearman's rho correlation was performed to assess the relationship between the Total score and the three domains of the PAQLQ (Activity Limitation, Symptoms and Emotional Function), along with the CHQ Summary Scores, Physical Summary Score (PHS) and Psychosocial Summary Score (PSS).

Spearman's rho correlation was also performed to assess the relationship between the total score and the two domains of the PACQLQ (Activity Limitation and Emotional Function),

along with the CHQ Summary Scores, Physical Summary Score (PHS) and Psychosocial Summary Score (PSS).

*Statistical Analysis for Comparison of QOL Scales and Measures of Asthma Severity*

General linear regression analysis was performed to assess the association between the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) and percent predicted values for FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>, maternal education, asthma medication use in the last 12 months and parental smoking.

General linear regression was also performed to assess the association between the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) and their subscales or domains with mean diurnal peak flow variability for the 2-week home monitoring period adjusting for age, sex and height.

*Power Calculation*

The expected power was calculated for each research question using G Power software, Erdfelder, Faul, & Buchner, 1996. Alpha was defined as 0.05.

*Power calculation for Research Question 1*

*Is there a correlation between the QOL scores measured on the PAQLQ in children with asthma and QOL scores of their caregivers measured on the PACQLQ?*

For this research question there are 77 cases of asthma. Based on a similar study the correlation reported was  $r = 0.61$  (Mussafi, et al, 2007). With a subject pool of 77 children for the PAQLQ and 77 parents with the PACQLQ available in the study, the projected power for this research question with a similar effect size would be 99.9%.

*Power Calculation for Research Question 2*

*Is there an association between QOL as measured on a generic QOL assessment tool, the CHQ-PF50, and QOL measured on asthma specific QOL assessment tools, the PAQLQ and the PACQLQ in children with asthma and their caregivers?*

For this research question we also have 77 subjects who completed the PAQLQ and the PACQLQ and 76 subjects who completed the CHQ-PF50. From the literature, based on similar studies we have found the correlation to be  $r = 0.45$  (Warschburger et al., 2004) and  $r = 0.70 - 0.75$  (Flapper et al., 2006). With a subject pool of 77 children and parents, who completed the PAQLQ (children), PACQLQ (parents) and 76 parents who completed the CHQ-PF50 (parents) available, the anticipated power to find a significant association will be 98.5%.

#### *Power Calculation for Research Question 3*

*Is there an association between QOL measurements (PACQLQ, PAQLQ and CHQ-PF50) and measures of asthma severity as measured by percent predicted lung function (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>) or by the mean diurnal peak flow variability during a two-week home monitoring period?*

A comparison of PAQLQ and FEV<sub>1</sub> and PEFR has been assessed in a single study producing ( $r = 0.25-0.26$ ) with and ( $r = 0.31-0.27$ ), respectively (Juniper et al, 1996(a)). With a fixed sample size of 77 subjects for the PAQLQ and PACQLQ and 76 subjects for the CHQ-PF50 available in this analysis, to test associations with FEV<sub>1</sub>, the power to find a similar association will be 69%. To test associations between the PAQLQ and peak flow variability based on findings from previously studies we should have 95% power to find a similar association.

For this research question we also have 76 caregivers who completing the CHQ-PF50 and 77 children completing measures of lung function. From the literature based on similar

studies we have found the correlation to be  $r = 0.32\text{--}0.47$  (Poachanukoon et al., 2006),  $r = 0.31\text{--}0.43$  [Juniper et al., 1996 (a)],

In summary, based on the above power calculation and previous research findings regarding potential effect sizes we appear to have a sufficient sample size for a medium effect size with a power of 69-99.9%. The most conservative correlation exists with Research Question 3, specifically the association between  $\text{FEV}_1$  and measures of QOL. However all research questions, with the exception of  $\text{FEV}_1$  demonstrate a power of greater than 95%. We should have sufficient power to answer most research questions.

#### *Ethical Approval*

Letters of ethical approval for this study by university institutions are located in Appendix A. The original case control study was approved on December 3, 2004 by the University of Saskatchewan Biomedical Research Ethics Board (reference # 04-184) and the University of Alberta's Health Research Ethics Board – Panel A (5471). The current study was approved on July 11, 2012 by the University of Saskatchewan Biomedical Research Ethics Board (reference # 12-200) and renewed on July 9, 2013.

Local approval was received from school boards of schools approached during the study period for recruitment and testing of subjects. Written informed consent (assent) was completed by all study participants and a caregiver. See Appendix B.

## **CHAPTER FOUR**

### **Results**

#### *Descriptive Analysis of Study Population*

There were 102 children who participated in the original case-controlled study as cases. They were mostly male (66.7%) versus (33.3%) female. The mean age of children in the study population is 11.3 years ( $SD = 3.05$ ). Only 2 of the study participants were non-Caucasian. More mothers (80.4%) than fathers (51.0%) had an education level greater than Grade 12. Approximately 65.7% of children lived in town while 34.3% lived on either a farm or acreage. Mothers were most likely to have completed the survey questionnaire (88.2% of respondents).

Of the children within the study population, 77 have a physician diagnosis of asthma which will be examined for the current study. Table 4.1 provides findings for demographic variable for the current study population.

Table 4.1 Comparison of selected demographic variables

	Asthma n=77
	Mean (sd)
Age (years)	11.2 (2.98)
Height (cm)	150.7 (16.98)
	n (%)
Sex	
(male)	51 (66.2)
(female)	26 (33.8)
Mothers education	
(high school)	53 (68.8)
(Post-secondary degree)	24 (31.2)
Fathers education	
(high school)	66 (85.7)
(Post-secondary degree)	11 (14.3)
Missed days from School (child)	
(Yes)	11 (14.2)
(No)	66 (85.7)
Missed days from work (parent)	
(Yes)	10 (12.9)
(No)	67 (87.0)
Questionnaire completed by	
Mother	69 (89.6)
Other	8 (10.4)
Location of home	
Farm or acreage	24 (31.2)
Town	53 (68.8)

#### *Descriptive Analysis of Pulmonary Function and Peak Flow*

All cases in the study population had relatively high mean lung function values (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>). Table 4.2 provides crude and percent predicted information about the study population. Average percent predicted for pulmonary function variables were greater than 100.0%. Table 4.3 provides information comparing crude and percent predicted values of pulmonary function variables for children with asthma.

Table 4.2 Crude and percent predicted values of pulmonary function characteristics for study population (n=77)

	Percent Predicted Mean (95% CI)	Adjusted* Mean (95% CI)
FVC (L)	113.69 (81.45-145.15)	3.40 (3.16 - 3.65)
FEV <sub>1</sub> (L)	109.27 (76.45-143.61)	2.83 (2.63 - 3.03)
ratio (%)	---	83.59 (82.39 - 84.78)
FEF <sub>25-75</sub> Litres/second	100.77 (44.83-147.64)	3.02 (2.79 - 3.25)

FVC = Forced vital capacity, FEV<sub>1</sub> = Forced expiratory volume in 1 second, FEF<sub>25-75</sub> = Forced expiratory flow between 25<sup>th</sup> and 75<sup>th</sup> percent of FVC, ratio (FEV<sub>1</sub>/FVC) = FEV<sub>1</sub> as a proportion of FVC expressed as a percent, CI=Confidence Interval.

\*adjusted for age, sex and height

Table 4.3 Crude and percent predicted values of pulmonary function characteristics among children with asthma (n=77)

	Asthma n=77 Mean (95% CI)
FVC	
Litres*	3.35 (3.25-3.46)
Percent Predicted	113.69 (110.93-116.44)
FEV <sub>1</sub>	
Litres*	2.80 (2.71-2.90)
Percent Predicted	109.27 (106.47-112.08)
ratio	
Litres*	84.08 (82.64-85.53)
Percent Predicted	---
FEF <sub>25-75</sub>	
Litres*	3.04 (2.86-3.22)
Percent Predicted	2.99 (2.48-3.29)

FVC = Forced vital capacity, FEV<sub>1</sub> = Forced expiratory volume in 1 second, FEF<sub>25-75</sub> = Forced expiratory flow between 25<sup>th</sup> and 75<sup>th</sup> percent of FVC, ratio (FEV<sub>1</sub>/FVC) = FEV<sub>1</sub> as a proportion of FVC expressed as a percent, CI=Confidence Interval.

\*adjusted for age, sex and height

Table 4.4 Crude diurnal peak flow variability of children with asthma (n=77)

	Asthma (n=77)
Median	7.01
Minimum-maximum	1.76 – 43.82
Range	42.06
Mean (SD)	5.60 (7.10)

### *Internal Consistency Reliability Testing for Quality of Life Measurement Tools*

Internal consistency reliability was tested for the three quality of life measurements tools, the PAQLQ, PACQLQ and CHQ-PF50. The three tests used were Cronbach's Alpha, Spearman-Brown and Guttman Split-half. Table 4.5 provides findings regarding the internal consistency reliability for the three quality of life measurement tools.

Cronbach's Alpha is a measure used to statistically test internal consistency between scores on individual items. Values of this measure above 0.70 are usually acceptable, and 0.80 or more is excellent. All three QOL measurement tools demonstrated excellent internal consistency (0.907-0.919).

The Spearman-Brown correlation coefficient is a nonparametric test measuring internal consistency and statistical dependence between two variables. It assesses how well the relationship between two variables can be described as a monotonic function. The Spearman-Brown coefficient assesses the direction of association between two variables, and increases as the two variables become closer together. All three QOL measurement tools demonstrated excellent internal consistency (0.884-0.931).

The Guttman Split-half coefficient is a measure of reliability where a comparison of the population is completed when split into two equal halves and considers the amount of variance in each item. All three QOL measurement tools demonstrated excellent internal consistency reliability (0.872-0.925). Results from testing internal consistency reliability show that all three QOL measurements showed good to excellent values on all three measures of internal consistency reliability.

Table 4.5 Internal consistency reliability for QOL measurement tools

	Cronbach's Alpha	Spearman-Brown Coefficient	Guttman Split-half Coefficient
PAQLQ (n=77)	.919	.891	.891
PACQLQ (n=77)	.909	.884	.872
CHQ-PF50 (n=76)	.907	.931	.925

#### *Descriptive Analysis for Quality of Life Measures*

*CHQ-PF50.* No single overall score was available for the CHQ-PF50. All parents (n=77) completed the CHQ-PF50, with questions from all 14 domains. One participant did not complete a single question on the General Health domain resulting in a study population of 76. The mean, (SD), median and ranges for the CHQ-PF50 Physical Summary Score were 53.4(5.54), 51.2, respectively. For the Psychosocial Summary, the mean (SD), median and range of scores were 50.9(10.47), 53.6, respectively. Table 4.6 provides findings of the descriptive statistics for the Physical Summary Score and Psychosocial Summary Scores. The Physical Summary Score and Psychosocial Summary Scores are produced using select domain scores. Table 4.7 provides findings regarding the descriptive statistics of the CHQ-PF50 grouping each of the 14 domains into the appropriate category for their respective summary scores.

Table 4.6 Descriptive statistics of CHQ-PF50 Physical Summary Score and Psychosocial Summary Score (n=76)

	Physical Summary Score (standard deviation)	Psychosocial Summary Score (standard deviation)
Mean (SD)	53.4(5.54)	50.9(10.47)
Median	51.2	53.6
Interquartile Range	42.31-64.42	40.48-71.88

Table 4.7 Descriptive statistics of CHQ-PF50 sub scale scores (n=76)

	Mean	Median	Interquartile Range
<b>Physical Summary Score Domains</b>			
General Health	80.33	85.0	66.47-100
Physical Functioning	95.53	98.7	75.42-100
Bodily Pain	82.99	79.6	82.43-100.0
General Health (last 12 months)	69.98	70.2	54.83-85.13
Role-Physical	96.54	99.4	95.8-100.0
<b>Psychosocial Summary Score Domains</b>			
Global Behaviour	73.25	84.6	58.35-84.7
Role-Emotional/Behaviour	93.22	94.9	86.7-100
Behaviour	71.95	76.1	53.12-76.7
Self-Esteem	82.63	87.5	65.4-87.5
Parent Impact Emotional	78.03	83.3	66.7-83.3
Parent Impact Time	91.20	99.5	88.7-100.0
<b>Domains Not Included in Summary</b>			
<b>Scores</b>			
Family Activities	85.60	90.6	69.2-100.0
Family Cohesion	77.01	85.0	60.0-85.0

Quality of life for children with asthma (n=77) was also assessed using the PAQLQ. Domain and total scores were calculated for the questionnaires. Three domain scores are produced using the PAQLQ, Symptoms, Activity limitation and Emotional function. Table 4.8 provides information regarding the descriptive statistics of the PAQLQ, grouping each of the 24 questions into the appropriate category for their respective domain score.

Table 4.8 PAQLQ scores for domains and individual questions (n=77)

	Mean (SD)	Median	Range Min-max
PAQLQ Activity Limitation Domain	5.9(0.90)	6.20	5.8-6.2
Bothered by physical activity	5.8(1.19)	6.00	5.6-6.1
Bothered by animals	6.2(1.54)	7.00	5.9-6.6
Bothered by activities	6.1(1.08)	7.00	5.9-6.4
Feel like couldn't keep up with others	6.1(1.51)	7.00	5.7-6.4
Activities bothered by asthma	5.7(1.48)	6.00	5.3-6.0
PAQLQ Symptom Domain	6.1(0.88)	6.40	5.9-6.3
Bothered by coughing	5.5(1.57)	6.00	5.2-5.9
Feel tired because of asthma	6.1(1.39)	7.00	5.8-6.5
Bothered by asthma attacks	6.6(1.21)	7.00	6.3-6.8
Bothered by wheezing	6.1(1.30)	7.00	5.8-6.4
Bothered by tightness in chest	6.2(0.99)	7.00	6.0-6.4
Bothered by shortness of breath	6.1(1.04)	6.00	5.9-6.3
Wake during night	6.2(1.51)	7.00	5.9-6.6
Feel out of breath	5.7(1.25)	6.00	5.4-6.0
Trouble sleeping at night	6.4(1.22)	7.00	6.1-6.7
Difficulty taking deep breath	5.9(1.34)	6.00	5.7-6.3
PAQLQ Emotional Function Domain	6.5(0.79)	6.88	6.3-6.6
Frustrated by asthma	6.2(1.35)	7.00	5.8-6.5
Worried, concerned or troubled	6.5(0.90)	7.00	6.3-6.7
Feel angry	6.5(1.20)	7.00	6.2-6.8
Feel irritable	6.3(1.25)	7.00	6.0-6.6
Feel different or left out	6.8(0.73)	7.00	6.6-7.0
Frustrated couldn't keep up	6.2(1.41)	7.00	5.9-6.6
Feel uncomfortable	6.5(1.06)	7.00	6.2-6.7
Feel frightened by asthma attack	6.6(1.25)	7.00	6.3-6.9
PAQLQ Total Score	6.2(0.76)	6.48	6.0-6.4

The third measure of QOL, the PACQLQ, was used to assess parental QOL, for parents of children with asthma. Domain and total scores were calculated for the questionnaire. Table 4.9 provides information regarding the descriptive analysis of the PACQLQ, grouping each of the 13 questions into the appropriate category for their respective domain score.

Table 4.9 PACQLQ scores for domains and individual questions (n=77)

	Mean (SD)	Median	Range min-max
PACQLQ Activity Limitation Domain	6.5(0.87)	7.00	6.3-6.7
Need to change plans	6.6(0.86)	7.00	6.4-6.8
Interfere with work	6.6(0.89)	7.00	6.4-6.8
Have sleepless nights	6.4(1.16)	7.00	6.1-6.6
Awakened at night	6.4(1.18)	7.00	6.1-6.6
PACQLQ Emotional Function Domain	6.5(0.65)	6.78	6.4-6.6
Feel helpless or frightened	6.1(1.28)	7.00	6.4-6.8
Feel frustrated or impatient	6.5(0.93)	7.00	6.3-6.7
Feel upset because of asthma symptoms	6.3(1.41)	7.00	6.1-6.6
Asthma interfere with relationships	6.9(0.32)	7.00	6.8-7.0
Feel angry	6.8(0.51)	7.00	6.7-6.9
Concerned with child's performance	6.4(1.06)	7.00	6.1-6.6
Concerned with child's medication	6.4(1.14)	7.00	6.2-6.7
Concerned with being overprotective	6.5(0.87)	7.00	6.3-6.7
Concerned with leading normal life	6.6(0.99)	7.00	6.3-6.8
PACQLQ Total Score	6.5(0.68)	6.77	6.3-6.6

### *Research Questions*

#### *Research Question 1*

*Is there a correlation between the QOL scores measured on the PAQLQ in children with asthma and QOL scores of their caregivers measured on the PACQLQ?*

No significant relationship was found between the domain or total scores on the PAQLQ and the PACQLQ. Table 4.10 provides findings regarding the relationship between the PAQLQ and PACQLQ. Comparisons were also made between children age 6-12 and children age 13-17. Table 4.11 provides findings between these two groups.

Table 4.10 Spearman's rho correlation of QOL domain scores on PAQLQ and PACQLQ (n=77)

	PAQLQ Activity Limitation Domain	PAQLQ Symptom Domain	PAQLQ Emotional Function Domain	PAQLQ Total Score
PACQLQ Activity Limitation Domain	0.010	-0.036	0.095	0.011
PACQLQ Emotional Function Domain	0.169	0.095	0.147	0.142
PACQLQ Total Score	0.153	0.083	0.133	0.128

No significant correlations were found between the PAQLQ and PACQLQ total and domains scores.

Table 4.11 Comparison of QOL scores PAQLQ and PACQLQ between children and adolescents (n=77)

	n	Mean	Standard Deviation	p value
<b>PAQLQ Total score</b>				
Age 6-12	47	6.1	0.79	
Age 13-17	25	6.3	0.69	0.341
<b>PAQLQ Activity Limitation Domain</b>				
Age 6-12	47	5.9	0.92	
Age 13-17	25	6.1	0.85	0.399
<b>PAQLQ Symptom Domain</b>				
Age 6-12	47	6.1	0.91	
Age 13-17	25	6.1	0.84	0.818
<b>PAQLQ Emotional Function Domain</b>				
Age 6-12	47	6.3	0.89	
Age 13-17	25	6.7	0.51	0.057
<b>PACQLQ Total Score</b>				
Age 6-12	50	6.4	0.76	
Age 13-17	27	6.7	0.41	0.010
<b>PACQLQ Activity Limitation Domain</b>				
Age 6-12	50	6.3	0.98	
Age 13-17	27	6.8	0.45	0.003
<b>PACQLQ Emotional Function Domain</b>				
Age 6-12	50	6.4	0.73	
Age 13-17	27	6.7	0.43	0.032

Overall QOL scores were lower for children ages 6-12 than for those ages 13-17 in all domains. Significant associations were seen with the PACQLQ Total Score ( $p = 0.01$ ), Activity Limitation Domain ( $p < 0.01$ ) and Emotional Function Domain ( $p < 0.05$ ) and the two age groups. Parents of children age 6-12 scored their child's quality of life lower in both of the PACQLQ domains and the overall score compared to parents of children age 13-17. A significant association ( $p = 0.057$ ) was also found between the PAQLQ Emotional Function Domain score and the two age groups of children. Children age 6-12 scored lower on the Emotional Function domain than children age 13-17.

## *Research Question 2*

*Is there a correlation between QOL as measured on a generic QOL assessment tool, the CHQ-PF50, and QOL measured on an asthma specific QOL assessment tools, the PAQLQ and the PACQLQ in children with asthma and their caregivers?*

A significant relationship was seen between the PAQLQ Emotional Domain score and the CHQ-PF50 Psychosocial Summary score (0.302, p<0.01). Table 4.12 provides findings regarding the relationship between the PAQLQ and the CHQ-PF50.

Table 4.12 Spearman's rho correlation of QOL scores on PAQLQ domains and CHQ-PF50 summary scores (n=76)

	PAQLQ Activity Limitation Domain	PAQLQ Symptom Domain	PAQLQ Emotional Function Domain	PAQLQ Total Score
CHQ-PF50				
Physical Summary Score	0.085	0.085	-0.003	0.096
CHQ-PF50 Psychosocial Summary Score	0.173	0.220	0.302**	0.239

\*\* Correlation is significant at the 0.01 level (2-tailed)

Significant relationships were found with the CHQ PSS and both domains of the PACQLQ and the PACQLQ total score. Table 4.13 provides findings regarding the relationship between the PACQLQ and the CHQ-PF50.

Table 4.13 Spearman's rho correlation of QOL scores on PACQLQ domains and CHQ-PF50 summary scores (n=76)

	PACQLQ Activity Limitation Domain	PACQLQ Emotional Function Domain	PACQLQ Total Score
CHQ-PF50			
Physical Summary Score	-0.073	0.100	0.067
CHQ-PF50 Psychosocial Summary Score	0.362**	0.377**	0.364**

\*\* Correlation is significant at the 0.01 level (2-tailed)

### *Research Question 3*

*Is there an association between QOL measurements (PACQLQ, PAQLQ and CHQ-PF50) and asthma severity as measured by percent predicted lung function (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>) or by the mean diurnal peak flow variability during a two-week home monitoring period?*

#### *Quality of Life and Spirometry Results.*

No significant relationships were found between the FVC percent predicted and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50). Table 4.14 provides findings for the linear regression assessing associations of FVC percent predicted and the three measures of QOL (PAQLQ, PACQLQ, CHQ-PF50). No significant relationships were found between the FEV<sub>1</sub> percent predicted and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50). A trend was observed between the PAQLQ Activity Limitation Domain and the FEV<sub>1</sub> percent predicted ( $p = 0.08$ ). Table 4.15 provides findings for the linear regression assessing associations of FEV<sub>1</sub> percent predicted and the three measures of QOL (PAQLQ, PACQLQ, CHQ-PF50). No significant relationships were found between the FEF<sub>25-75</sub> percent predicted and the three QOL

measures (PAQLQ, PACQLQ, CHQ-PF50). Table 4.16 provides findings for the linear regression assessing associations between FEF<sub>25-75</sub> percent predicted and the three measures of QOL (PAQLQ, PACQLQ, CHQ-PF50). No significant relationships were found between the FEV<sub>1</sub>/FVC ratio percent predicted and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50). Table 4.17 provides findings for the linear regression of the percent predicted FEV<sub>1</sub>/FVC ratio and the three measures of QOL (PAQLQ, PACQLQ, CHQ-PF50).

Table 4.14 Linear regression assessing associations between FVC percent predicted and measures of quality of life

Quality of Life Variables	Beta (SE)	r <sup>2</sup>	p value
<b>CHQ-PF50 (n=76)</b>			
CHQ-PF50 (PHS)	0.295(.328)	0.091	0.38
CHQ-PF50 (PSS)	0.079(.212)	0.068	0.71
<b>PAQLQ (n=77)</b>			
Total	-3.231(3.679)	0.079	0.39
Domain			
Activity Limitation	-3.832(2.115)	0.164	0.08
Symptoms	-0.067(3.798)	0.049	0.99
Emotional Function	-1.866(3.126)	0.063	0.56
<b>PACQLQ (n=77)</b>			
Total	1.087(2.063)	0.068	0.72
Domain			
Activity Limitation	1.684(2.408)	0.080	0.49
Emotional Function	0.460(2.993)	0.064	0.88

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\*Adjusted for maternal education, asthma medication use in last 12 months, parental smoking.

Table 4.15 Linear regression assessing associations between FEV<sub>1</sub> percent predicted and measures of quality of life

Quality of Life Variables	Beta (SE)	r <sup>2</sup>	P value
CHQ-PF50 (n=76)			
CHQ-PF50 (PHS)	-0.012(.338)	0.108	0.97
CHQ-PF50 (PSS)	0.059(2.15)	0.111	0.79
PAQLQ (n=77)			
Total Domain	-3.942(3.684)	0.153	0.30
Activity Limitation	-3.849(2.135)	0.219	0.08
Symptoms	-1.158(3.824)	0.116	0.77
Emotional Function	-2.358(3.140)	0.133	0.46
PACQLQ (n=77)			
Total Domain	0.648(3.010)	0.110	0.83
Activity Limitation	0.664(2.462)	0.111	0.79
Emotional Function	0.502(3.036)	0.109	0.87

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\*Adjusted for maternal education, asthma medication use in last 12 months, parental smoking.

Table 4.16 Linear regression assessing associations between FEF<sub>25-75</sub> percent predicted and measures of quality of life

Quality of Life Variables	Beta (SE)	r <sup>2</sup>	P value
CHQ-PF50 (n=76)			
CHQ-PF50 (PHS)	-0.769(.639)	0.174	0.24
CHQ-PF50 (PSS)	-0.001(.418)	0.128	0.99
PAQLQ (n=77)			
Total Domain	-7.335(7.140)	0.180	0.32
Activity Limitation	-2.974(4.359)	0.160	0.50
Symptoms	-6.923(7.277)	0.175	0.35
Emotional Function	-5.395(6.047)	0.172	0.38
PACQLQ (n=77)			
Total Domain	-2.740(5.826)	0.136	0.64
Activity Limitation	-3.178(4.746)	0.143	0.51
Emotional Function	-1.878(5.887)	0.132	0.75

\*Adjusted for maternal education, asthma medication use in last 12 months, parental smoking.

Table 4.17 Linear regression assessing associations between FEV<sub>1</sub>/FVC ratio percent predicted and measures of quality of life

Quality of Life Variables	Beta (SE)	r <sup>2</sup>	P value
<b>CHQ-PF50 (n=76)</b>			
CHQ-PF50 (PHS)	-0.089(.197)	0.022	0.65
CHQ-PF50 (PSS)	0.027(.113)	0.018	0.81
<b>PAQLQ (n=77)</b>			
Total	-0.614(2.185)	0.085	0.78
Domain			
Activity Limitation	0.081(1.320)	0.082	0.95
Symptoms	-1.008(2.214)	0.089	0.65
Emotional Function	-0.485(1.841)	0.084	0.79
<b>PACQLQ (n=77)</b>			
Total	-0.405(1.788)	0.042	0.82
Domain			
Activity Limitation	-1.020(1.451)	0.058	0.49
Emotional Function	0.094(1.805)	0.041	0.96

\*Adjusted for maternal education, asthma medication use in last 12 months, parental smoking.

*Quality of Life and Mean Diurnal Peak Flow Variability Results.*

A significant relationship between the PAQLQ total score and the mean diurnal peak flow variability was seen ( $p = 0.05$ ) with the linear regression analysis. Table 4.18 presents these findings.

Table 4.18 Comparison of QOL scores and mean diurnal peak flow variability\*

Quality of Life Variables	Beta	Standard Error	$r^2$	p value
<b>CHQ-PF50 (n=76)</b>				
CHQ-PF50 (PHS)	0.009	0.010	0.159	0.38
CHQ-PF50 (PSS)	-0.008	0.006	0.170	0.16
<b>PAQLQ (n=77)</b>				
Total	2.216	1.123	0.188	0.05
Domain				
Activity Limitation	0.136	0.078	0.156	0.09
Symptoms	0.058	0.080	0.125	0.48
Emotional Function	0.102	0.094	0.133	0.28
<b>PACQLQ (n=77)</b>				
Total	-1.115	1.199	0.133	0.36
Domain				
Activity Limitation	-0.082	0.120	0.110	0.50
Emotional Function	-0.070	0.106	0.104	0.51

CHQ-PF50 = Child Health Questionnaire, PAQLQ = Pediatric Asthma Quality of Life Questionnaire, PACQLQ = Pediatric Asthma Caregivers Quality of Life Questionnaire.

\*All analyses were adjusted for age, sex and height (cm).

### *Summary of Major Findings*

- A higher percentage of children with asthma were in the age group 6-12.
- All three of the QOL measurement tools demonstrated excellent internal consistency reliability.
- The lowest domain score (indicating poorer QOL) on the PAQLQ was the Activity Limitation Domain [mean 5.9(0.90), range 5.8-6.2].
- The lowest single question score on the PAQLQ was in the Symptom Domain relating to bothered by coughing [5.5(1.57), range 5.2-5.9].
- PACQLQ scores on the Activity Limitation Domain ranged from (6.1-6.8), mean 6.5. The lowest mean score was found for the question regarding sleepless nights and feeling helpless or frightened. The highest mean score was found on the question regarding need to change plans. Associations between the Activity Limitation and Emotional Function domain and total scores on the PAQLQ and on the PACQLQ were not statistically significant.
- Higher scores on the Emotional Function domains of both the PAQLQ and PACQLQ were associated with higher scores on the CHQ-PF50 Psychosocial Summary Scores.
- No correlations were found with either the PAQLQ or PACQLQ and the CHQ-PF50 Physical Summary Scores.
- Significant correlations were found between the PAQLQ Total score and mean DPV. A borderline significant relationship was found between the PAQLQ Activity Limitation Domains score with mean DPV.
- No significant relationships were found between FEV<sub>1</sub> percent predicted and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) with overall scales and subscales, a

borderline significant relationship was found between FEV<sub>1</sub> percent predicted and the PAQLQ Activity Limitation Domain score.

- No significant relationships between FVC percent predicted, FEV<sub>1</sub>/FVC ratio, or FEF<sub>25-75</sub> and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) although a borderline significant relationship was found between the FVC percent predicted and the PAQLQ Activity Limitation Domain.

## **CHAPTER FIVE**

### **Discussion and Conclusions**

The purpose of this investigation was to examine the relationship between QOL measures of rural children with asthma and their parents. In particular this study investigated the relationship between three measures of quality of life of children with asthma (PAQLQ, PACQLQ, CHQ-PF50) and measures of asthma severity (diurnal peak flow variability and lung function). The findings from this secondary analysis of previously collected data suggest that measures of quality of life are associated with certain measures of asthma severity.

This chapter will discuss major findings related to specific research questions, assess strengths and limitations of the study and provide recommendations for future research.

#### *Characteristics of the Study Population*

The study population consisted children with physician diagnosed asthma (n=77). Although children between the ages of 6-17 were included in the study 2/3 of children were in the age group of 6-12 years. Children diagnosed with asthma and their parents were more likely to be absent from either school or work because of chest related illness and had a lower mean FVC and FEF<sub>25-75</sub>. These findings for absenteeism are supported by others (Laforest, 2004; Austin, 2003; Fillmore et al, 1997).

Three measures of QOL were used to assess QOL in the children with asthma and their parents, the PAQLQ, PACQLQ and the CHQ-PF50. All three QOL measurements were tested for internal consistency reliability using Cronbach's Alpha, Spearman Brown's Correlation and Guttman Split-half and demonstrated good to excellent scores. The highest being the PAQLQ (Cronbach's Alpha 0.919) and the lowest being the CHQ-PF50 (Cronbach's Alpha 0.907).

### *Assessment of Associations between QOL Measured by the PAQLQ and the PACQLQ*

Quality of life is a very individualized concept to assess. To provide a more comprehensive picture of the QOL of the child with asthma both parental and child perceptions of quality of life are required. In this study, QOL for children with asthma and their parents was assessed using well-known asthma-specific QOL questionnaires, the PAQLQ and PACQLQ.

At the domain levels of each scale, it was difficult to compare the quality of life results between the parents (PACQLQ) and children (PAQLQ) because the domains on each quality of life questionnaire were not exactly the same. While both the PAQLQ and PACQLQ include Activity Limitation, and Emotional Function domains the PAQLQ also includes a Symptom domain. As a result no comparisons could be completed using the PAQLQ Symptom domain and the PACQLQ. Although similar quality of life questions are present on both the PAQLQ and PACQLQ they may be scored in different domains of the questionnaires. For example, the PAQLQ contains questions related to how often the child wakes during the night or had trouble sleeping at night in the past week. The PACQLQ contains questions asking were you awakened during the night or did you have sleepless nights because of your child's asthma. These questions are grouped into the symptom domain for the PAQLQ whereas similar questions for the PACQLQ they are grouped into the Emotional Function domain. This presents a challenge in comparing the two asthma-specific quality of life questionnaires.

Overall the children's QOL was good. Scores on the 7-point Likert scale of the PAQLQ ranged from 5.2-6.7, with a mean of 6.1. The lowest question scores were found on the PAQLQ Symptom Domain for a question relating to bothered by cough. The children's scores on the PAQLQ Activity Limitation Domain on the 7-point Likert scale ranged from 5.3-6.4, with a mean of 5.9, while parent scores on the PACQLQ Activity Limitation Domain, on the 7-point

Likert scale ranged from 6.1-6.8, with a mean of 6.5. Of the three domain scores on the PAQLQ, the children's lowest mean score was on the Activity Limitation Domain. Several research studies found similar results with children scoring lowest on the Activity Limitation Domain of the PAQLQ, indicating that the child's rating of their quality of life is largely influenced by limitations to their activity (Eiser et al., 2001; Annett et al., 2003; Erickson et al., 2002; Williams et al., 2000 & Williams et al., 2003). Parental quality of life was perceived as better than the child's. Scores on the 7-point Likert scale of the PACQLQ ranged from 6.1-6.8, with a mean of 6.5. The lowest scores were found on the Emotional Function Domain question regarding sleepless nights.

Having sleepless nights is consistent with previous literature indicating this is the single most important quality of life influencer for parents of children with asthma. A study by Kieckhefer & Ratcliffe, 2000, found that caregivers of children with asthma reported sleepless nights and greater anxiety about their child than parents of children without asthma. This lack of sleep appeared to increase the stress of living with asthma and affected the family dynamics of parents caring for children with asthma. Caregivers of children with asthma have been shown to have higher rates of emotional distress, uncertainty and fears related to the illness due to the demands associated with caring for a chronically ill child (Kieckhefer & Ratcliffe, 2000; Frankel & Wamboldt, 1998; Everhart et al; 2008). These findings were similar to the current study which showed the two lowest scores to be in the Emotional Function domain of the PACQLQ, related to feeling helpless or frightened about their child's asthma and sleepless nights.

When assessing the relationship between the two asthma-specific measures of QOL, the PAQLQ and PACQLQ, no significant correlations were found between the PAQLQ and PACQLQ Total or Domain scores. Previous literature has found similar results with an

inconsistent relationship between parental and child report of QOL (Brunner et al., 2003; Butz et al., 2005; Renzoni et al., 1999; Sweeting & West, 1998; Williams et al., 2003).

A study by Guyatt et al., (1997), found that younger children's quality of life scores on the PAQLQ were more closely related to the parents' quality of life on the PACQLQ than those of adolescents. In the current study, children were sub-divided into two groups, age 6-12 and age 13-17, scores on both scales were compared by age group. Children did not differ by age group for their perception of quality of life relating to the Activity Limitation and Symptom domains and total quality of life scores. There was a trend for younger children to have lower mean scores in the Emotional Function domain of the PAQLQ. However, parents of children with asthma age 6-12 scored lower on both domains of the PACQLQ, the Activity Limitation and Emotional Function Domains and the Total score on the PACQLQ.

Several studies including a systematic review concluded that parental perceptions of QOL may not be sufficient in accounting for the subjective nature of the child's QOL measurement. These studies recommend the child's perception of their own QOL must be considered when assessing QOL (Butz et al., 2005; Drotar, 2004; Eiser & Morse, 2001; Frankel & Wamboldt, 1998; Keickhefer & Ratcliffe, 2000; Petrou, 2003; Osman & Silverman, 1996). Findings from this study also suggest that more than one quality of life questionnaire may be necessary to complete a comprehensive assessment of quality of life as it influences both the child and their family.

#### *Assessment of Association between QOL Measured by Generic and Asthma Specific QOL Questionnaires*

In the current study QOL for children with asthma and their parents was assessed using both generic measures of quality of life (CHQ-PF50) and asthma-specific (PAQLQ, PACQLQ)

measures of quality of life. Spearman's rho correlations were completed between the three measurements of QOL (PAQLQ, PACQLQ, CHQ-PF50). No significant correlations were found between the asthma-specific measures of QOL, (PAQLQ, PACQLQ) and the generic measurement of QOL (CHQ-PF50). Higher scores on the PAQLQ Emotional Function Domain were associated with higher scores on the CHQ-PF50 Psychological Summary Score (0.302, p<0.01). In addition, higher scores on the PACQLQ Emotional Function Domain were also associated with higher scores on the CHQ-PF50 Psychological Summary Score, (0.377, p<0.01, respectively). No significant correlations were found with the CHQ-PF50 Physical Summary Score and the PAQLQ or the PACQLQ.

The CHQ-PF50 correlates with both the PAQLQ and PACQLQ questionnaires on emotional measures of QOL but not physical measures of QOL. No previous studies could be found comparing the association of QOL in children with asthma and parental QOL using the CHQ-PF50. Findings from this study suggest that the CHQ-PF50 could be used to assess emotional aspects of QOL in children with asthma and their parents. However, with no significant correlations between the Physical Summary Score on the CHQ-PF50 and the PACQLQ or the PAQLQ it may not accurately assess the physical symptoms and activity limitation associated with asthma. This raises the question as to whether the CHQ-PF50 is a valuable tool in assessing the QOL of children with asthma and their parents with its limited variability.

#### *Assessment of Associations between QOL Measurements and Asthma Severity*

In the current study three psychometric tools were used to assess QOL (PAQLQ, PACQLQ and CHQ-PF50) of children with asthma and their caregivers. The PACQLQ and CHQ-PF50 were completed by the parents and the PAQLQ was completed by the child with

asthma. The measures of asthma severity assessed for all children with asthma were diurnal peak flow variability, over a two-week monitoring period and lung function including FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub> measured at a single point in time.

*Quality of Life and Spirometry.*

Linear regression analysis was completed assessing associations between the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) and percent predicted values for lung function (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>), adjusting for maternal education, asthma medication in the last 12 months and parental smoking. Although no significant relationships were found between FEV<sub>1</sub> percent predicted and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) with overall scales and subscales, a borderline significant relationship was found between FEV<sub>1</sub> percent predicted and the PAQLQ Activity Limitation Domain score ( $r^2 = 0.22$ ,  $p = 0.08$ ). The finding of no statistically significant relationship is consistent with previous literature examining the relationship between asthmas severity (FEV<sub>1</sub> percent predicted) and the PAQLQ and PACQLQ total scores in Iranian children ages 7-17 years, (Zandieh et al., 2006) and Dutch children age 6-16 years (Brouwer et al., 2006). Juniper (1996) (a) completed a validation study of the PAQLQ on a convenience sample of 52 Canadian children ages 7-17 who were recruited through posters and pediatric clinics and found poor (non significant) correlations between FEV<sub>1</sub> percent predicted by spirometry and the PAQLQ Domain scores, Symptom Domain ( $r = 0.30-.60$ ,  $p = 0.01$ ), Activity Limitation Domain ( $r = 0.30-.60$ ,  $p = 0.02$ ), Emotional Function Domain ( $r = 0.30-.60$ ,  $p = 0.22$ ). At this point given the inconsistencies between studies, and the current study, FEV<sub>1</sub> would not be considered a good predictor of QOL for children with asthma.

The current study also found no significant relationships between FVC percent predicted FEV<sub>1</sub>/FVC ratio, or FEF<sub>25-75</sub> and the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50)

although a borderline significant relationship was found between the FVC percent predicted and the PAQLQ Activity Domain ( $p = 0.08$ ). The findings for FVC of no significant associations are similar to those found in the study by Zandieh et al. (2006). No previous literature could be found assessing associations between the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) and percent predicted values of the FEV<sub>1</sub>/FVC ratio, or FEF<sub>25-75</sub>.

No significant associations were found comparing generic measures of QOL on the CHQ-PF50 sub scale scores (PHS and PSS) and spirometric results. This is a new finding as no previous literature could be found assessing associations between the CHQ-PF50 and lung function percent predicted values (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, and FEF<sub>25-75</sub>). At this point given the limited study of the CHQ-PF50 and spirometric measures of asthma severity and the current study, this combination would not be considered a good predictor of QOL for children with asthma.

#### *Quality of Life and Diurnal Peak Flow Variability*

No significant associations were found between diurnal peak flow variability and the CHQ-PF50 Physical Summary Score or Psychosocial Summary Score or with the PACQLQ total score or domain scores. No previous studies from the literature could be found comparing the CHQ-PF50 or the PACQLQ with diurnal peak flow variability.

Significant associations were found with diurnal peak flow variability and the PAQLQ total score ( $r^2 = 0.19$ ,  $p = 0.05$ ) and the PAQCQ Activity Limitation Domain score ( $r^2 = 0.16$ ,  $p = 0.05$ ). This finding suggests that peak flow variability may be a useful tool in assessing activity limitation and overall quality of life in children with asthma.

*Post Hoc Analysis Assessing the Relationship between Minimum Morning Peak Flow and Quality of Life*

In a study by Reddell, (1995) consisting of 27 subjects with asthma, 18 subjects recorded their lowest reading in the morning. Reddell concluded that minimum morning peak flow expressed as percent recent best appears to be the most useful index for assessment of airway lability in stable asthma patients. It was hypothesized that the minimum morning peak flow expressed as percent recent best may be a useful measurement of asthma severity in assessing the relationship with QOL. We conducted a post hoc analysis to test this hypothesis.

The mean minimum morning peak flow expressed as percent recent best was 72.92 % with a standard deviation of 14.84. The range was 70.74, with the minimum percent 21.21 and the maximum percent 91.95. After performing a post hoc analysis to assess the association between the three QOL measures (PAQLQ, PACQLQ, CHQ-PF50) and the minimum morning peak flow expressed as percent recent best score significant relationships were found with the PAQLQ total score ( $r^2 = 0.18$ ,  $p = 0.02$ ), and all three domain scores, Activity Limitation Domain ( $r^2 = 0.22$ ,  $p = 0.004$ ), Symptom Domain ( $r^2 = 0.16$ ,  $p = 0.09$ ), Emotional Function Domain ( $r^2 = 0.16$ ,  $p = 0.07$ ). Table 5.1 presents these findings. This finding suggests that minimum morning peak flow expressed as percent recent best measurements may be a useful tool in assessing QOL for children with asthma.

Table 5.1 Comparison of QOL scores and minimum morning peak flow\*

Quality of Life Variables	Beta	Standard Error	$r^2$	P value
<b>CHQ-PF50 (n = 76)</b>				
CHQ-PF50 (PHS)	0.006	0.003	0.147	0.10
CHQ-PF50 (PSS)	0.001	0.002	0.124	0.74
<b>PAQLQ (n = 77)</b>				
Total	-0.064	0.028	0.183	0.02
Domain				
Activity Limitation	-0.067	0.022	0.220	0.00
Symptoms	-0.041	0.024	0.155	0.09
Emotional Function	-0.052	0.028	0.160	0.07
<b>PACQLQ (n = 77)</b>				
Total	0.015	0.030	0.096	0.62
Domain				
Activity Limitation	-0.012	0.0365	0.099	0.73
Emotional Function	0.019	0.031	0.098	0.54

CHQ-PF50 = Child Health Questionnaire, PAQLQ = Pediatric Asthma Quality of Life Questionnaire, PACQLQ = Pediatric Asthma Caregivers Quality of Life Questionnaire.

\*All analyses were adjusted for age, sex and height (cm). Peak flow expressed as percent recent best

### *Assessment of Quality of Life of Rural Children with Asthma*

All children and their families included in the study population were considered to be residing in a rural community. Of the 77 children with asthma in the study 53 (68.8%) were living in town and 24 (31.2%) had their home on either a farm or acreage. Limited research has been conducted examining QOL in rural children with asthma. Guyatt et al., (1997) reported important differences between parental and child perceptions in 7 to 10 year old children and 11 to 17 year old children. Although this Canadian study included both rural and urban children with asthma, researchers did not report the differences in QOL between the urban and rural children with asthma and their parents. A second study of rural children with asthma, completed in the United States found that parents of children with asthma experiencing night-time asthma symptoms reported lower QOL scores on the CHQ-PF50 than parents of children with asthma who did-not experience night-time symptoms. This finding is consistent with the findings from this study.

### *Limitations of the Study*

The current study is a secondary analysis of a study conducted between 2005 and 2007. As the data is previously collected all of the data is predetermined and other important variables in this analysis could not be examined. For example, only two objective measures of asthma severity were available and one of these, spirometry, was collected at a single time point. Multiple measurements of spirometry would have been useful in determining the relationship between spirometry as an indicator of asthma severity with QOL.

A low participation rate was experienced in the original study which may make the study less generalizable to community populations of children with asthma. The participation rate of 41.4% in the case control study was low and could potentially not be representative of the overall

study population. Previous work in this geographical area had shown relatively high participation rates. This study required a much greater commitment by families than previous studies in the area. However, when compared to the overall cross-sectional population group from where the case control population was drawn; there were few differences between groups (Lawson, Dosman, Rennie, Beach, Newman et al., 2009). The only differences which would be minimally influential on results were among children who were selected as potential cases, those who completed the case-control study were less likely to have a father who currently smokes and were younger compared to those who did not complete the case-control study (Lawson, et al., 2009).

#### *Strengths of the Study*

All three quality of life measurement tools demonstrated excellent internal consistency reliability (0.907-0.919). The combination of generic and disease-specific scales provides researchers and clinicians with additional insight about the child with asthma's overall well-being. All testing was administered according to the specified guidelines by the QOL scale developers.

All data collection interviews were completed by one interviewer, the primary investigator of the study. The PAQLQ was completed by the children with asthma. If assistance was required, support was provided by the interviewer assisted rather than the parent. This method of data collection prevented parental bias or influence for the children's response garnering a true representation of the child's own perceived quality of life.

Although both measures of asthma severity are effort dependent, significant efforts were taken by the primary investigator to minimize error. The collection of diurnal peak flow was completed over a two-week monitoring period using a portable Piko peak flow meter. This

device is capable of recording the previous 96 maneuvers and therefore no documentation of results was necessary by the children or parents. Education was provided to the child and parent at the home visit which included oral and written instructions for daily completion of the peak flow monitoring. The peak flow monitoring protocol was based on that of the Peak Flow Working Party of the European Respiratory Society (Quanjer et al., 1997) and was used in this study. The collection of peak flow data over the two week monitoring period allowed for multiple times of data collection as opposed to a single entry point with spirometry. In addition the collection of peak flow data over the two week monitoring period is current collection of data which did not require recall of information.

In collection of lung function data using spirometry, a dry-rolling spirometer was used to conduct the testing following the ATS guidelines (American Thoracic Society, 1995). Calibration of the spirometer was performed prior to testing each day and was recalibrated if there was an extended length of time between testing or if the temperature of the room changed by  $\geq 2^{\circ}\text{C}$ .

The current study examined asthma severity by both a single point in time through spirometry and over a two-week period by the collection of diurnal peak flow measurements, allowing for the calculation of peak flow variability.

The combination of generic and disease-specific scales provides researchers and clinicians with additional insight about the child with asthma's overall well-being.

#### *Recommendations for Future Research*

There are several recommendations that would be important to consider with regards to future research. These include:

- Conduct further investigation of the relationship between diurnal peak flow variability, and minimum morning peak flow expressed as percent recent best measurements and QOL in children with asthma.
- Conduct research examining measurements of spirometry at several points in time in relationship to measures of QOL.
- Consider using the PAQLQ, to gain the child's perspective of their QOL in research studies rather than relying on parental perceptions of their child's QOL.
- Conduct studies investigating QOL in urban children with asthma and compare those to the rural findings.

*Significance of Findings*

*Significance for Quality of Life Research*

Findings from this study suggest that more than one quality of life questionnaire may be necessary to complete a comprehensive assessment of QOL for children with asthma, as it influences both the child and their family. While findings from this study suggest that the CHQ-PF50 could be used to assess emotional aspects of quality of life in children with asthma and their parents it may not accurately assess the physical symptoms and activity limitation associated with asthma and may not be a valuable tool in assessing the quality of life of children with asthma and their parents with its limited variability.

*Significance for Health Care Professionals*

Health care professionals will be facing challenges in providing treatment to patients with chronic lung disease because of their increasing frequency and severity and the projected trends and economic impact (Ait-Khaled, Enarson, & Bousquet, 2001).

Findings from this study suggest that measurements of lung function (FVC and FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub>) may not be useful in assessing QOL of children with asthma and a more useful measurement of QOL may be in measuring peak flow variability or minimum morning peak flow expressed as percent recent best measurements. DPV measurements may be more useful in children with severe asthma than mild asthma. DPV is also a more cost-effective method of measuring asthma severity in stable asthma patients (Reddel, 1995).

These findings indicate that families may be able to monitor their child's asthma at home non-invasively and economically by using a peak flow monitor and observing for fluctuations which could indicate decreases in QOL. Providing this information to their health care provider could provide an interpretable trend to be reviewed at clinic appointments and in tertiary care centers.

This study found that activity limitation was the most influential factor of quality of life in children with asthma, while report of sleepless nights and feeling helpless or frightened was the most influential factor of quality of life for parents of children with asthma. Therefore assessing QOL of the parent may not be reflective of the child's QOL and QOL should be assessed from both the child's and parents' perception.

#### *Support for Theoretical Framework*

This study suggests that QOL of children with asthma is influenced by a variety of factors and affects the entire family. This finding is consistent with the concepts outlined in the Systems Theory Model (Wright & Leahey, 2009) in that a change in one family member affects all family members and the family as a whole is greater than the sum of its part. Assessing the individual QOL for both the child with asthma and their parents' is provided a very subjective

perception of their own QOL. Findings from this study suggest that more than one measurement of quality of life is needed to adequately assess QOL.

The third concept of the model, *a change in one family member affects all family members*, (Wright & Leahey, 2009) were evident while analyzing the research findings. For children with asthma in this study, the most influential factor for QOL was limitations in their activity. Whereas, for parents of children of asthma the most influential factor for QOL was interruptions to sleep or sleepless nights and feeling helpless or frightened. This is an important distinction to consider when evaluating QOL for children with asthma. This validates that a change in one member of the family affects all members of the family and reinforces the need to assess more than a single measurement of QOL to adequately represent the QOL for the family.

A families' ability to adapt to changes in managing the child's asthma is essential in creating balance and stability which is reflected in the fourth concept of the Systems Theory Model (Wright & Leahey, 2009). This study highlights the importance of assessing both the parent and the child's quality of life in demonstrating that discrepancies exist when measuring both perspectives.

#### *Significance for Nursing*

The prevalence of asthma increases as communities adopt modern lifestyles and become urbanized which will contribute to nurses providing care to more patients with asthma (Bousquet, Ndiaye, Annesi-Maesane & Vignola, 2003). Nurses are required to adapt to barriers such as economic costs, differences between health care systems and drug and device availability and accessibility (Bousquet et al., 2005), which may be increased in rural populations. Research also indicates nurse-led outpatient management of childhood asthma can be provided at a lower cost than medical care by pediatricians (Kamps, Roorda, Kimpel, Overgoor, van Heisdingen et

al., 2004). The findings from this research support the use of home peak flow monitoring as an indicator of asthma severity and may be reflective of the child's quality of life. This research supports the use of a single measurement of morning peak expiratory flow which is a cost-effective and easily accessible technology for rural areas. This study highlights the importance of assessing both the parent and the child's quality of life in demonstrating that discrepancies exist when measuring both perspectives and emphasizes the need for nurses and health care professionals to involve the child with asthma in assessments of their own quality of life to provide a comprehensive evaluation of quality of life.

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## Appendix A: Participant Information, Assent & Consent Forms



### PARTICIPANT INFORMATION & ASSENT FORM

Exposure to endotoxin and the lung: Humboldt Case-Control Study

**(Effects of endotoxin and tobacco smoke exposure on asthma and asthma-like symptoms in children and adolescents)**

**Title:** "Effects of endotoxin and tobacco smoke exposure on asthma and asthma-like symptoms in children and adolescents."

**Researchers:**

Mr. Josh Lawson 1-306-966-2978 (PhD student)  
Dr. A. (Senthil) Senthilselvan 1-780-492-6505 (Supervisor of the PhD student)  
Dr. Jim Dosman 1-306-966-8286 (Study researcher and doctor)

**Sponsor:** Canadian Institutes of Health Research

**Introduction.** This form may use words you do not understand. Please ask the study doctor or his assistant to explain any words or information you do not understand.

You are being asked to take part in a research study. The study will test how things in the air affect your lungs. A research study is something like a science project in school. The people in charge of this study want to learn something new about our lungs.

**Why would we like you in this study?** We would like to include you because you have had something happen because of your lungs in the past year. For example, you may have had wheezing, shortness of breath or visited a doctor or hospital because of a lung problem. You may also be in the study if you have had none of these things. We are going to ask almost 500 children and teenagers to take part in this study.

**What will you have to do?** The researchers would like to see how things in the air affect your lungs. You will be asked to answer questions about your health and what is around you. You will also be asked to blow into a machine, and give a small sample of spit. We would also like to come to your home and collect dust from your living room floor and bed mattress. Testing may take about 1½ hours in total. Finally, you may also be asked to blow into a small device a few times a day for two weeks. This will take about five minutes each morning and night.

**Can you quit?** You do not have to be in this study at all if you do not want to, and you can quit this study at any time. Nobody will be mad at you if you do not want to do this study or if you quit at any time. It will not affect your school or medical care.

**Possible benefits.** By being part of this study, you will get results from completing the lung tests. You will receive these for your records. A more general benefit is that the results could help the future health of others.

**Possible risks.** The lung tests are common tests. They are forceful and may make you feel uncomfortable for a short time. This may include tightness in the chest, dizziness, or coughing. By sitting still for a few minutes, these feelings should leave. If you become sick because of this test, you will get appropriate medical care at no cost.

**Who will know?** The information about you and what you tell the study doctor or his staff will only be seen by a few people. The written information about you will be seen by the study doctor and his staff. It may also be seen by people who make sure that the study is being done correctly. Access to this information may include copying and taking copies away.

Reports based on results of this study may be presented for medical or scientific purposes but we will not report your name. If information about the study is sent anywhere, it will not have your name on it. A secret code will be used instead.

**Do you have more questions?** You can ask questions at anytime. You can ask your mom and dad about anything you don't understand or ask them to contact us. If you or your parent/legal guardian have any questions or concerns or require more information, you or your parent/legal guardian can contact:

Mr. Josh Lawson	1-306-966-2978
Dr. A. (Senthil) Senthilselvan	1-780-492-6505
Dr. Jim Dosman	1-306-966-8286

If you have any questions about your rights as a research participant or concerns about the research project you may contact:

Biomedical Research Ethics Board  
c/o the Office of Research Services  
University of Saskatchewan  
Phone: 1-306-966-4053

OR

Health Research Ethics Board  
*University of Alberta*  
Phone: 1-780-492-0839

**Your signature.** We would like you to sign this form to show that you agree to take part. Your mom and dad will also be asked to sign this and another form agreeing for you to take part in the study.



## ASSENT



I have read this paper or have had it read to me. I understand what I have to do in this study and I agree to take part in it.

---

Child's name (Print)

---

Child's signature

---

Date

---

Parent/Legal guardian's name (Print)

---

Parent/Legal guardian's signature

---

Date

Please Check which statement applies (to be completed by the person administering the assent):

- The subject is capable of reading and understanding the assent form and has signed the above documentation of assent to take part in this study.
- The subject is not capable of reading the assent form, however, the information was explained verbally to the subject who has verbally given assent to take part in this study.

---

Name of person administering assent (Print)

---

Signature of person administering assent

---

Date



## INFORMATION LETTER & CONSENT FORM

Exposure to endotoxin and the lung: Humboldt Case-Control Study  
**(Effects of endotoxin and tobacco smoke exposure on asthma and asthma-like symptoms in children and adolescents)**

Researchers:

Mr. Josh Lawson

Department of Public Health Sciences, University of Alberta  
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Dr. Jim Dosman

Institute of Agricultural, Rural and Environmental Health, University of Saskatchewan  
(306) 966-8286

**This research is being completed by Josh Lawson as part of a PhD dissertation. He is a student at the University of Alberta. His supervisor is Dr. Senthilselvan who is a professor in the Department of Public Health Sciences, University of Alberta. The principal investigator of the funded project is Dr. James Dosman. Dr. Dosman is a respiratory doctor and director of the Institute of Agricultural, Rural and Environmental Health at the University of Saskatchewan.**

### Contact

Any questions about your child's rights as a research subject or concerns about your experiences while participating in this study can be directed to one of the following:

*Biomedical Research Ethics Board  
c/o the Office of Research Services  
University of Saskatchewan  
Phone: 1-306-966-4053  
Health Research Ethics Board  
University of Alberta  
Phone: 1-780-492-0839*

**Research description and purpose:** We are inviting you and your child to take part in a research project. This study is being done to look at how the home environment can affect lung health. One of our main interests is endotoxin. This is a substance in bacteria found in the indoor and outdoor environments. This research project is part of a larger project entitled "Endotoxin and the lung." Please feel free to ask any questions that you or your child may have.

**Procedures:** If you agree to allow your child to be in the study the testing will include:

- Completion of questionnaires. This includes information on your child's home, behaviour and health as well as quality of life. You will be asked to complete some of the questionnaires.
- Completion of simple tests of breathing. This measures how much air your child can blow out in a single breath and how fast he/she can do it (lung function). This test is a common screening test that may cause mild temporary discomfort such as dizziness, coughing, and mild shortness of breath for a few seconds following the test. Remaining seated for a few seconds should relieve these symptoms. In the event that your child becomes ill as a result of participating in the course of this procedure, necessary medical treatment will be made available at no cost.
- If your child has asthma or asthma symptoms, another breathing test will include measuring breathing in the morning and night without the presence of a research technician (repeated breathing tests). This will continue daily for two weeks. It will take about 10 minutes each in the morning and evening. This is a simple breathing test often used in patients with asthma. It may result in mild temporary discomfort such as dizziness, coughing, and mild shortness of breath for a few seconds following the test. Remaining seated for a few seconds should relieve these symptoms. In the event that your child becomes ill as a result of participating in this test, necessary medical treatment will be made available at no cost. A diary will be completed to record symptoms, medication use and exposures with the repeated breathing tests.
- Collection of saliva is done to study how much the child is exposed to tobacco smoke. This involves soaking a cotton swab in the mouth for a short time.
- Collection of dust from the play area floor and the mattress of the child's bed is done to measure indoor exposures including endotoxin.

**Role of your child:** Your child has been invited because he/she took part in a previous study. We wish to do more in depth testing to see how different exposures affect lung health. For this part of the study, we require both children with asthma or asthma symptoms, and children without asthma or asthma symptoms. As part of this study, the researchers will need to conduct tests on your child. These will include measuring your child's height and weight, completing breathing tests, collecting saliva and collecting dust from the play area floor and dust from the mattress of the child's bed as well as completing some questionnaires. Testing will take about 1½ to 2 hours. If your child has asthma or asthma symptoms, you will be asked to complete extra breathing tests.

**Confidentiality:** All information will be held confidential, except when professional code of ethics or legislation (or the law) requires reporting. While absolute confidentiality

cannot be guaranteed, every effort will be made to keep all personal information confidential. Your child's name and any information that can identify your child or your family will never be used in any presentations or publications of the study results. All information from this study will be used for research purposes only and will be grouped with the information from other children when reported.

The information you provide will be kept for at least five years after the study is done. The information will be kept in a secure area (i.e. a locked filing cabinet). Your name or any other identifying information will not be attached to the information you give. Information identifying the personal source of these data will be kept separately and in a locked file at the University of Saskatchewan.

**These results will be used only for the purpose of this research project and will be under the responsibility of Dr. A. Senthilselvan at the Department of Public Health Sciences, University of Alberta and Dr. J. Dosman at the Institute of Agricultural Rural and Environmental Health, University of Saskatchewan. Only people who are part of the research team will have direct access to your records.**

You will be given a copy of the consent form for your records.

**Freedom to withdraw:** Your child's participation in this study is free and voluntary. Your child also has the right to quit the study at any point. Your child can refuse to answer any questions or take part in any testing. If you decide not to allow your child to be part of this study, it will not compromise you or your child's health care.

**Benefits and risks:** A personal benefit of the study is the completion of lung tests. The results will be provided to you so that you may keep them for your records. A more general benefit is that results could help the future health of others. Risks of the procedures are described above under procedures.



## CONSENT FORM & SIGNATURES



Study title: Effects of endotoxin and tobacco smoke exposure on asthma and asthma-like symptoms in children and adolescents

<b>Part 1: Researcher Information</b>		
<b>University of Saskatchewan Principal Investigator:</b> Dr. J. Dosman <b>Affiliation:</b> Institute of Agricultural, Rural and Environmental Health, University of Saskatchewan <b>Contact Information:</b> 306-966-8286		
<b>University of Alberta Principal Investigator:</b> Dr. A. Senthilselvan <b>Affiliation:</b> Department of Public Health Sciences, University of Alberta <b>Contact Information:</b> 780-492-6505		
<b>Student Investigator:</b> J. Lawson <b>Affiliation:</b> Department of Public Health Sciences, University of Alberta & Institute of Agricultural, Rural and Environmental Health, University of Saskatchewan <b>Contact Information:</b> 306-966-2978		
<b>Part 2: Consent of Subject</b>		
Do you understand that your child has been asked to be in a research study?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Have you read, or had read to you, the attached information sheet and received a copy?	<input type="checkbox"/>	<input type="checkbox"/>
Do you understand the benefits and risks involved in taking part in this research study?	<input type="checkbox"/>	<input type="checkbox"/>
Have you had an opportunity to ask questions and discuss the study?	<input type="checkbox"/>	<input type="checkbox"/>
Do you understand that your child is free to refuse to participate or withdraw from the study at any time? Your child does not have to give a reason and it will not affect your child's health care.	<input type="checkbox"/>	<input type="checkbox"/>
Has the issue of confidentiality been explained to you? Do you understand who will have access to your records/information?	<input type="checkbox"/>	<input type="checkbox"/>
<b>Part 3: Signatures</b>		
<b>I have explained this consent to my child and he or she can participate in testing as initialled above.</b>		
Name of Parent or Guardian	Signature of Parent or Guardian	Date
<b>I agree to take part in this study</b>		
Name of Child	Signature of Child	Date
I explained this form to the subject and their parent and I believe that those signing this form understand what is involved in the study and voluntarily agree to participate.		
Name of Research Assistant	Signature of Research Assistant	Date

Appendix B: Screening Questionnaire

**SCREENING QUESTIONNAIRE**

**Please answer all of the questions**

1. In the past 12 months, has this child's chest ever sounded wheezy or whistling when they had a cold?..... Yes \_\_\_\_\_  
\_\_\_\_\_ No \_\_\_\_\_
2. In the past 12 months, has this child's chest ever sounded wheezy or whistling apart from colds?..... Yes \_\_\_\_\_  
No \_\_\_\_\_
3. In the past 12 months, has this child's chest ever sounded wheezy or whistling most days or nights?..... Yes \_\_\_\_\_  
No \_\_\_\_\_
4. In the past 12 months, has this child ever been short of breath with wheezing? (speech limited to one or two words between breaths)..... Yes \_\_\_\_\_  
No \_\_\_\_\_
5. In the past 12 months, has this child's chest ever sounded wheezy during or after exercise?..... Yes \_\_\_\_\_ No \_\_\_\_\_  
\_\_\_\_\_
6. Has your child **EVER** had wheezing or whistling in the chest at any time in the past?..... Yes \_\_\_\_\_ No \_\_\_\_\_  
\_\_\_\_\_
7. In the past 12 months, has your child seen a physician for asthma?..... Yes \_\_\_\_\_ No \_\_\_\_\_  
\_\_\_\_\_
8. In the past 12 months, has your child visited an emergency room for asthma?..... Yes \_\_\_\_\_ No \_\_\_\_\_  
\_\_\_\_\_
9. In the past 12 months, has your child been hospitalized or been to an intensive care unit for asthma?..... Yes \_\_\_\_\_  
No \_\_\_\_\_
10. In the past 12 months, has your child taken medication for asthma?..... Yes \_\_\_\_\_ No \_\_\_\_\_  
\_\_\_\_\_

11. In the past 12 months, has your child had an episode of asthma?  
..... Yes \_\_\_\_ No \_\_\_\_  
\_\_\_\_\_

12. Has your child **EVER** been diagnosed as having asthma by a doctor?  
..... Yes \_\_\_\_ No \_\_\_\_  
\_\_\_\_\_

**Thank you very much for taking the time to complete this questionnaire.**

**Research assistant to complete:**

**SUBJECT A CASE:**

\_\_\_\_ Yes \_\_\_\_ No

**SUBJECT AGREES TO PARTICIPATE:**

\_\_\_\_ Yes \_\_\_\_ No