Published in final edited form as:
Qual Life Res. 2010 December ; 19(10): 1517–1527. doi:10.1007/s11136-010-9715-4.

Predicting moderate improvement and decline in pediatric asthma quality of life over 24-months

Robert D. Annett, Ph.D.
University of New Mexico Health Sciences Center

Bruce G. Bender, Ph.D.
National Jewish Medical and Research Center

Betty Skipper, Ph.D.
University of New Mexico Health Sciences Center

Celeste Allen, MD
Children's Hospital and Research Center Oakland

Abstract

Objective—Determine factors associated with 24-month change in quality of life in children with asthma and their parents during the Childhood Asthma Management Program (CAMP).

Methods—Participants from 4 CAMP clinical centers were administered the Pediatric Asthma Quality of Life questionnaire and protocol measures of asthma symptoms, lung function, and psychological measures.

Results—Multivariate logistic regression analyses determined predictors of moderate change in quality of life. Subclinical levels of depression predicted moderate improvement in child-reported quality of life. Level of depressed affect together with clinical asthma features predicted moderate decline. Improvement in parent quality of life was predicted by perception of illness burden, whereas family features and a child missing school predicted moderate decline.

Conclusions—This ancillary study provided an opportunity to examine the determinants of 24-month change in parent and child of quality of life within a subset of the CAMP participants. Moderate changes in quality of life occur in clinical studies and have both psychosocial correlates as well as illness characteristics.

Keywords

Asthma; Childhood Asthma Management Program; Quality of life

Introduction

Because quality of life reflects disease control from the patient's perspective, its measurement has become an important objective of asthma management and research (NHLBI, 2007). Still, pediatric asthma researchers are faced with several challenges in understanding the results from quality of life measures used in longitudinal studies, including discerning the meaning of changes in scores derived with these measures. The extent to which score changes are affected by treatment medications, asthma education, or psychological factors (e.g., family, parent, and child psychological functioning) has seldom

Address correspondence to: Robert D. Annett, Ph.D., Department of Pediatrics, University of New Mexico Health Sciences Center, Albuquerque, NM, 87131-5311; 505-272-5551; 505-272-6845 (fax); rdannett@unm.edu..

been examined in the research literature and relatively little guidance is available to researchers to assist in interpretation of the meaning of score improvement or decline over time. In the case of one quality of life measure, information on the meaning of quality of life change scores has been provided by Juniper (1994), who conceptualized the “minimally important difference” in quality of life scores among individuals with asthma. Understanding of the meaning of an increase in asthma quality of life scores or decline has, however, been missing for most instruments and could be important in interpreting the results from clinical studies of asthma treatments.

Several factors may account for quality of life score differences that occur between groups and within individuals with asthma. Sawyer, Spurrier, & Kennedy (2001) studied a large group of children with mild to moderate asthma, examining the interplay between disease severity, family functioning, and quality of life. The findings from this study suggested a dose-response relationship between asthma severity and child-reported quality of life: higher levels of family functioning (e.g., higher cohesion) resulted in higher quality of life scores. Additionally, family functioning was significantly associated with all aspects of the parent-completed measure of general quality of life. Van Dellen and colleagues (2007) examined a multicultural cohort of children with asthma and found no differences in quality of life among children of different ethnic origins, once asthma symptom control and socioeconomic status were included as covariariates in the regression analyses. Other studies have revealed differences on quality of life scores between parents and children with asthma (Erickson, Munzenberger, Plante, Kirking, Hurwitz, & Vanuya, 2002). Parent psychological functioning, including the presence of parent anxiety or depression, contributed to perceptions of quality of life scores for children with asthma (Price, Bratton, & Klinnert, 2002). Overall, this literature indicates that asthma severity and family functioning as well as fundamental differences between parents and children contribute to asthma quality of life scores. Unfortunately, there has been no empirical literature that informs researchers as to the meaning of improvement or decline in quality of life as reported by parents or children with asthma.

Research attempting to connect clinical asthma features (lung functioning, medication usage, symptom reports, and nocturnal awakenings) with quality of life reports has demonstrated varying patterns of association. Increased features of clinical asthma have been associated with reports of decreased of quality of life scores (Juniper, Wisniewski, Cox, Emmett, Nielsen, & O'Byrne, 2004) and improvements in clinical symptoms of asthma being associated with a positive change in quality of life scores (Kamps, Brand, Kimpen, Maillé, Overgoor-van de Groes, van Helsdingen-Peek, & Roorda, 2003). Other research would suggest that the association between clinical asthma features appears to be complicated by whether the child or the parent is the reporter of quality of life. For example, no relationship between clinical asthma characteristics (e.g., daily diary report of asthma symptoms) and child quality of life has been observed in children with well-controlled asthma (Annett, Bender, Lapidus, DuHamel, & Lincoln, 2001). Yet, child asthma symptoms have been found to be minimally associated with parent quality of life (Annett, Bender, DuHamel, & Lapidus, 2003). Findings such as these suggest that the child's psychological functioning may influence their reports of quality of life and that parent reports may be influenced by both clinical asthma symptoms and psychosocial factors. The relative contributions of clinical asthma characteristics, child psychological functioning and psychosocial features to child and parent reported improvement or decline in quality of life remains uncertain.

The current report presents results from an ancillary study examining moderate improvement and moderate in quality of life over a specific 24-month interval (between the 12 and 36-month clinic visits). We hypothesized that moderate improvement in child quality

of life would be associated with self-reports of psychological functioning (anxiety and depression), independent of lung function and treatment characteristics. In contrast, we predicted that moderate decline in quality of life would be associated with lung function and treatment characteristics. Our second aim was to characterize the influences of change in parent-reported quality of life over the same 24-month interval. We hypothesized that moderate improvement would be associated with family psychosocial and child psychological functioning, and that moderate decline would be associated with lung function and treatment characteristics.

Method

CAMP Design

The objective of the Childhood Asthma Management Program (CAMP) trial was to assess the long-term effectiveness of two types of anti-inflammatory medications in children with asthma of mild to moderate severity. Details of study design and recruitment have been published (CAMP, 1998, 1999). Enrollment for CAMP occurred over a period of 21 months. Participants returned for regularly scheduled follow-up appointments beginning from their date of randomization. Information for the present analyses comes from the 12-month and 36-month follow-up visits at 4 of the 8 CAMP centers that voluntarily participated in a quality of life ancillary study by additionally administering a quality of life questionnaire to parent and child participants (other CAMP centers chose not to participate in this ancillary study).

Participants

The CAMP population consisted of 1,041 participants (at 8 clinical centers) who had completed 4 pre-randomization screening visits. A total of 279 parents and 281 children participated in this ancillary study completing quality of life questionnaires and CAMP psychosocial health outcomes questionnaires during the 12-month follow-up visit at 4 participating clinical centers. At the 36-month visit 369 parents and 368 children completed the same set of questionnaires. The study did not open simultaneously at all centers, resulting in a different number of participants at the two visits. Previous work suggests that the participants were representative of the CAMP population socioeconomic characteristics and were comprised of a greater percentage of children with moderate asthma at the time of medication treatment assignment (Annett, Bender, Lapidus, DuHamel & Lincoln, 2001). Only questionnaires completed by the same individuals at both follow-up visits were used in subsequent analyses. (Tables 1, 2, & 3 provide the number of participants with complete quality of life domain and total scores at both time points.) The mean age of child participants at the time of the 36-month data collection was 11.4 years (SD 2.2 years; range 8–16 years). Male child participants comprised 59% of the ancillary study sample. Ethnicity, which was identified in the pre-randomization visit, included: 66% white, 9% black, 16% Hispanic, and 14% other or mixed (including Native American).

Procedures

Human subject institutional review boards at participating sites reviewed CAMP procedures and ancillary study procedures. Informed consent/assent was obtained from participants before randomization into the trial and a second consent/assent was used when participants were enrolled in to the quality of life ancillary study during the child's 12-month visit. All eligible participants were invited to enroll in the ancillary study. A smaller number of participants were initially invited to participate due to delays in opening the ancillary study at several centers.

Parents competed a battery of psychosocial health outcomes questionnaires specified in the CAMP protocol at the 12-month and 36-month visits. Parents in the ancillary study also completed the Caregiver's Pediatric Asthma Quality of Life Questionnaire (Juniper, 1994). A psychometrist certified in CAMP procedures administered the Pediatric Asthma Quality of Life Questionnaire (Juniper, 1994) to child participants following directions provided by Juniper (1994). These measures were completed *before* the initiation of CAMP clinic visit procedures (e.g., spirometry) at the 12 and 36-month follow-up visits. Follow-up clinic visits also included a structured interview, conducted by either a nurse coordinator or pediatric asthma physician-specialist, which assessed changes in the child's asthma history. Other than the quality of life data, only data from the 36-month follow-up was employed in the subsequent analyses.

Psychosocial Health Outcomes Measures

Quality of Life Questionnaires—The Pediatric Asthma Quality of Life Questionnaire (PAQLQ; Juniper, 1994) is a 28-item questionnaire designed for children/adolescents with asthma (age range 7–17) that asks them to reflect on characteristics of their asthma during the past week. The PAQLQ employs a 7-point Likert scale and has been reported to detect changes in asthma status (Guyatt, Juniper, Feeny, & Griffith, 1997). The items in the PAQLQ were derived from a questionnaire for adults with asthma. The initial items require the child/adolescent to identify three activities that they feel have been impacted by asthma during the past week. The respondent then needs to indicate the extent to which they have been “bothered” by or how frequently the symptom (e.g., feel out of breath) has occurred. The PAQLQ has three rationally derived domains: Activity Interference (4 items), Asthma Symptoms (15 items) and Emotional Response to Asthma (9 items). Scores within each domain are the mean for a participant (range: 1 to 7; higher scores indicate higher quality of life). Concurrent validity for the PAQLQ has suggested that children's reports of quality of life are closely associated with child feelings of anxiety (Annett, Bender, Lapidus, DuHamel, & Lincoln, 2001), socioeconomic status (Erickson, Munzenberger, Plante, Kirking, Hurwitz, & Vanuya, 2002), and that acute changes in quality of life scores will occur with asthma treatments (Everden, Campbell, Harnden, McGoldrick, Bodalia, Manion, & Reynia, 2004). Long-term changes in quality of life have not been associated with improvements in asthma control (Kamps, Brand, Kimpen et al, 2003).

The Caregiver's Pediatric Asthma Quality of Life Questionnaire (CPAQLQ; Juniper, 1994) is a 13-item disease specific measure that uses a 7-point Likert scale (endpoints: “extremely bothered” to “not bothered”, and “very, very worried/concerned” to “not worried/concerned”) to assess parent perceptions of the extent to which they have been bothered or concerned by their child's asthma symptoms and functioning during the past week. The authors recommend that a total mean score of the items completed (range 1 to 7; higher scores indicate higher quality of life) be examined to assess change and provide a global rating of parent perception quality of life.

Other CAMP Parent Questionnaires—Measures completed by parents as part of the main CAMP protocol assessed child behavior, family functioning and perceived burden of illness. Questionnaires included the Child Behavior Checklist (CBCL; Achenbach, 1991), Family Environment Scale (FES; Moos, 1981), MOS Social Support Survey (Sherbourne & Stewart, 1991), and Impact on Family Scale (IOF; Stein & Riessman, 1980). The CBCL and FES both have well characterized psychometric characteristics that include norm-referenced scores. Variables used from the CBCL included: Total Competence, Internalizing, Externalizing and Total Problems scores. The FES is comprised of 90 true-false items that are scored and coded into 10 variables. The variables selected for analysis in this study included: Cohesion (measure of family support), Expressiveness (openness in family

communication), Conflict (measure of expression of anger and conflict with the family), Independence (measure of family members' self sufficiency), and Control (extent to which rules and procedures are used in family life). The MOS Social Support Survey (MOS-SSS; Sherbourne, & Stewart, 1991) is a 20-item measure using a 5-point Likert scale (anchors: *None of the Time* to *All of the Time*) to assess the properties of family supports available and the impact of a child's illness upon family functioning. The MOS-SSS was developed to measure these properties in families where a member has a chronic illness. Research has suggested that the total score on the MOS-SSS is related to treatment adherence (Kravitz, Hays, Sherbourne, DiMatteo, Rogers, Ordway, & Greenfield, 1993). Scores on this measure range from 20 to 100 (higher scores reflect greater social support) and Cronbach's a for the total score has been reported as 0.97 (Hays, Sherbourne, & Mazel, 1995). The IOF was developed to measure parent perception of a chronically ill child's impact upon family life and was originally developed for the Pediatric Ambulatory Care Treatment Study (Stein & Jessop, 1984). It includes 24 questions about the economic burden, social burden, personal strain, and coping strategies that families experience and used a 4-point Likert scale (from *Strongly Agree* to *Strongly Disagree*). The total IOF score used in the present study measures overall impact of a child's illness upon the family (Stein & Jessop, 2003), with scores ranging from 24 to 96, and has a Cronbach's $_{a\tilde{=}88}$ Stein & Riessman, 1980).

Other Child CAMP Questionnaires—Child participants were administered a battery of questionnaires to assess their self-reported emotional functioning. The measures completed included: the Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds & Richmond, 1985), Children's Depression Inventory (CDI; Kovacs, 1981), and Social Anxiety Scale for Children-Revised (SASC-R; LaGreca & Stone, 1993). The RCMAS contains 37-items that elicit child-report of anxiety using a “Yes” or “No” format. While there are three specific domains (physiological experience of anxiety, worries, and social concerns) only the total score (a global measure of individual anxiety) and “Lie” score (tendency to exaggerate or minimization of symptoms) were utilized in this study. The CDI is a 27-item measure of feelings that are associated with depressive affect. Only the total raw score was utilized in subsequent analyses. The SASC-R has 22-items that comprise 3 factors: negative evaluations from the child's peer group (FNE; e.g., I worry about being teased), social avoidance of new situations (SAD-N; e.g., I feel shy around kids I don't know), and generalized social avoidance (SAD-G; e.g., It's hard for me to ask other kids to play with me). The specific procedure for administering these measures within the CAMP study has previously been described (Annett, Bender, Lapidus, DuHamel, & Lincoln, 2001).

Spirometry—Spirometry was measured at each visit by a CAMP certified coordinator (nurse or pulmonary function technician). This procedure consisted of a child breathing into a spirometer so that maximal expiration of the lungs can be ascertained. The spirometer yields a measurement of forced expired volume in one second (FEV1), the maximum volume of air that can be exhaled (FVC), and index of airflow limitation (FEV1/FVC ratio). These measures allow for the calculation of how effectively and how quickly the lungs can be emptied. Within the CAMP study, these measures were obtained both before and after the administration of a bronchodilator (Albuterol). Only pre-bronchodilator FEV1 percent predicted and prebronchodilator FVC percent predicted were used in the data analyses.

Interview—Parents and children were interviewed at annual visits to ascertain reports about events in the interval since the most recent CAMP visit, which occurred on average 4 months previously. These events included: the number of asthma-specific telephone calls to the child's primary care physician, the number of times the child had been seen at the primary care physician's office due to asthma, the number of emergency room or urgent care visits because of asthma symptoms, days of school missed due to asthma, frequency of night

time awakenings due to asthma, Albuterol use in response to asthma symptoms (excluding preventative use for exercise), days of prednisone use because of asthma symptoms and a global rating of the frequency with which asthma symptoms had interfered with the child's usual daily activities. Finally, smoking exposure was ascertained by asking about the presence of parent smoking and others smoking within the home.

Data Analysis—Previous work by Juniper and colleagues (Juniper, Guyatt, Willan, & Griffith, 1994; Juniper, Guyatt, Feeny, Ferrie, Griffith & Townsend, 1996b) indicated that a "minimally important difference" in quality of life was developed through intra-individual difference scores, with a change of ±1.0 classified as a moderate change and change greater than +1.5 representing a large change. Unfortunately, this procedure does not differentiate between improvement and decline in quality of life. The principal objective of this study was to examine the current variables (obtained at the 36-month follow-up) that were associated with moderate improvement compared to "no change" or moderate decline compared to "no change" in quality of life reported by children and parents. Change was calculated by subtracting the 12-month follow-up scores in each quality of life domain and total score from the 36-month follow-up scores. Change score values of −1 to +1 were considered "no change"; change score values less than -1.0 were grouped as moderate decline in quality of life and change scores greater than +1.0 were categorized as moderate improvement in quality of life. This procedure was employed with both parent and child quality of life questionnaires.

Separate dichotomous outcome variables were calculated to (1) compare the moderately improved group to the no change group and (2) compare the group where quality of life moderately declined to the no change group. These dichotomous variables were then used as dependent variables in stepwise multivariate logistic regression analyses to explore variables that predict moderate change (improvement and decline) in quality of life compared to no change. The goodness-of-fit of the model was tested with the Wald statistic to demonstrate the significance of individual coefficients in the model. For independent variables with prevalence rates above 15% in the "no change" category for total quality of life, there is at least 80% power for detecting odds ratios above 2.5 for moderate improvement and 4.3 for moderate decline. Analyses were completed using SPSS Version 16.

Our analyses used current measures of child and family psychological functioning as well as current measures of lung function and the most recent reports of treatment characteristics, all of which were obtained at the 36-month follow-up visit. The larger number of participants at the 36-month follow-up visit provided complete and current data on psychological functioning and treatment characteristics (e.g., current lung function), thus the 36-month data were employed as independent variables in all analyses. In our analyses of child-reported information we used independent variables such as child age and CAMP treatment arm (2 active medications and placebo) in conjunction with current lung function data, current asthma treatment characteristics (e.g., recent doctor visits that occurred due to asthma), and current child reports of anxiety and depressive symptoms. Similarly with data from parents, our approach was to examine the association of child age, CAMP treatment arm, current lung function data, current environmental exposure to smokers, current asthma treatment characteristics, current family characteristics, and current child behavior with quality of life change categories.

Multivariate logistic regression analysis was selected because it does not require normally distributed independent variables and does not assume homogeneity of variance across the independent variables. Our preliminary examination of independent variables used in the analyses indicated non-normal distribution of psychological variables including the CBCL, RCMAS, CDI, SASC-R, MOS, IFS, and FES, as well as the lung function data and

interview data. In addition, we observed that both dependent variables (PAQLQ and CPAQLQ) were skewed towards the high end of the available range (e.g., CPAQLQ total Mean score 6.35 (SD 0.77); range 2.46–7.00). In view of this observation, data recoding occurred for the independent variables selected for analysis from the 36-month follow-up. With the parent and child-completed questionnaires recoding of data was completed in order to form meaningful categories of the independent variables (available from the authors). Child psychological variables included age and results from the RCMAS, CDI, and SASC-R. Parent-completed variables included CBCL composite scores, FES composite scores, IOF total score, MOS-SSS composite score, and smoking exposure. Treatment arm, lung function data, and clinic interview data were employed with both child and parent logistic regression analyses.

Results

CAMP treatment condition

Treatment group had been randomly assigned at the time of randomization into the CAMP trial. Data employed in the subsequent analyses included only those participants where both 12-month and 36-month quality of life data was available. Thus examination revealed child quality of life data for each of the three treatment conditions as follows: Budesonide N=83; Nedocromil N=87, and placebo N=110. For treatment condition and parent quality of life, complete data was obtained for Budesonide (N=82), Nedocromil (N=85), and placebo (N=111). The proportion of individuals in each treatment condition is the same as that observed in the larger CAMP trail (CAMP, 2000).

Predicting child quality of life improvement

In order to explore the meaningful predictors of improvement in child quality of life domain scores (Total Score, Activity Interference, Asthma Symptoms, and Emotional Response to Asthma), logistic regression was used with the child age, medication treatment arm (2 anti-inflammatory medications and placebo), self-reported predictors (RCMAS Total, RCMAS Lie, CDI Total, and SASC-R scores: FNE, SAD-N SAD-G) and asthma treatment characteristics. Moderate improvement in total quality of life was found to occur with 53 children, with 211 in the category for no change in their total quality of life. Table 1 presents these results for each child quality of life domain where significant findings were observed. Examination of this table reveals that improvements in domains of child-reported quality of life were affected by several different variables. However, improvement in the Asthma Symptoms domain was not associated with any predictor variable. When raw scores on the CDI were greater than 1 standard deviation above the sample mean, the likelihood of the child reporting improvement in Total Quality of Life increased (Odds Ratio 2.5; 95% CI 1.26–4.93). Similarly, when scaled scores on the RCMAS Lie scale increased to over 12 and the child reported higher CDI scores, the likelihood of the child reporting improvements in their Emotional Response to Asthma increased (Odds Ratio 3.08; 95% CI 1.31–7.21; Odds Ratio 3.47; 95% CI 1.54–7.81, respectively). It appears that an increased score on the CDI, which was subclinical, increased the odds of a child reporting improvements in their global quality of life and emotional response. Similarly, reports of increased use of prednisone between clinic visits was associated with an increased likelihood of a child reporting a decrease in the extent to which asthma interfered with their activities (Odds Ratio 2.08; 95% CI 1.11–3.88). In summary, improvement in total quality of life and the emotional quality of life domain over the 24-month interval was associated with psychological aspects of a child's functioning. Children's report of improvement in physical functioning was linked to the use of prednisone during this interval.

Predicting child quality of life decline

Results of the logistic regression analyses predicting decline in child-reported quality of life are presented in Table 2. There were only 14 children where a moderate decline in total quality of life occurred during the study interval. The likelihood of a child reporting declining total quality of life were greater when a higher CDI score was coupled with low pre-bronchodilator FEV^1 and increased frequency of asthma interfering with the child's activities (Odds Ratio 4.04; 95% CI 1.23–13.27; Odds Ratio 4.3; 95% CI 1.31–14.15; Odds Ratio 5.84; 95% CI 1.23–27.73, respectively). The analyses also revealed that child-reports of asthma interfering with activity predicted declines in 2 domains of the PAQLQ: Activity Interference and Asthma Symptoms (Odds Ratio 3.87; 95% CI 1.49–10.06; Odds Ratio 4.44; 95% CI 1.43–13.77, respectively). In contrast, decline in a child's Emotional Response to Asthma score was significantly associated with pre-bronchodilator FEV^1 (Odds Ratio 3.72; 95% CI 1.00–13.86), increased telephone calls to the child's physician (Odds Ratio 4.31; 95% CI 1.25–14.82), and high CDI scores (Odds Ratio 7.43; 95% CI 2.16–25.58). Thus, when a decline in quality of life scores was observed, increased levels of depressed affect (as measured by the CDI) occurred in conjunction with diminished lung function and increased reports of asthma interference with activity or increased family phone calls to the doctor.

Predicting parent quality of life

Parent-reported quality of life total scores were examined to determine the predictors of improvement and decline (see Table 3). Improvement in total quality of life was found to occur with 34 parents, with 230 having no change in quality of life and 13 reporting a decline in their total quality of life score. Improvements in quality of life total scores were associated with the impact that the child's illness was having upon the family (Odds Ratio 2.3; 95% CI 1.02–5.07) and a normal level of family control (Odds Ratio 0.33; CI 0.11–0.99). Specifically, greater family burden was significantly associated with improvements in parent quality of life only when burden was allied with normal levels of family control. Decline in parent quality of life total score was increased by a child missing school (Odds Ratio 5.65; 95% CI 1.45–22.03), high levels of family independence (Odds Ratio 7.28; 95% CI 1.71–31.06), and low levels of family support (Odds Ratio 15.88; 95% CI 4.04–62.45). In summary, the likelihood of parent improvement in quality of life are increased when normal levels of family control are associated with higher reports of family burden of illness. When declines in parent quality of life were observed, these were associated with an increased number of school days missed due to asthma occurring with higher levels of family independence and lower levels of family support.

Discussion

The CAMP trial has provided a large-scale framework for examining asthma medication treatment outcomes pertaining to children with mild and moderate asthma. The results presented provide new insight for researchers into variables associated with moderate improvement and decline in quality of life outcomes. Within the current analyses, a focus on change that has occurred in quality of life between the 12-month and 36-month follow-up CAMP visits has been examined, with results indicating that change in children's self-reported quality of life are associated with several specific disease and behavioral characteristics. Moreover, change that occurs in a child's Total Score and Emotional Functioning domain of quality of life over a 24-month period was likely to be associated with specific aspects of child psychological functioning when moderate improvements in quality of life occur. Striking in these findings was how medication treatment arm did not contribute to changes (improvement or decline) in child or parent quality of life during the interval assessed. Rather, the use of steroid therapy during the preceding 4 months was the

single determinant of moderate improvement in child-reported participation in the Physical Activities domain of quality of life. In contrast, a combination of poor lung function, reports of asthma interfering with the child's life, and specific child psychological functioning were the factors most strongly associated with moderate decline in child-reported quality of life total score.

Child report of subclinical depressive symptomatology was observed as an associated feature of both improvement and decline in quality of life. Child acknowledgement of depressive symptoms in this study were found to be remarkably low (overall mean raw score = 4.7, SD 4.9) suggesting that children participating in the CAMP study were reporting subclinical depressive symptoms compared to the normative population for the CDI. Our findings may be interpreted as suggesting that reports of subclinical scores on the CDI can be associated with both improvement and decline in quality of life. It is the other features associated with subclinical depressed affect that determine the valence of the moderate change in quality of life. While this line of reasoning may be perceived as controversial, there is emerging evidence suggesting that children with asthma may have increased subclinical levels of depressed affect that can be associated with physiological functioning. Von Leupoldt, Ehnes, and Dahme (2006) have demonstrated that individuals with asthma experience change in lung function in response to both positive and negative emotional stimuli. It may be that children with asthma develop subclinical affective symptoms in response to the challenges of managing their disease. Other lines of research indicate that children with asthma who exhibit higher amounts of anxiety have increased symptom perception skills (Chen, Hermann, Rodgers, Oliver-Welker, & Strunk, 2006), a finding that could be considered consistent with the current results.

Two major conclusions can be drawn from the present findings: 1) subclinical levels of depressed affect, as reported by children, can be associated with improvement in quality of life when there is no co-occurring change in lung function; and 2) when subclinical levels of depressed affect are observed in association with asthma treatment changes and/or changes in lung function, there is likely to be a decline in child-reported quality of life. Unlike studies that have suggested a decline in lung function when children experience some negative emotion (e.g., Miller & Wood, 1997; Neild & Cameron, 1985; Ritz, Claussen, & Dahme, 2001), our findings suggest a more nuanced psychological picture where subclinical levels of depressed affect (as represented in this study by symptoms on the CDI) can be a useful tool for helping trigger intervention that lead to improved control of asthma and thus improvement in quality of life.

Parent reports of their quality of life were obtained within the clinic visit when child-reported quality of life assessments were obtained. Using a total quality of life change score during the 24-month interval, greater report of perception of disease burden (as represented by the IOF score) was associated with improvement in parent quality of life. This finding must be understood within the context of family factors, and specifically the report of the extent to which rules and procedures (represented by the FES Control scale) are used to guide family life. When parents report improvement in their quality of life, this is associated with increased awareness of burden of disease and normal levels of parental control. It may be inferred that the awareness of illness burden results in increased parent commitment to developing rules and procedures for managing and helping the child manage their asthma. Again, the data from the participants in the CAMP ancillary study reveal the influences of both family characteristics and perception of illness burden as contributors to the parent perception of improvement in quality of life.

A striking difference was observed when parents report a moderate decline in quality of life. School days missed combined with higher levels of family member independence and a

restricted range of social supports each contribute to decline over the 24-month interval. Thus when the parent reports a decline in quality of life, this is very likely to be associated with an increased expectation of independence (represented by the FES Independence scale) for the child with asthma, which occurs in combination with the child missing school and lower levels of social support. Within the context of an asthma clinical setting, finding a change in parent quality of life total score of at least one point would potentially suggest targets for psychosocial intervention, such as helping the parent to make modifications in the family support system and the expectations for child independence.

The results from this study contribute to the understanding of change in quality of life scores for children with asthma. Perhaps the most significant of these contributions is that child and parent reports of quality of life moderate improvement and decline are affected by different sets of features. Previous reports on predictors of child and parent quality of life have suggested that child-reported anxiety is the predominant feature influencing quality of life (Annett, Bender, Lapidus, DuHamel & Lincoln, 2001), and that parent perception of illness burden significantly influences their report of the quality of life of their child with asthma (Annett, Bender, DuHamel & Lapidus, 2003). Results in this current investigation extend the previous findings by demonstrating that moderate change in quality of life over a 24-month interval is influenced by distinct features, depending upon whether the child or the parent is the source of the observation.

There are several features of the CAMP study that merit recognition in these findings. First, the interval of examination within this study is extensive. No studies to date have examined quality of life change over such an lengthy period of time for children involved in a clinical trial where changes in disease characteristics and treatment were thoroughly mapped (see CAMP, 2000). Additionally, participants in this study were engaged in an intervention aimed at assessing differences in asthma medication treatments. As such, these participants were receiving a high level of surveillance of their asthma symptoms and active intervention for asthma exacerbations. The CAMP study participations have previously been described in significant detail (CAMP, 1999) and appear to represent the preponderance of asthma severity in childhood (i.e., children with mild to moderate asthma). There are several limitations to the study results, including that study participants did not include children with more severe asthma. Additionally, quality of life was measured while asthma medication treatments were occurring, rather than being assessed before treatment began and again during treatment. Yet, one of the unique findings from this study was how 12 to 36-month change in quality of life was not impacted by CAMP treatment condition, raising the question of under what conditions treatment condition may impact quality of life for children with asthma and their parents. However, the unique examination of improvement and decline during medication treatment provides a contribution to the understanding of variables contributing to quality of life changes that occur for this subset of CAMP participants.

In summary, moderate improvement and decline in quality of life do occur when children with mild and moderate asthma participate in a controlled clinical research treatment program. Furthermore, these changes can be observed in reports from children about their quality of life and from the reports from parents about parent quality of life. Depending upon whether the child or the parent is the focus of the quality of life endpoint, different asthma disease features and psychological characteristics were observed to predict improvement or decline. This study has highlighted how subjective, intra-individual change of one point in a quality of life questionnaire is associated with measures of both psychological functioning and disease features. These findings propose a broadening of the procedures for assessing moderate improvement and decline in subjective reports of disease-

related functioning to include measures of psychosocial parameters as well as disease characteristics.

Acknowledgments

Supported by the Agency for Health Care Policy and Research (R03 HS09123-01) and contract from the Department of Health and Human Services, National Heart, Lung, and Blood Institute (NHLBI-HR-90-13). CAMP has been supported by contracts NO1-HR-16044, 16045, 16046, 16047, 16048, 16049, 16050, 16051, and 16052 from the National Heart Lung and Blood Institute. Additional support was received from the General Clinical Research Centers at the University of New Mexico (NCRR-GCRC grant M01-RR00997) and National Jewish Medical and Research Center (NCRR-GCRC grant M01-RR00051).

REFERENCES

Achenbach, TM. Manual for the Child Behavior Checklist/4–18 and 1991 Profile. Univ. VT Dept. of Psychiatry; Burlington, VT: 1991.

Annett RD, Bender BG, DuHamel T, Lapidus J. Factors Influencing Parent Reports On Quality of Life For Children With Asthma. Journal of Asthma. 2003; 40:577–587. [PubMed: 14529108]

Annett RD, Bender BG, Lapidus J, DuHamel T, Lincoln A. Predicting Children's Quality of Life in a Clinical Trial: What do Children's Reports Tell Us? Journal of Pediatrics. 2001; 139:854–861. [PubMed: 11743513]

Boulet LP, Phillips R, O'Byrne P, Becker A. Evaluation of asthma control by physicians and patients: Comparison with current guidelines. Canadian Respiratory Journal. 2002; 9:417–423. [PubMed: 12522488]

Chen E, Hermann C, Rodgers D, Oliver-Welker T, Strunk RC. Symptom Perception in Childhood Asthma: The Role of Anxiety and Asthma Severity. Health Psychology. 2006; 25:389–395. [PubMed: 16719611]

Childhood Asthma Management Program Research Group. Long-Term Effects of Budesonide or Nedocromil in Children with Asthma. New England Journal of Medicine. 2000; 343:1054–63. [PubMed: 11027739]

Childhood Asthma Management Program Research Group. The Childhood Asthma Management Program (CAMP): Design, Rationale and Methods. Controlled Clinical Trials. 1999; 20:91–120. [PubMed: 10027502]

Childhood Asthma Management Program Research Group. Recruitment of participants in the Childhood Asthma Management Program (CAMP). I. Description of methods. Journal of Asthma. 1998; 36:217–237.

Erickson SR, Munzenberger PJ, Plante MJ, Kirking DM, Hurwitz ME, Vanuya RZ. Influence of sociodemographics on the health-related quality of life of pediatric patients with asthma and their caregivers. Journal of Asthma. 2002; 39:107–117. [PubMed: 11990227]

Everden P, Campbell M, Harnden C, McGoldrick H, Bodalia B, Manion V, Reynia S, FACT study group. Eformoterol Turbohaler compared with salmeterol by dry powder inhaler in asthmatic children not controlled on inhaled corticosteroids. Pediatric Allergy & Immunology. 2004; 15:40–7. [PubMed: 14998381]

Guyatt GH, Juniper EF, Feeny DH, Griffith LE. Children and adult perceptions of childhood asthma. Pediatrics. 1997; 99:165–8. [PubMed: 9024440]

Hays, RD.; Sherbourne, CD.; Mazel, RM. User's Manual for Medical Outcomes Study (MOS) Core Measures of Health-Related Quality of Life. RAND Corporation, MR-162-RC; 1995. (available at www.rand.org)

Jacobson NS, Truax P. Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. Journal of Consulting and Clinical Psychology. 1991; 59:12–19. [PubMed: 2002127]

Juniper, EF. The Paediatric Asthma Quality of Life Questionnaire: Background information and interviewing tips. McMaster University; Hamilton, Ontario: 1994.

Juniper EF, Chauhan A, Neville E, Chatterjee A, Svensson K, Mork AC, Stahl E. Clinicians tend to overestimate improvements in asthma control: an unexpected observation. Primary Care Respiratory Journal. 2004; 13:181–4.

Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring Quality of Life in the Parents of Children with Asthma. Quality of Life Research. 1996a; 5:27–34. [PubMed: 8901364]

Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. Quality of Life Research. 1996b; 5:35–46. [PubMed: 8901365]

Juniper EF, Guyatt GH, Feeny DH, Griffith LE, Ferrie PJ. Minimum skills required by children to complete health-related quality of life instruments for asthma: comparison of measurement properties. European Respiratory Journal. 1997; 10:2285–2294. [PubMed: 9387955]

Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific Quality of Life Questionnaire. Journal of Clinical Epidemiology. 1994; 47:81–7. [PubMed: 8283197]

Juniper EF, Wisniewski ME, Cox FM, Emmett AH, Nielsen KE, O'Byrne PM. Relationship between quality of life and clinical status in asthma: a factor analysis. European Respiratory Journal. 2004; 23:287–91. [PubMed: 14979505]

Kamps AW, Brand PL, Kimpen JL, Maillé AR, Overgoor-van de Groes AW, van Helsdingen-Peek LC, Roorda RJ. Outpatient management of childhood asthma by paediatrician or asthma nurse: randomized controlled study with one year follow up. Thorax. 2003; 58:968–73. [PubMed: 14586050]

Kovacs M. Rating scales to assess depression in school aged children. Acta Paedopsychiatrica. 1981; 46:305–315. [PubMed: 7025571]

Kravitz RL, Hays RD, Sherbourne CD, DiMatteo MR, Rogers WH, Ordway L, Greenfield S. Recall of recommendations and adherence to advice among patients with chronic medical conditions. Archives of Internal Medicine. 1993; 153:1869–1878. [PubMed: 8250648]

LaGreca AM, Stone WL. The social anxiety scale for children-revised: Factor structure and concurrent validity. Journal of Clinical Child Psychology. 1993; 22:17–27.

Von Leupoldt A, Ehnes F, Dahme B. Emotions and respiratory function in asthma: A comparison of findings in everyday life and laboratory. British Journal of Health Psychology. 2006; 11:185–198. [PubMed: 16643693]

Miller BD, Wood BL. Influence of specific emotional states on autonomic reactivity and pulmonary function in asthmatic children. Journal of the American Academy of Child and Adolescent Psychiatry. 1997; 36:669–677. [PubMed: 9136502]

Moos, RH.; Moos, BS. Family Environment Scale Manual. Consulting Psychologists Press, Inc.; Palo Alto, CA: 1981.

National Heart Lung and Blood Institute; National Asthma Educations and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Institutes of Health; Bethesda, MD: 2007. Publication 07-4051

Neild JE, Cameron IR. Can emotional stress cause bronchoconstriction? Biological Psychology. 1985; 22:184–185.

Price MR, Bratton DL, Klinnert MD. Caregiver negative affect is a primary determinant of caregiver report of pediatric asthma quality of life. Annals of Allergy Asthma & Immunology. 2002; 89:572–577.

Reynolds, CR.; Richmond, BO. Revised Children's Manifest Anxiety Scale (RCMAS) Manual. Western Psychological Services; Los Angeles: 1985.

Ritz T, Claussen C, Dahme B. Experimentally induced emotions, facial muscle activity, and respiratory resistance in asthmatic and non-asthmatic individuals. British Journal of Medical Psychology. 2001; 74:167–182.

Sawyer MG, Spurrier N, Kennedy D. The relationship between the quality of life of children with asthma and family functioning. Journal of Asthma. 2001; 38:279–284. [PubMed: 11392368]

Sherbourne CD, Stewart AL. The MOS Social Support Survey. Social Science and Medicine. 1991; 32:705–714. [PubMed: 2035047]

Stein REK, Jessop DJ. Does pediatric home care make a difference for children with chronic illness? Findings from the Pediatric Ambulatory Care Treatment Study. Pediatrics. 1984; 73:845–853. [PubMed: 6728584]

Stein REK, Jessop DJ. The Impact on Family Scale revisited: Further psychometric data. Journal of Developmental & Behavioral Pediatrics. 2003; 24:9–16. [PubMed: 12584480]

Stein REK, Riessman CK. The development of an Impact-on-Family scale: Preliminary findings. Medical Care. 1980; 18:465–472. [PubMed: 7401703]

van Dellen QM, Stronks K, Bindels PJE, Ory FG, Bruil J, van Aalderen WMC, the Peace Study Group. Health-related quality of life in children with asthma from different ethnic origins. Journal of Asthma. 2007; 44:125–131. [PubMed: 17454327]

Table 1

Summary of Logistic Regression Analysis Predicting Moderate Improvement in Child-Reported Quality of Life Outcomes

Improvement in Quality of Life Total Score Compared to No Change (N=276)					
	B	**SE**	**Odds Ratio**	**Wald Statistic**	**P**
Variable					
Age *	−0.14	0.07	0.87	4.12	.05
CDI Score *					
+/− 1SD			1.00		
>1 SD	0.92	0.35	2.50	6.92	.009

Improvement in Activity Interference Score Compared to No Change (N=277)					
	B	**SE**	**Odds Ratio**	**Wald Statistic**	**P**
Variable					
Prednisone *					
No days			1.00		
> 1 Day	0.73	0.32	2.08	5.25	.02

Improvement in Emotional Response to Asthma Score Compared to No Change (N=264)					
	B	**SE**	**Odds Ratio**	**Wald Statistic**	**P**
Variable					
Age *	−0.18	0.08	0.84	5.56	.02
RCMAS Lie *					
SS < 7			1.00		
SS 7–12	0.55	0.43	1.73	1.63	NS
SS > 12	1.12	0.44	3.08	6.67	.01
CDI Score *					
+/− 1SD			1.00		
> 1 SD	1.24	0.41	3.47	9.03	.003

Key:

- CDI Score: CDI Total raw score
- Prednisone: Report from CAMP questionnaire (completed by parent and child together at 36 month follow-up visit) regarding days of Prednisone use since last CAMP clinic visit
- RCMAS Lie: Revised Children's Manifest Anxiety Scale Lie Score (scaled score)

Table 2

Summary of Logistic Regression Analysis Predicting Moderate Decline in Child-Reported Quality of Life Outcomes

Decline in Total Score Compared to No Change (N=223)

	B	SE	Odds Ratio	Wald Statistic	P
Variable					
CDI Score *					
+/− 1SD			1.00		
>1 SD	1.40	0.61	4.04	5.29	.02
Pre-BD FEV *					
≥ 80% Pred			1.00		
< 80% Pred	1.46	0.61	4.30	5.76	.02
Asthma *					
None			1.00		
> 1	1.76	.80	5.84	4.93	.03

Decline in Activity Interference Score Compared to No Change (N=214)

	B	SE	Odds Ratio	Wald Statistic	P
Variable					
Asthma *					
None			1.00		
≥ 1	1.35	0.49	3.87	7.69	.006

Decline in Emotional Response to Asthma Score Compared to No Change (N=221)

	B	SE	Odds Ratio	Wald Statistic	P
Variable					
Pre-BD FEV *					
≥ 80% Pred			1.00		
< 80% Pred	1.31	0.67	3.72	3.83	.05
Phone calls *					
None			1.00		
> 1 Call	1.46	0.63	4.31	5.38	.02
CDI Score *					
+/− 1SD			1.00		

Decline in Emotional Response to Asthma Score Compared to No Change (N=221)

	B	SE	Odds Ratio	Wald Statistic	P
> 1 SD	2.01	0.63	7.43	10.09	.001

Decline in Asthma Symptoms Score Compared to No Change (N=221)

	B	SE	Odds Ratio	Wald Statistic	P
Variable					
Asthma *					
None			1.00		
≥ 1	1.49	0.58	4.44	6.66	.01

Key:

- CDI Score: CDI Total raw score
- Pre-BD FEV: Pre-bronchodilator FEV1 at 36-month follow-up visit
- Asthma: Report from CAMP questionnaire (completed by parent and child together) regarding how many times asthma has interfered with activity since last CAMP clinic visit (Greater than or equal to 1 time)
- Nights awakened: Report from CAMP questionnaire (completed by parent and child together at 36 month follow-up visit) regarding nights awakened by asthma symptoms since last clinic visit
- Prednisone: Report from CAMP questionnaire (completed by parent and child together at 36 month follow-up visit) regarding days of Prednisone use since last CAMP clinic visit

Qual Life Res. Author manuscript; available in PMC 2013 January 25.

Qual Life Res. Author manuscript; available in PMC 2013 January 25.

Table 3

Summary of Logistic Regression Analysis Predicting Domains of Parent-Reported Quality of Life Outcomes

Moderate Improvement in Quality of Life Total Score Compared to No Change (N=260)					
	B	**SE**	**Odds Ratio**	**Wald Statistic**	**P**
Variable					
FES Control*	−1.01	0.56	0.33	3.91	.05
IOF *					
−/+ 1 SD			1.00		
>1 SD	0.82	0.41	2.28	4.06	.04

Moderate Decline in Quality of Life Total Score Compared to No Change (N=238)					
	B	**SE**	**Odds Ratio**	**Wald Statistic**	**P**
Variable					
School *					
No Days			1.00		
≥ 1 Day	1.73	0.70	5.65	6.21	.01
FES Independ *					
T ≤ 60			1.00		
T > 60	1.99	0.74	7.28	7.20	.007
MOS Support *					
≥ −1SD			1.00		
< −1SD	2.77	0.70	15.88	15.67	.001

Key:

- FES Control: Family Environment Scale Control subscale
- IOF: Impact on Family Scale
- School: Report from CAMP questionnaire (completed by parent and child together) regarding days of school missed due to asthma since last CAMP clinic visit
- FES Independ: Family Environment Scale Independence subscale
- MOS Support: MOS Social Support Survey (≥ −1SD: Within normal range support)