ASTHMA IN YOUNG CHILDREN

EPIDEMIOLOGY, BURDEN OF ASTHMA AND EFFECTS OF A PARENTAL INFORMATION PROGRAM

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ABSTRACT

Background: The prevalence of asthma is usually estimated on the basis of the results of questionnaires. A comparison with prevalence according to medical records has not been reported before. Adherence to medical advice and prescriptions are generally poor in chronic diseases like asthma. There is a lack of intervention studies to improve adherence.

Aims: 1: To perform an epidemiological analysis of the asthma prevalence and the use of the healthcare system in a Swedish region. 2: To compare the parental assessment of children’s asthma according to a questionnaire with physicians’ diagnosed asthma. 3: To perform an intervention with additional information and support to parents of preschool children with newly diagnosed asthma in order to improve adherence. 4: To evaluate the effects on quality of life and separately analyze the answers of the mothers and the fathers. 5: To analyze any remaining intervention effects after 6 years.

Methods: Firstly, all outpatient clinics had computerised patient records and thus these visits could be studied as well as admissions to hospital for asthma. In 1999 a questionnaire was answered by 75% of the parents of 6295 children 1-6 years of age. Secondly, a controlled, prospective intervention study where the parents of 60 children were randomised to either a control group (CG) or to an intervention group (IG) which had group meetings in close connection to the diagnosis. Outcome was measured by questionnaires and by classification of the children according to clinical examination, blood tests, symptoms and medication. Adherence rate was calculated with the help of diaries and weighing the inhalers used. Fathers and mothers answered separately the Paediatric Caregiver’s Quality of Life Questionnaire. Children were followed up after 6 years and objective measurements of lung function were added to the other parameters.

Results: The burden of asthma was mainly handled by the outpatient clinics. According to the parental questionnaire 5.9% had asthma in 1999, according to the medical records 4.9%. With register diagnosis as gold standard the sensitivity of the questionnaire was 77%. The questionnaire identified half of the children with a medical record of asthma. Forty percent of the children claimed by their parents to be asthmatic had no medical record of asthma. One third of the children with newly diagnosed asthma had risk of developing persistent asthma.

The intervention resulted in an improvement of the parents’ view on adherence issues and on adherence per se. The children in the IG had less exacerbation days despite having lower inhaled steroid doses. There were no major gender differences in indices of quality of life, but according to individual questions mothers were more affected by their children’s asthma. After 6 months the mothers in the IG showed improvements in all indices. At the 6 year follow-up 71% still had asthma. The IG had fewer contacts with nurses than the CG and they had lower inhaled corticosteroid (ICS) doses. The IG parents still had a more positive view on adherence questions and their quality of life was better. The children who were older than 2 years of age at inclusion had a higher risk of developing persistent asthma. Intermittent ICS was used by 81%. The lung function was preserved. The burden on the health care system was low. Hospital admittances due to asthma in the region are the lowest in the country.

Conclusions: A parentally completed questionnaire provided an acceptable estimation of the prevalence of asthma in children 2-6 years of age compared to asthma registered in medical records although in half of the cases the individual child was not identified. Straightforward and timely information to parents of children with asthma has long-term positive effects which can be mediated through equalization of the parent’s roles in handling their child’s asthma. The hospital admissions due to asthma are very few, possibly as a result of the intervention and improved medical care in the paediatric outpatient clinics. Asthma diagnosed before age 2 has a better prognosis. Most children with a high risk of persistent asthma can be successfully treated with intermittent ICS.

Key words: Asthma, Pre-school children, Prevalence, Questionnaires, Quality of life, Intervention.
LIST OF PUBLICATIONS

I. The burden of asthma – as reflected by the prevalence defined by doctor's diagnosis and the use of health care services by pre-school children in a Swedish region
Carl-Axel Hederos, Staffan Janson, Carl-Gustaf Bornehag, Gunilla Hedlin

II. Comparison of clinically diagnosed asthma with parental assessment of children’s asthma in a questionnaire
Carl-Axel Hederos, Mikael Hasselgren, Gunilla Hedlin, Carl-Gustaf Bornehag

III. Group discussions with parents have long-term positive effects on the management of asthma with good cost-benefit
Carl-Axel Hederos, Staffan Janson, Gunilla Hedlin

IV. A gender perspective on parents' answers to a questionnaire on children's asthma
Carl-Axel Hederos, Staffan Janson, Gunilla Hedlin

V. Long-term Positive Effects of an Intervention to Improve the Adherence of Preschool Children with Asthma – Results of a 6-year Follow-up
Carl-Axel Hederos, Staffan Janson, Gunilla Hedlin
Submitted for publication
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<tr>
<td>ACQ</td>
<td>Asthma Control Questionnaire</td>
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<td>DBH</td>
<td>The Dampness in Buildings and Health study</td>
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<td>CG</td>
<td>Control Group</td>
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<tr>
<td>EBM</td>
<td>Evidence based medicine</td>
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<td>FENO</td>
<td>Fraction of exhaled NO</td>
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<tr>
<td>GINA</td>
<td>Global Initiative for Asthma</td>
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<td>GP</td>
<td>General Practitioner</td>
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<td>ICD</td>
<td>International Classification of Diseases</td>
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<td>ICS</td>
<td>Inhaled corticosteroids</td>
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<td>IG</td>
<td>Intervention group</td>
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<td>ISAAC</td>
<td>The International Study of Asthma and Allergies in Childhood</td>
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<tr>
<td>MID</td>
<td>Minimally important difference</td>
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<td>PACQLQ</td>
<td>Paediatric Asthma Caregiver’s Quality of Life Questionnaire</td>
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<td>PAQLQ</td>
<td>Paediatric Asthma Quality of Life Questionnaire</td>
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<td>QoL</td>
<td>Quality of life</td>
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<td>SABA</td>
<td>Short acting beta-2 agonists</td>
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<td>SPT</td>
<td>Skin Prick Test</td>
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<td>WQ</td>
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1 PREFACE

In 1979 I became a specialist in paediatrics and from the mid 80’s I have been working at an out-patient clinic at the Gripen Primary Care Centre in Karlstad. During the late 80’s and early 90’s we noticed that children with allergic problems and asthma became more frequent and at the end of the 90’s over half of our appointments were due to allergy and more than 1/3 had asthma as their main problem. During these years I was the head of this centre and initiated the registration of referrals and diagnoses to get a better picture of what was happening. I also had an interest in reflecting over problems that I met in my clinical practice and had written some articles on different subjects when I met Agneta Andersson-Ellström, a gynaecologist who then worked at our centre and was interested in research. She now is my mentor. Together we initiated what was later to be called the Primary Care Research Unit where Professor Staffan Janson is now the head and my co-supervisor. In 1997 I qualified as a specialist in Paediatric Allergology and during this time I worked with an old friend from my time as a registrar in Karlstad, Professor Gunilla Hedlin, now working at Karolinska Institutet in Stockholm. We discussed how to improve the situation for young children with asthma. As clinicians we know that we have good medications to offer the asthmatic child but a great problem is how to increase adherence. In order to try to improve the situation we started a research project in 1998 and Gunilla agreed to be my main supervisor. My teacher in biostatistics, Professor Pagano from Harvard University, emphasized two things: “always question the data” and “statistics is telling a story”. I will try to use his advice when telling the story of our investigation of the prevalence and burden of asthma in southern Värmland and how we succeeded in improving the adherence to therapy and advice.
2 INTRODUCTION

Asthma is the most common chronic disease in childhood and can have very serious consequences for the child and the family and it can potentially even be life-threatening (1) (2). The burden of asthma is heavy not only for the individual and the family but also for society (1) (3-6). Today we have very effective symptomatic medications and anti-inflammatory treatments that in most cases can control the disease. There are however some patients that can be characterized as severe asthmatics as they have ongoing or frequent symptoms in spite of standard therapy (7) (8). Even more problematic is the fact that most patients who have serious acute attacks of asthma are usually classified as mild or moderate asthmatics (9) in spite of having severe exacerbations, often due to poor adherence to the treatment with inhaled corticosteroids (ICS) (10).

Several large studies have found that many patients with asthma, both adults and children, have symptoms that influence their daily life in a negative way. A recent Australian survey revealed that one-third of asthmatic children have disturbed sleep and 60% miss school days or experience activity limitations because of their disease (11). A European telephone study on children and adults found similar figures with nearly half of the patients reporting daytime symptoms at least once a week, 25% of patients reported an unscheduled urgent care visit and 7% reported overnight hospitalization due to asthma during the last year. More patients had used prescribed quick-relief medication (63%) than inhaled corticosteroids, ICS, (23%) during the last 4 weeks. Nearly 50% of patients who reported severe persistent symptoms considered their asthma to be completely or well controlled implying that patient’s perception of asthma control did not match their symptom severity (12). Only half of the children considered by their parents to have well-controlled asthma actually had good control, while at the same time the proportion of children defined as having severe persistent asthma was three times higher than that perceived by parents. Similar results are reported from all over the world (13) and are, according to a recent study from the United States, still valid (14). Evidence suggests that even physicians overestimate the degree of asthma control in children (15) (16).

In a summary on this subject the authors conclude that less than half of the children fulfilled the criteria for control of asthma according to the Global Initiative for Asthma (GINA) guidelines. There is a considerable tendency to use too little ICS. Both physicians and parents underestimate the degree of asthma symptoms of the child and there are big differences in asthma treatment between countries (17). According to the latest GINA guidelines (18) the new approach to asthma management should be based on the goal to achieve and maintain control of the disease, rather than underline the importance of asthma severity. Probably the most important explanation for the
rather disappointing situation discussed above is poor adherence to medication and lifestyle advice on to avoid asthma exacerbations (19).

Many studies have confirmed that adherence is usually below 50 % and that this is the situation for most chronic diseases like cardio-vascular diseases, psychiatric diseases, epilepsy and rheumatic diseases (20). It is relatively easy to improve short-term adherence with a variety of simple interventions but efforts to increase long-term adherence have been less successful. Thus, an increase in long-term adherence could be beneficial in order to improve the situation for children with asthma.
3 BACKGROUND

3.1 THE PREVALENCE OF ASTHMA

3.1.1 Asthma definition

The prevalence of asthma is dependent on how this condition is defined. The latest definition of asthma as launched by GINA 2006 is “a chronic inflammatory disease of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.” (18).

Lately the whole concept of asthma as a definition of a distinct disease (21) has been challenged (22). It has been proposed that asthma is probably not “a single disease, but rather a complex of multiple, separate syndromes that overlap” (23).

For children in the preschool ages the definition and diagnosis of asthma is even harder as more than 1/3 of all children in this age group have experienced wheeze at least once in connection with an upper respiratory infection but only some 20 % of these wheezers will go on to have persistent asthma (24-29). However, half of all asthma patients are formally diagnosed before age six (30). In the younger age groups wheezing is most often triggered by airway infections whereas in school children inhaled allergens are the commonest cause of asthma attacks (31) (32).

“Wheezing” in infancy in relation to upper airway infection generally has a good prognosis but it is still an important risk factor for the development of asthma later in life, in contrast to "coughing" and "shortness of breath" where the prognostic value is less clear (33). Wheezing is a term that cannot be translated directly into many other languages e.g. Swedish and therefore you have to describe the phenomenon or use a video to demonstrate the symptom (34). The label “asthma” for wheezing symptoms in this age group has important consequences both for the parents and for the treatment strategies that should be applied.

According to several prospective long-term cohort follow-up studies (24) (35-43) there are three categories of wheezing that can be identified:

- Transient early wheezers. Sometimes associated with prematurity. Parental smoking is another risk factor. This type of wheezing is often outgrown in the first 3 years.
- Persistent early-onset wheezing. Recurrent episodes of wheezing that start before age 3 and are associated with acute viral infections (often respiratory syncytial virus during the first 2 years and later rhinovirus infections). This type often has a family history of atopy. These asthmatic symptoms generally persist up to at least 12 years of age.
Late-onset wheezers. These children often start with eczema and have a family history of atopy. They often develop allergy themselves and have airway pathology characteristic of asthma. The asthma symptoms generally persist throughout childhood and into adult life.

The diagnosis of asthma in the preschool ages is largely based on clinical judgment and an assessment of physical findings and symptoms as there is no single diagnostic test that is possible to perform in these young children. Techniques for lung function testing have been described even for preschoolers, but they have not been accepted in clinical practice (44). In the future the measurement of exhaled NO might become an aid in the diagnostic procedure in this age group as well as in older children (45) (46).

There have even been suggestions that today the most practical way to diagnose asthma in preschool children is probably just to accept a doctor’s diagnosis (21). There are symptoms that are strongly suggestive of a diagnosis of asthma, like activity-induced cough or wheeze, frequent episodes of wheeze (more than once a month) especially if there is no seasonal variation, nocturnal cough without signs of viral infection and symptoms that persist after age three.

Some children never wheeze but still they have good therapeutic effect of short acting beta-2-agonists (SABA). Another approach to diagnosing asthma is consequently to try a treatment period with SABA and ICS. If the child has a marked clinical improvement and deterioration when the medication is stopped, the diagnosis can be confirmed ex juvantibus (18).

Based on the results of the Tucson cohort a clinical index has been proposed for predicting persistent asthma in children younger than three years of age (47). The presence of one major (parental history of asthma or eczema in the child) and two or three minor risk factors (eosinophilia, wheezing without colds, and allergic rhinitis) is considered highly predictive. In Sweden we traditionally have used the following diagnostic criteria during the preschool years: three or more episodes of wheezing before two years of age or the first wheezing episode after the age of two or the first episode of wheezing in a child with other atopic diseases (48).

### 3.1.2 Different ways of measuring the prevalence

Usually the prevalence of asthma in children is estimated on the basis of responses to written questionnaires (WQs) but there are several other methods. Another approach to estimate prevalence based on parent’s answers is through telephone surveys (49). However, there are reports that indicate that WQs or other types of parental assessments of asthma do not correlate well with the prevalence of symptoms, clinical findings or pulmonary function tests results (50-52) or even with what their adolescent children have reported themselves (53).
In addition, children that the parents think have been given an asthma diagnosis by a doctor, sometimes several years before, might be included as well as children that have recently started to have asthma symptoms and have not yet been identified by a physician. Other investigators have found acceptable validity, even in preadolescent children, between parental reports of symptoms and other measures like assessment of airway inflammation, lung function or children’s own rating (54).

Another way of determining the prevalence of asthma involves analysis of purchases of asthma medication which really identifies those in need of asthma treatment (55) (56). The problem with this is that many children are treated with medicines that were prescribed last year and some of the medication can even have been meant for brothers or sisters. Still another indirect way is studies of medical records which represent one possibility of catching those who have been in contact with the health care services and have been diagnosed with asthma (57). This approach can miss those who are successfully treated at home and seldom have to visit a doctor and also those that are undiagnosed. According to studies in adults there are around three times more undiagnosed than diagnosed asthmatics (58) (52).

One probable explanation why studies of the medical records of adult patients have indicated a prevalence of asthma lower than that suggested by corresponding questionnaires is failure of physicians to diagnose the disease (58) (59). According to a Norwegian study 37% of children fulfilling criteria for asthma disease were undiagnosed (60). A study from Germany concerning the situation 10 years ago among young school children found that only half of the children with asthma symptoms had been diagnosed and only 21% of the children with an diagnosis were on ICS treatment (55).

The best alternative to establish the prevalence and incidence is to perform prospective studies (43) (61). However, these are time-consuming and complicated and for practical purposes WQs will continue to be used.

Although validation of one of the most well-known questionnaires, the International Study of Asthma and Allergies in Childhood (ISAAC) WQ, has been performed in school children, employing clinical investigations, the use of this same WQ with pre-school children has not been validated clinically (62). However, the reproducibility of answers to similar questions has been validated for other WQs designed for this age group (63).

There is also a discussion about what type of questions in a WQ that yields the best outcome in order to find children with clinical asthma. It has been proposed that questions about symptoms are best for screening purposes and diagnosis-based questions are most suitable for risk-factor studies (64) (65). Youden's Index (sensitivity + specificity - 1) is said to be the best single measure of the validity of a specific method when the aim of a study is to compare the differences in prevalence of clinically significant asthma between populations (66).
3.1.3 Results of earlier prevalence studies

The asthma prevalence has risen worldwide during the last decades according to many investigations and is around, or even above, 10 % for school-children and adults in most developed countries (1) (18) (67). Studies, using objective methods like spirometry and skin prick tests, have questioned this increase (68) (69). There are now indications of a shift in this trend at least in some countries and especially in teenagers, with a stabilization or even a decrease of the prevalence in some countries (70-78).

However, in other countries the prevalence still seems to be rising (79) (80). The cause of the rise (and also the potential stabilization) is unclear even if several hypotheses have been launched. The theory of a Th2-dominance of the immunologic response as the explanation has been contradicted by the parallel increase of autoimmune diseases such as type-1 diabetes and inflammatory bowel disease where there is a Th1-dominance (81).

No one hypothesis, including the hygiene theory, can explain all the contradictory evidence. Furthermore, there is interplay between different factors that constitute our “Westernized” style of living (82).

WQs in preschool ages are few. One Australian study found a prevalence of 22 and 18 % respectively in two cities (63). Asthma was defined as ever having been diagnosed with asthma and having cough or wheeze during the last 12 months and having used an asthma medication in the last 12 months. An English study performed with questions and methods that were the same on two occasions, 1990 and 1998, showed that diagnosed asthma rose from 11 to 19 % and there was also an increase in transient early wheezers (3% to 5%), persistent wheezers (5% to 13%), and late-onset wheezers (6% to 8%), and in all severity groups (25).

A medical record study from Italy found a prevalence of 6.3% among males and 4% among females younger than 5 years of age (57).

Today there are 18 birth cohort studies on asthma and allergy in Europe (83) and many more around the world. One of the first and most well-known is the Tucson study from Arizona, US, which started in 1980 (35). At the age of six years, 19.9 percent of the children had had at least one episode of lower respiratory illness with wheezing during the first three years of life but had no wheezing at six years of age, 13.7 % had wheezed both before three years of age and at six years of age, 15.0 percent had not wheezed before the age of three years but had wheezed at the age of six years.

A German cohort study found a prevalence of doctor diagnosed asthma at 7 years of age of 6.1% (84) and they concluded that sensitization to perennial allergens (e.g. house dust mite, cat and dog hair) developing in the first 3 years of life was associated with a loss of lung function at school age (39). It was children with persistent and late-onset asthma who at age 7 years showed a significant impairment of expiratory flow volumes (38).
A Norwegian study that started in 1992 used an asthma definition that required a minimum of two positive criteria, (i) a doctor's diagnosis of asthma, (ii) wheeze and/or chest tightness, (iii) use of anti-asthmatic treatment (24). They found that the lifetime prevalence of asthma at the age of 10 was 20.2%; current asthma 11.1%, a doctor’s diagnosis of asthma 16.1% and ever having wheezed 30.3%. In this cohort, allergic sensitization was also more common among children with current asthma.

The Swedish prospective cohort study called BAMSE (43) noted a prevalence of 7% at age 4 (85). The IFWIN study from England found a prevalence of 24.1% doctor diagnosed asthma among children with heredity for allergy (42).

In contrast to cross-sectional studies the prospective ones can produce estimations of incidence. One of the earliest was a cohort of English children born in 1958. The incidence rate per year in children 0-7 years was 26/1000 persons/year as reported at 7 years of age and with asthma defined as a report of ever having had asthma or wheezy bronchitis (86).

There are a lot of studies considering the prevalence of asthma in school children from countries all over the world, especially since the ISAAC study started. The prevalence has varied between, but also within, countries with the highest prevalence about 20 times higher than the lowest and the range 1.6-36.8% (70) (87).

From Scandinavia there are several reports published during the 1990’s that found a prevalence of 6 - 12% (60) (88-93) and there is also a documented rise in prevalence from 2.5% in 1979 to 5.7% in 1991 (89) .

According to prospective investigations the asthma incidence in school children is 9/1000 persons/year and the incidence of wheezing 38/1000 persons/year (61). Prevalence is always higher among boys during the preschool ages but this gender difference levels off around puberty and later on there is a female preponderance. This gender difference might be explained by the fact that young boys have more narrow airways and their airway muscle tone is higher (94).

In summary the prevalence of asthma differ greatly between countries and over time. This is partly due to various definitions and methods in measuring, but probably there exist real differences which are a challenge for further investigations.

### 3.2 THE BURDEN OF ASTHMA

A large study on the development of children’s health in the Nordic countries revealed that the three most common chronic illnesses were asthma, allergy and eczema (95). In the USA asthma is classified as the most common chronic disease of significant severity for children and remains the third most frequent cause of hospitalization (96). Several aspects of the
burden of asthma on society can be considered: the effect on the health care system, the effect on the family, and finally the consequences for the individual himself. The impact of the disease on the individual child includes not only effects on the physical health, but also effects on the social and emotional life (97). Several questionnaires with the intention to measure issues of quality of life (QoL) have been constructed. There are generic self-report questionnaires for measuring and comparing the health-related QoL of general and specific groups of children with different diseases (98). These instruments are less sensitive to particular conditions and in order to compare the results of an intervention in e.g. asthma a disease-specific instrument such as the Paediatric Asthma Caregiver’s Quality of Life Questionnaire (PACQLQ) is preferable (99).

### 3.2.1 Health care system: Economic burden

It has been calculated that the worldwide costs for asthma are equal to the combined costs for treating tuberculosis and HIV (30). The health care expenditures for asthma in developed countries are 1-2% of the total health care costs (100). An American investigation with a large number of children with mild-to-moderate persistent asthma and normal or near-normal lung function found that the median total annual asthma-related cost was 564 dollars. Low-income status and non-white race were the strongest correlates for increased asthma-related costs.

Indirect costs represented 54.6% of total costs. Medicines accounted for 52.6% of direct costs (101).

It has been calculated that the cost in Australia ranges from A$85 to A$884 (68–700US dollars) per patient, depending on asthma severity and in the United Kingdom the estimated annual costs of childhood asthma on the Health Service are between 100 million and 150 million Pounds sterling (5). The economic burden for the Swedish society for children with asthma has been calculated to 500 millions kronor/year (48).

### 3.2.2 Health care system: Comorbidity

Another aspect of the burden of asthma is the association of asthma with other illnesses like otitis media, sinusitis, and allergic rhinitis. In a large investigation with children between ages 1 and 17 years children with asthma were more likely than children without asthma to have comorbidity (26% vs. 9%). Children with asthma had a 47% probability of being in the highest total cost quintile compared to a 29% likelihood once adjusted for comorbidity. The outcome measures in this study were non-urgent outpatient care, pharmacy fills, urgent care visits, and hospital care along with the associated total costs (102).
3.2.3 Health care system: Hospital admittances

A study of paediatric hospital admittances for asthma between 1980 and 1995 from Norway found that the admittance rate increased significantly among children aged 0-3 years, and 75% of all children were younger than 4 years. First admissions increased throughout the study, whereas readmissions, as well as the mean duration of hospital stay, decreased significantly. This decrease could be contributed to the fact that prophylactic treatment with inhaled steroids increased over 1980-89 (103).

A report from Finland during the same time period found that hospital admissions as a result of asthma had increased by 2.8-fold. The mean length of hospital stay had more than halved (from 7.3 to 2.6 days) and the increase in hospital admissions was most pronounced in the 0-4 year age-group. They also saw a significant reduction in hospital admissions among the 10-14 year age-group (p <0.001) probably due to more extensive use of ICS (104). The launching of a national program for the treatment of asthma with regular pre-scheduled ambulatory control visits is considered to be the explanation for this development in Finland (105).

Likewise in a study from Gothenburg during the same time the number of hospital days per year gradually decreased to less than a third, and admissions decreased by 45%. This decrease was most marked in the children older than 5 years but it was also seen in the group of 2 to 5 year-old children (106).

In a Finnish study treatment days declined 50% between 1996 and 2004 (107). A steady state seems to have been reached during recent years. Consequently, there are strong indications that proper medication can control symptoms and thus decrease the personal burden of asthma (108).

3.2.4 Psychological burden on the family

It has been argued that intrafamilial stress and a family history of psychological problems is common in children with asthma (109). Poorer self-esteem and social abilities have been noted in asthmatic children with comorbid anxiety disorders (110). Children with asthma, especially those with severe asthma, are said to be at greater risk for internalizing psychological disorders than healthy controls (111). Severely negative life events can increase the risk of acute asthma attacks (112).

However, studies in Sweden have found that these differences are often secondary to asthma and structured family therapy can have positive effects on the clinical outcome (113) (114). Early onset of severe asthma can negatively impact the psychological adaptation, with development of more anxious and depressive features (115). It has been reported that children use more approach coping than avoidant coping when dealing with asthma. This seems to be an adequate way of handling the situation as this positively predicted psychological functioning and improves QoL for both the children and their mothers (116). It has been noted that parents, especially mothers, with self-reporting poor global health tend to report
their children with poor global health and illness (117). The QoL of the parents of asthmatic children is depended on that of the children and vice versa (118). According to this study patients who assess the quality of their lives as poor would benefit from psychological evaluation and support. A joint paediatric and psychiatric intervention can improve the clinical control and also the quality of life (6) as well as decrease the over-all cost (119). Even more limited methods of intervention such as individual or family group meetings can reduce the psychosocial burden of having a child with asthma (120).

The lives of children with asthma and their families have been illustrated and discussed in two recent theses from Sweden (121) (122). They used both qualitative and quantitative methods and found that the parents lived a strenuous life, many times fearing that their child might die during a severe asthma attack. Mothers tended to act in a protective manner and expressed feelings of sadness and uncertainty, while fathers acted more in a liberating manner and found it easier to accept the situation.

The mothers felt that they should always be available for the asthmatic child, which led to a decreased availability for the other members of the family resulting in feelings of being forsaken and a lack of understanding. In spite of this the parents rated their QoL as relatively high. The children strived to live a normal life and their core concern was not letting the asthma get the upper hand over life. Boys tended to distance themselves from the disease while girls stated that their asthma influenced their lives to a high degree, but both genders used the strategy of challenging the disease. In an early interview study with parents of children with chronic diseases the parents of asthmatic children stated that they often felt misunderstood by the physicians and that their child’s problems were severely underestimated (123).

3.2.5 Effects on the individual: Socio-economic differences

In a study from the 90’s in the USA no significant differences in asthma prevalence between race and poverty groups could be found but asthma-related morbidity was higher among black and poor children. White non-poor children had the highest level of out-patient care use for asthma after accounting for disease severity, and black poor children had the lowest level. Black children and poor children had a higher risk of activity limitation (124). In an investigation with 6-year-old children from the inner-city of Chicago 10.8% were diagnosed with asthma and they had evidence of a high burden of illness: over 40% reported having had disturbed sleep due to wheezing more than 1 to 2 nights/week and 86.6% reported acute care visits for respiratory symptoms in the past year. Only 12.2% of these asthmatics used inhaled anti-inflammatory medication (125).

School attendance is lower in children with asthma. One American investigation noted that 75% of non-cases reported never missing school compared with 19%, 33%, and 54% of active, suspected, and non-active asthma cases (126) and the total annual missed school days...
in the USA was 14 million (96). This is a result of the fact that approximately one-third of children with asthma have had five or more episodes of wheezing in the previous 12 months (5).

In summary asthma is the most prevalent chronic disease in childhood with a heavy burden on the health care system, nowadays primarily on the out-patient clinics, and also on the family and the individual child.

3.3 ADHERENCE

“Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments” (127). The problem of how to convince the patient of the importance of preventing and treating his disease is not a new one. Communication is the basis for all diagnostic and therapeutic procedures and even Hippocrates was skeptical of the honesty of his patients: “You need to be aware of the weaknesses of patients as they often have lied about taking the medications prescribed”.

3.3.1 Definition of adherence

This phenomenon was earlier called compliance which was originally a military term implying obedience. In 1979 Haynes defined it as ”The extent to which a persons behavior (in terms of taking medications, follow diets or executing life-styles changes) coincides with medical or health advice” (19). A discussion emerged during the 90’s about how to look upon the relationship between the doctor and his patient. This is mirrored in a headline from British Medical Journal in September 1999: “Paternalism or partnership? Patients have grown up – and there’s no going back” (128).

Another way of describing the relationship between doctor and patient was launched by The Royal Pharmaceutical Society of Great Britain in 1997, called concordance. It is defined as ”a state or condition of agreement or harmony” and ”a therapeutic alliance reached through negotiation” (129) (130).

A third term that was introduced is adherence and this term took into consideration the new relationship between patients and their physicians. This relationship became evident as the internet eventually became part of everyday life for most people. Parents of our patients had often prepared themselves with information from the net before consulting their doctor, thus putting stress on him/her to be well updated. The consultation became more of a discussion where it was important for the physician to find out the view of the parent (and child) before suggesting advice or a medication that the parent/child could then accept or not.
The definition of adherence as proposed by the WHO is “The extent to which a person’s behaviour - taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health provider” (127). This has been described by Falk in 2001 as “adherence is influenced by the disease, the medication, the patient, the physician and the environment” (131). Falk also has proposed that William Osler’s aphorism “The practice of medicine is an art, based on science” should now be changed to “The practice of medicine is a communicative skill, based upon evidence based medicine”. In this text we will refer to adherence when discussing these issues.

3.3.2 Problems with adherence
Poor adherence is a major problem that can result in poor asthma control, exacerbations, a decreased QoL and economic consequences e.g. due to increased hospitalization both for children and for adults (127). It has been proven that good adherence is important for a positive clinical outcome (132) but adherence in chronic diseases such as asthma is seldom over 50% (19) (133). It has been calculated that 70% of the poor adherence is a voluntary, intentional choice (134). In order to improve adherence we have to take into consideration the fact that patients and parents conduct experiments with their regimen components in an effort to balance the burden of treatment with the burden of asthma to attain control of their lives and a good QoL (135) (136). This often involves a certain amount of non-adherence to the suggestions of the physician and has been described as:
Actual treatment = perceived disease burden/perceived treatment burden (134)

Another study showed that 25% of the patients trusted the prescription while 35% were afraid to take it continuously. Twenty-eight percent thought that medicines are harmful and dangerous while 12% believed that medicines are harmful but necessary (137). Some ten percent of the medicines that are sold at the pharmacies are returned unopened each year. In 2002 it was estimated that in Sweden we could save 15 000 millions kronor/year if medicines were used in a proper way (138).

It is difficult to measure adherence accurately as patients can manipulate the result and tend to report inaccurately when they have failed to follow the treatment advice (139). On the other hand, when patients reveal that they have not followed the recommendations they describe their behaviour accurately (140).

Objective methods, such as counting remaining pills at clinical visits, are preferable but they can also be manipulated. The best method is probably the electronic monitoring device (141), which records the date and time when a medication container is opened. Moreover, this is expensive which precludes its use in many situations. The WHO concludes that “a multi-method approach that combines feasible self-reporting and reasonable objective measures is the current state-of-the-art in measurement of adherence behaviour” (127).
3.3.3 Earlier intervention studies

According to the latest Cochrane review on the subject there are only nine intervention studies concerning asthma that fulfil the criteria for evidence based medicine (EBM) (19). Of these, only one concerning adult patients could document positive objective effects on the asthma symptoms. The interventions in these studies were all rather short-term, complex, time-consuming and thus expensive, making them less attractive for clinical applications (142). In a recent review (133) another investigation with children with positive clinical effects was found. In this study the intervention consisted of a combination of informational and behavioural components (143).

There are a lot of investigations on this subject that do not fulfill EBM criteria but can still give hints on methods to improve adherence. In the Harvard Community Plan a nurse gave personal instructions on asthma management and maintained regular telephone contact with the families which resulted in a 70% lower annual rate of emergency-department visits and hospital admissions related to asthma (144). Another program with four small-group sessions of about 2 hours each with parents of children under the age of 7 years, including promotion of the psychosocial well-being of the family, resulted in more symptom-free days for the children and more nights of uninterrupted sleep for the parents (145). Two sessions with direct instructions for children aged 4-6 years were included in this program.

The issue of adherence is further complicated by the fact that poorer adherence to a more effective treatment, e.g. ICS compared to anti-leukotriens, can give equally good result (146). There is evidence from behavioural science demonstrating the efficacy of specific strategies. It is now well-known that education either alone (147) (148) or combined with telephone reminders are poor interventions (149) (150), but a combination including scheduled return visits to the physician gives better results (151). Patients need to be informed, skilled and motivated to cope with the demands imposed by their illness (127), however, these improvements often lead to an increase in the cost of asthma care (152). Studies in adults highlight the fact that a majority of patients want to take an active, or at least a collaborative, role in their treatment (153).

Thus, the situation concerning adherence in chronic diseases like asthma is poor and there is a need for improvements.

3.4 THE VALUE OF EARLY INSTITUTED AND CONTINUOUS TREATMENT WITH INHALED CORTICOSTEROIDS

There was a consensus, after the paradigm shift during the 70’s, that early instituted medication with inhaled corticosteroids (ICS) was valuable in the treatment of asthma in order to stop the inflammation in the airways. There is one long-term follow-up study of early, continuous, treatment with ICS in pre-school children that supported this conclusion, as it revealed that this could stop the deterioration of the lung function (154). Later studies could
not confirm the effect on lung function but showed less symptoms and exacerbations in school-age children (155) as well as in adults (156). An investigation with early, continuous ICS in mild asthma in children over five years of age and adults confirmed the good results concerning symptoms and moreover, also revealed improved lung function after three years (157).

3.4.1 Is intermittent ICS treatment good enough?

In a review concerning mild asthma it was concluded that therapy with ICS decreased bronchial inflammation, but had only a slight effect on structural remodelling, and, when stopped, inflammation immediately recurred. Continuous low-dose ICS therapy should be the baseline treatment for persistent mild asthma combined with a step-up dose when the child had symptoms (158). However, there are a few investigations in adults that have indicated that intermittent, symptom-guided ICS could be sufficient to adequately control mild/moderate asthma (159) (160).

Short-term, intermittent ICS instituted 3 days after initiation of wheezing in infants had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing (161). A large study with newly diagnosed asthmatic infants followed for several years showed no effect of early treatment with ICS on either symptoms or lung function (162) and another found a good effect on symptoms while the ICS was taken but no persistent effect on lung function or symptoms when the treatment was stopped (163).

Thus, the perception that early instituted ICS will stop the airway remodeling has been challenged by several investigations published during the last years. On the other hand, a recent review (164) summarized that “by age 3, the dice is cast and lung function tracks lifelong” so it is obviously very important to treat the young child optimally and at least to try to give the parents the best information available and support them in order to improve the adherence.

3.5 RATIONALE FOR THIS THESIS

During the process of our investigation there was a consensus that early treatment with ICS was valuable. However, adherence is poor in chronic diseases and this is also the case in patients with asthma. There is a lack of randomized intervention studies aimed at increasing the adherence to medication in pre-school asthmatic children that fulfill the criteria for EBM. In my clinical work I had experienced the problems with poor adherence and I felt that trying to change this situation was an inspiring challenge.

EBM, that is the demand for scientific proof of efficacy of treatments, is one major trend in contemporary medical debate on health management. Another theme is partnership medicine
or, concerning public health, empowerment with user-oriented health care where the emphasis is on collaboration between the care giver and the patients/families (128) (165) (166). We had applied this method earlier in a group setting in connection with our work with parents of adopted children. We were inspired by the work of K. Reichenberg and his team in Gothenburg with parents of children with asthma (6) and we decided to use a similar method in order to try to improve the adherence in newly discovered asthma in pre-scholars.

In our region, all out-patient clinics have used computerized records since the early 90’s and each visit by a patient is recorded with an International Classification of Diseases (ICD-code). This gave me the incitement of performing an epidemiological study. There are only a few investigations of the epidemiology of asthma in pre-school children and to our knowledge there is no study that has tried to compare the results of questionnaire based investigations with asthma according to medical records. The results from the Tucson follow up study show that asthma prevalence and lung function after 16 years are comparable to the 6 year follow-up (41). This underlines the importance of better management during the pre-school years.

There is an on-going debate about the best way of treating newly discovered, and especially mild, asthma (158). In clinical practice we had used a treatment plan based on long-term, intermittent ICS, guided by symptomatology. The effectiveness of this type of ICS-treatment strategy is of interest as, until now, the only positive studies are on adults (159).

In summary we thought that there was a need for an intervention study in order to improve adherence in asthma and also a possibility to study the prevalence in a new way and finally to perform an investigation with the intention to follow the children prospectively for several years and evaluate the effects of the intervention and of the ICS treatment used.
4 AIMS

This thesis has two main themes. One aim is to compare two different ways of estimating prevalence of asthma in pre-school children. A second aim is to investigate if an intervention with information and extra support to parents of young children with newly diagnosed asthma would result in better adherence, and as a consequence reduce asthma exacerbations and improve quality of life for the asthmatic children and their parents.

Specific aims are:

To perform an epidemiological analysis of the asthma prevalence and the utilization of the health care system in the southern part of Värmland (paper I).

To compare parental assessments of children’s asthma diagnosis with doctor’s diagnoses (paper II).

To evaluate the results of the intervention on adherence to therapy and advices (paper III).

To evaluate the effects of the intervention on parent’s quality of life and to separately analyse the answers with a gender perspective (paper IV).

To analyse any sustained effects of the intervention at a 6 year follow up (paper V).
## 5 METHODS AND SUBJECTS

Table 1. Summary of the investigations in this thesis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of analysis</th>
<th>Population</th>
<th>Period of time</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper I: The burden of asthma- as reflected by the prevalence defined by doctor’s diagnosis and the use of health care services by pre-school children in a Swedish region</td>
<td>Admissions to the hospital</td>
<td>Children 0-18 years old. County of Värmland</td>
<td>1988 and 1998</td>
<td>Manual analysis of medical records in the hospital</td>
</tr>
<tr>
<td></td>
<td>Visits to out-patient clinics</td>
<td>9410 children 0-6 years old. Southern part of Värmland</td>
<td>1998</td>
<td>See above + computerized data in medical records of out-patient clinics</td>
</tr>
<tr>
<td></td>
<td>Prevalence of asthma</td>
<td>9410 children 0-6 years old</td>
<td>1998</td>
<td>As above</td>
</tr>
<tr>
<td>Paper II: Comparison of the prevalence of clinically diagnosed asthma among Swedish pre-school children with parental assessment of their children’s asthma in response to a questionnaire</td>
<td>Prevalence of asthma</td>
<td>6295 children 1-6 years old</td>
<td>1999</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td>Prevalence of asthma</td>
<td>See above</td>
<td>1999</td>
<td>Responses to a questionnaire</td>
</tr>
<tr>
<td></td>
<td>Comparison of prevalence</td>
<td>As above</td>
<td>1999</td>
<td>Analysis with personal identification numbers</td>
</tr>
<tr>
<td></td>
<td>Prevalence of asthma (on treatment)</td>
<td>418 children (asthma according to medical records/questionnaires)</td>
<td>1999</td>
<td>Responses to a complementary questionnaire</td>
</tr>
<tr>
<td>Paper III: Group discussions with parents have long-term positive effects on the management of asthma with good cost-benefit</td>
<td>Intervention to improve adherence</td>
<td>60 children</td>
<td>1998 and 1999</td>
<td>Clinical examinations, diaries, blood tests, lung function tests, chest X-ray, questionnaires</td>
</tr>
<tr>
<td>Paper IV: A gender perspective on parents’ answers to a questionnaire on children’s asthma</td>
<td>Quality of life</td>
<td>119 parents</td>
<td>1998 and 1999</td>
<td>Responses to a questionnaire on quality of life</td>
</tr>
<tr>
<td>Paper V: Long-term positive effects of an intervention to improve the adherence of preschool children with asthma – results of a 6-year follow-up</td>
<td>Long-term effects of an intervention</td>
<td>60 children</td>
<td>1999 - 2005</td>
<td>Clinical examinations, diaries, blood tests, lung function tests, NO measurements, dry air tests, questionnaires</td>
</tr>
</tbody>
</table>
5.1 PAPERS I AND II

All out-patient clinics in the southern part of the Värmland region have computerized medical records and every visit is registered with a diagnosis according to the ICD-10 code. Papers I and II are based on reports by all five paediatricians and all of the 70 general practitioners (GP) working in this area during both 1998 and 1999, including whether the asthma diagnosis was new or not. In addition the (non-computerized) patient records of the Paediatric Department at the Central Hospital of Karlstad were analyzed during these years and in 1988 both for admittances and for out-patient clinic visits.

5.1.1 Identification and referral of patients

We used the criteria for asthma diagnosis referred to above: three or more episodes of wheezing before 2 years of age or the first wheezing episode after the age of 2 or the first episode of wheezing in a child with other atopic diseases (48).

The children could be diagnosed by the GP, but according to the regional guidelines (167) he/she should refer a child with suspected asthma to the nearest paediatrician for further evaluation and confirmation of the diagnosis. During these years all children with a diagnosis of asthma were referred to the out-patient clinic at Gripen Primary Care Centre where my two colleagues and I took a history and performed clinical examinations.

If the child fulfilled the criteria above and was < 4 years old a skin prick test (SPT) with egg white and cat allergen extracts (Soluprick®, ALK-Albello A/S, Denmark) was carried out. If the child was > 4 y of age we included birch, timothy, mugwort, dog, horse, cat and Dermatophagoides pteronyssinus. The test was considered positive if the mean diameter of the wheal was > 3 mm. If the child was able to perform a peak expiratory flow or a spirometry with reversibility, this was also performed.

If the children had experienced asthma without symptoms of upper respiratory tract infection and/or had an atopic heredity (parents or brothers/sisters) and/or proven allergy with positive SPT and/or other atopic disease they were considered to have a high risk of developing persistent asthma (35) (168) and were invited to participate in the intervention study described below.

In 1998 our region had a population of 117 653 inhabitants and 9410 were under 7 years of age (seven age groups). The analysis in 1999 was made with 5 age groups (1-6 years of age) including 6 295 children.

5.1.2 The first questionnaire (in year 2000)

In study II we wanted to compare asthma diagnosis according to the medical records with the parental responses to questions regarding their children’s respiratory symptoms and doctor
diagnosed asthma in a WQ distributed in March 2000. The WQ was based on the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (62) and was sent to all the parents with children 1 – 6 years of age in 1999 in the county of Värmland. The total number of children were 14 077 but we only analyzed the 75% of the 6 295 who answered the WQ and who lived in the southern part of Värmland. The parents of 53 of these 4749 children did not respond to the question, “Has your child been diagnosed with asthma by a doctor?” This was the only question modified compared with the original questionnaire. The WQ also had many questions about background factors concerning the home environment and was used in the first phase of the Dampness in Buildings and Health study (DBH) which is on-going in our county (169). The children included in the WQ could then be matched with the children in the medical records on the basis of their personal identification numbers without any missing.

5.1.3 The second questionnaire (in 2003)

This was a complementary WQ (see table 4) to the parents of all the 418 children with asthma according to the medical records and/or the DBH WQ in order to better explain the discrepancies found between these two data sets. This WQ constituted the third data set and was distributed during 2003 and could be answered anonymously. If we did not receive an answer two reminders were sent.

5.1.4 Analysis of data

The data collected was used for estimation of the prevalence during each year. During 1998 we also performed a calculation of the asthma incidence. The admittances to the hospital in 1988 and 1998 with asthma, obstructive bronchitis and bronchiolitis were manually summarized and compared as a combination of diagnoses, as the nomenclature had changed during these years. The burden of asthma was further investigated by analyzing the visits to the different out-patient clinics, including the clinic at the hospital.

5.2 Paper III – V

According to calculations of the supposed incidence of asthma in these age groups we decided to include 60 children, as we had the intention to stop the inclusions within two years. This number was also based on power calculations (see Statistical analysis) which estimated that this number would be feasible.
5.2.1 The intervention study
The intervention consisted of additional information and support in a group setting and we requested that both the mother and father should be present. The sessions took place in the afternoon and lasted about 1.5 hours. The parents were randomised consecutively in groups of four to either the intervention or the control group by the nurse in charge as soon as a doctor decided that the child could be included. We chose to use this type of randomization so that we could start the intervention as soon as possible after the child was diagnosed. The parents were asked to come without their children. The parents could use the state-supported possibility to be free from work in order to enhance the health of their children, to finance these meetings.

We had three weekly meetings soon after the child was diagnosed and six months later we had a follow up meeting. Three paediatricians, three nurses and two psychologists were involved in these sessions and they were also in charge of the follow-ups, i.e. this study could not be blinded. One nurse was present at all occasions and the doctors and psychologists on 3 each. In order to minimise the effect of the personal charisma and skill and to be able to evaluate the effect of this method in its own right, the nurse worked together with the different doctors in due order. There was no selection of the parents referred to our clinic or in the recruitment to this study. The author of this thesis was in charge of 33, one colleague recruited 22 and the third physician included five children to the study.

5.2.2 The method used in the group discussions
We applied a method based on the concept of concordance (129), meaning that we tried to "speak the same language" as the parents and to reach an alliance with them on how to look upon the disease and its management. Our goal was to identify their "main worry" (170) and in addition to teaching them about asthma, we posed open questions such as: "What does asthma mean to you?". Our intention was to utilize peer education whereby the group was encouraged to share personal experiences (171) (172). In each group session the leaders had a list of subjects that should be covered during the discussion (See Appendix). We were convinced that communication of knowledge alone was not sufficient (173). To improve adherence we meant that we had to deal with the emotional aspects of the fact that their child had been diagnosed with a chronic disease such as asthma (174).

5.2.3 The treatment plan
The treatment recommended and the follow-up of all 60 children was the same except for the intervention group discussions. Each family received basic education about asthma and its treatment including how to use the Nebunette and information on environmental control at the first visit to the clinic. They also received a written treatment plan where the children
were told to begin taking high doses of ICS (0.2 mg of budesonide x 4) as soon as they caught a cold, and to subsequently reduce the dose gradually during the first week, stopping medication when the children no longer had any symptoms. When symptoms of asthma developed they were instructed to continue ICS for one month and, if they had experienced three or more exacerbations during a 12-month period, to continue this treatment for another six months.

5.2.4 The evaluation of the children
The children were seen by a paediatrician at inclusion, after three, six and 18 months respectively. The initial examination included a clinical examination, spirometry (when possible to perform), chest x-ray, examination of the patients’ records and questionnaires concerning issues of adherence, burden of asthma such as exacerbations, days away from day care centre/school, emergency visits to a doctor due to asthma and days in hospital care. The blood was analyzed for eosinophils and Eosinophil Cationic Protein (ECP). Skin prick tests were performed, if not performed earlier, as indicated above. RAST® testing (Pharmacia Diagnostics & Upjohn AB) with the same allergens (considered positive when the IgE-level was ≥0.7 kU/l) and Phadiatop® testing (Pharmacia Diagnostics & Upjohn AB) (considered positive if the value ≥ 1.0 kU/l) were also performed. Physical examination was performed at each of the follow-up visits, as well as peak flow measurements and spirometry when possible. After six and 18 months the same WQs as at inclusion were performed.

5.2.5 Estimation of adherence
The adherence to the inhaled medication was measured during six months between 12 and 18 months from inclusion by weighing the aerosol canisters and comparing the amount of ICS used with the medication the physicians had recommended and with the amounts the parents had documented in their diaries during the same period of time. The adherence was calculated from the following equation:
Registered number of ICS-doses x 100/ prescribed number of ICS-doses (175)

5.2.6 Estimation of quality of life
The parents answered the Paediatric Asthma Caregiver’s Quality of Life Questionnaire (PACQLQ) separately, either at home or during the visit to our clinic, at inclusion, after six and 18 months and we used this material for an analysis in paper IV. The PACQLQ is divided into two domains: the emotional functions and activities with nine and four questions respectively in each domain and an overall index is used for the sum of all answers (176). Responses to each item in the PACQLQ are given on a 7-point scale where one represents severe impairment and seven represents no impairment. For our investigation
we analyzed both the three indices and each question separately. According to the initial validation, a minimally important difference (MID) between two measurements of these indices should be 0.5 for caregivers overall quality of life, 0.64 for the emotional index and 0.67 for the activity index. Later publications using the PACQLQ have used 0.5 as a MID for all indices (177) and E. Juniper has concluded that no matter which method you use to estimate the MID it comes out around 0.5 on the 7-point scale (178).

We also used a WQ developed and validated in Norway (179) for measuring the parents’ view on the value of the group discussions. Another WQ (see table 13) which was constructed for another asthma study at Huddinge hospital (180) was answered by the parents in order to examine their views on issues important for adherence.

**5.2.7 The follow-up investigation**

The children then made regular visits to their own paediatrician and nurse during the subsequent years and their medical records were continuously updated and computerized. The examination after 6 years was performed during 2005 by the author together with a nurse. Here each child was examined and interviewed, in the company of one or both parents. The examination was the same as at the first visit, except that an objective assessment of adherence was not carried out. Chest X-ray was not performed as an evaluation of the first examination revealed that this was not necessary (181).

Exhaled NO was measured with the help of the NIOXMINO® Airway Inflammation Monitor (Aerocrine AB, Solna, Sweden), utilizing a 10-sec expiration at a constant flow rate of 0.05 l/s, and we performed dry-air tests (Aiolos AB, Karlstad, Sweden), in connection with which a fall in FEV1 of > 10% was considered pathological.

At the 6-year follow-up a separate questionnaire addressed to the child, the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) (182) was included. Another WQ, the Asthma Control Questionnaire (ACQ) (183) was also used and this was answered by the child and parent together. This WQ has 7 questions and each item has 7 points, 0 represents no problems and 6 very severe. The sum is divided by 7 and a value of < 0.75 is considered as being an indicator of good asthma control (184).

During the follow-up parents and doctors estimated adherence on a visual analogue scale (VAS).

**5.2.8 Complementary investigations**

At the time for the follow up we also contacted the parents of the six children that declined to participate in the study. We sent a letter and telephoned all the parents and they were willing to give information concerning the outcome and medication of their children.

In order to get a better picture of the socio-economic background of the parents in our intervention study we sent them additional written questions during the spring of 2007.
concerning their education and work situation as well as if they lived in a house of their own or in a flat during the time of inclusion in our study.
The regional Medical Research Ethics Committee gave ethical approval and all parents gave informed consent to these investigations.

5.3 STATISTICAL ANALYSIS
We decided to use a group of 60 children, as according to calculations made by E. Juniper, the constructor of the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) (182) this would give us a power of >80%. Data was analyzed with the SPSS statistical package for Windows (versions 10.0 - 14.0; SPSS, Chicago, IL, USA). Descriptive statistics were used to summarize mean scores and standard deviations. Trends and differences between the groups were tested for statistical significance employing non-parametric tests or t-tests, as appropriate. A p-value of ≤ 0.05 was considered to be statistically significant.
6 RESULTS

6.1 PAPER I – II

Analysis of the medical records from our catchments area during 1998 revealed that the prevalence of asthma among children 0 -7 y of age was 4.5% (95% CI = 4.1–4.9) whereof 59% were boys. For children 1- 6 y of age the prevalence was 4.8%, and the prevalence for this age group in 1999 was 4.9% (95% CI = 4.4-5.4). The incidence was only recorded in 1998 and was 2.2%.

Regarding the burden of asthma on the health care system we found that in 1998 the children with asthma had a mean of 2.1 visits/year per patient or 101/1000 children/year among children 1-6 year of age. The corresponding figure for 1999 in children 1-6 years of age was 2.4 visits/year per patient. One-third of all consultations in paediatric out-patient clinics concern asthma in children 0-18 y of age in our region.

The asthmatic children mainly consulted paediatricians working in primary care and 75% had no contact with either the hospital or a GP because of asthma during 1998. On average the GPs examined one child with asthma/year in these age groups. Twenty-seven of 40 newly diagnosed asthmatic children (68%) were not referred from the GP to a paediatrician in 1998 but came directly through e.g. emergency department visits. Eighty-six per cent of children with an established asthma diagnosis were under the care of paediatricians and 94% had visited a paediatrician at least on one occasion.

Admittances to the hospital because of asthma (including obstructive bronchitis and bronchiolitis) had decreased significantly from 5.4/1000/year to 4.2 between 1988 and 1998. The patients hospitalized for these diagnoses were also younger in 1998, 90% were <7 years of age as compared to 75% in 1988. The majority (61%) of the children hospitalized in 1998 had never had any symptoms of asthma before. Admissions for asthma constituted 3.2% of the total number of admissions this year.

Half of the children who were diagnosed with asthma in 1999 had visited a paediatrician in an out-patient clinic, 33% were diagnosed at the outpatient clinic of the hospital and 17% by a GP. The admission rate was twice as high in the 1-2 year age group compared to the older children.

During 1998 fifty-eight of 209 children (28%) with newly diagnosed asthma diagnosis fulfilled the criteria for having high risk of developing persistent asthma.

6.1.1 Comparison between the WQ and the medical records

In study II we compared the results of the study of the medical records from 1999 with the results of the DBH WQ covering the same period. According to the parents’ answers to the
DBH WQ the prevalence of doctor-diagnosed asthma was 5.9% (95% CI = 5.2-6.6) corresponding to 275 children. This is significantly higher (p<0.05) than the prevalence found in the medical records for the same period. The parents of 1599 children did not answer the WQ and according to medical records 93 of these had asthma which give a prevalence of 5.8% (95% CI = 4.8-7.2) among the non-responders. This prevalence is not significantly different from the responders or the clinical prevalence.

The comparison between the results of the medical record study and the WQ is summarized in table 2.

Table 2. Correspondence between the prevalence of asthma among 1-6 year-old children indicated by their parents’ responses to the Dampness in Buildings and Health questionnaire and by the medical records.

<table>
<thead>
<tr>
<th>CLINICAL DIAGNOSIS</th>
<th>DBH WQ</th>
<th>Asthmatic</th>
<th>Non-asthmatic</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children reported by their parents as having asthma</td>
<td>166</td>
<td>109</td>
<td>275</td>
<td></td>
</tr>
<tr>
<td>Children reported by their parents as not having asthma</td>
<td>50</td>
<td>4371</td>
<td>4421</td>
<td></td>
</tr>
<tr>
<td>Children whose parents did not answer the questionnaire</td>
<td>93</td>
<td>1506</td>
<td>1599</td>
<td></td>
</tr>
<tr>
<td>Total number</td>
<td>309</td>
<td>5986</td>
<td>6295</td>
<td></td>
</tr>
</tbody>
</table>

Matching the data from the medical records and from the DBH WQ, and assuming that the medical diagnostic code was correct, identified four groups of patients who were thought to have asthma:

The false-negative group, who had a clinical diagnosis of asthma, but whose parents denied this in responding to the DBH WQ (50)
The false positive group, who had no clinical diagnosis of asthma but whose parents stated the opposite in response to the DBH questionnaire (109)

The congruent group, for whom doctors and parents agreed on the diagnosis of asthma (166)

The non-responders, who had a recorded clinical diagnosis of asthma and whose parents did not answer the DBH questionnaire (93)

This table shows that of the 275 children reported by their parents to have a doctor diagnosed asthma actually only 166 (60%) had received the diagnosis from a doctor. Considering all discrepancies between the two data sets, including lack of response, the WQ was able to identify 54% (166/309) of the children with clinically diagnosed asthma. At the same time the WQ yielded 40% (109/275) false positive diagnosis.

Validation of the questions on respiratory symptoms reported by the parents in the DBH WQ against asthma diagnosis in the medical records is reported in table 3.

Table 3. Validation of the respiratory symptoms reported by parents in response to the Dampness in Buildings and Health questionnaire in relationship to clinically diagnosed asthma as gold standard.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma diagnosed by a doctor?</td>
<td>76.9</td>
<td>97.5</td>
<td>0.60</td>
</tr>
<tr>
<td>Wheezing during the past 12 months?</td>
<td>86.3</td>
<td>84.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Wheezing ever?</td>
<td>94.5</td>
<td>77.8</td>
<td>0.17</td>
</tr>
<tr>
<td>Coughing during the night?</td>
<td>27.9</td>
<td>93.0</td>
<td>0.11</td>
</tr>
</tbody>
</table>

The age-adjusted sensitivity of the question concerning diagnosis of asthma by a doctor was 22% for children 1-2 yr of age, rose to 66% in the 2-3-yr-old and was 83% among 5 to 6 yr old children.

The response rate to the DBH WQ was 75%, but the response rate amongst the children with a high risk for persistent asthma as defined above was 63%. On the other hand the sensitivity for this group was 100%.
The results of the complementary WQ directed to the parents of children who had asthma either according to medical records and/or according to the responses to the DBH WQ are summarized in table 4. The response rate to this WQ was 76%.

Table 4. Responses of parents of children who were asthmatics in 1999 (according to their parents and/or doctors) to the complementary questionnaire. Per cent within brackets. RR = Response rate

<table>
<thead>
<tr>
<th>Children with following characteristics:</th>
<th>False negative group</th>
<th>False positive group</th>
<th>Congruent group</th>
<th>The no response group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=50</td>
<td>n=109</td>
<td>n=166</td>
<td>n = 93</td>
</tr>
<tr>
<td>RR:90%</td>
<td>70%</td>
<td>87%</td>
<td>64%</td>
<td></td>
</tr>
<tr>
<td>Wheezing prior to 1999</td>
<td>29(64)</td>
<td>59(78)</td>
<td>133(92)</td>
<td>53(88)</td>
</tr>
<tr>
<td>Wheezing during 1999</td>
<td>25(56)</td>
<td>47(62)</td>
<td>124(86)</td>
<td>47(79)</td>
</tr>
<tr>
<td>Asthma prior to 1999</td>
<td>13(29)</td>
<td>44(58)</td>
<td>92(64)</td>
<td>26(44)</td>
</tr>
<tr>
<td>Asthma during 1999</td>
<td>11(24)</td>
<td>27(36)</td>
<td>95(67)</td>
<td>35(58)</td>
</tr>
<tr>
<td>Visit to a doctor because of asthma during 1999</td>
<td>13(29)</td>
<td>21(27)</td>
<td>91(63)</td>
<td>39(65)</td>
</tr>
<tr>
<td>Use of short-acting beta-2 agonists during 1999</td>
<td>30(67)</td>
<td>37(49)</td>
<td>131(91)</td>
<td>54(90)</td>
</tr>
<tr>
<td>Use of inhaled corticosteroids during 1999</td>
<td>15(33)</td>
<td>24(32)</td>
<td>120(83)</td>
<td>45(75)</td>
</tr>
<tr>
<td>Asthma in 2003</td>
<td>8(18)</td>
<td>21(27)</td>
<td>89(62)</td>
<td>29(48)</td>
</tr>
</tbody>
</table>

Finally, the results of the comparison of the study of the medical records and the WQs are summarized in fig 1.
**Fig 1.** Summary of the relationship between parental-reported (DBH WQ) and clinically diagnosed asthma and the complementary questionnaire.

<table>
<thead>
<tr>
<th>Population</th>
<th>6295</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DBH WQ:</strong></td>
<td></td>
</tr>
<tr>
<td>Responders</td>
<td>4696</td>
</tr>
<tr>
<td>Non-responders</td>
<td>1599</td>
</tr>
<tr>
<td>Asthma</td>
<td>275</td>
</tr>
<tr>
<td>Not asthma</td>
<td>4421</td>
</tr>
</tbody>
</table>

| Medical records: |      |
| Asthma           | 166  |
|                  | 50   |
|                  | 93   |
| Not asthma       | 109  |
|                  | 4371 |
|                  | 1506 |

| Complementary study: |      |
| Children in need of asthma medication | 133  |
|                              | 44   |
|                              | 20   |
|                              | 74   |

### 6.2 PAPER III

In January 1998 the first patient was included in the intervention study. In September 1999 the study was closed as we had 60 children included. Thirty-nine were recruited during 1998 and 21 during 1999. The parents of six children declined to participate. Fourteen of the
children included during 1999 had been diagnosed during 1998 and in total 53 who were included and five who declined fulfilled the criteria during 1998 for a high risk of persistent asthma (see above: paper I).

The background data for the participants is summarized in table 5. The background for the 6 children whose parents declined to participate showed that they differed in some respects from the 60 children; 5/6 were <2 years of age at the time they were asked to participate, 4/6 had atopic dermatitis, 5/6 had confirmed allergy and none had furry pets at home. The socio-economic background, parental smoking, number of brothers and sisters and use of day-care centre were comparable. Two of them did not have any signs of asthma at follow-up, one had severe asthma, one intermittent, one mild persistent and one moderate persistent asthma. The numbers of consultations through the years with physicians/nurses were comparable.

**Table 5. Background data for children in the intervention study.**

<table>
<thead>
<tr>
<th></th>
<th>Intervention group. n=32</th>
<th>Control group. n=28</th>
<th>Difference p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (months)</td>
<td>28</td>
<td>26</td>
<td>n.s.</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>boy</td>
<td>19</td>
<td>17</td>
<td>n.s.</td>
</tr>
<tr>
<td>girl</td>
<td>13</td>
<td>11</td>
<td>n.s.</td>
</tr>
<tr>
<td>Parents cohabiting</td>
<td>32</td>
<td>27</td>
<td>n.s.</td>
</tr>
<tr>
<td>Single child</td>
<td>5</td>
<td>9</td>
<td>n.s.</td>
</tr>
<tr>
<td>Day care centre</td>
<td>20</td>
<td>17</td>
<td>n.s.</td>
</tr>
<tr>
<td>House owner</td>
<td>26</td>
<td>22</td>
<td>n.s.</td>
</tr>
<tr>
<td>Furred animals in the home</td>
<td>15</td>
<td>5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smokers in the home</td>
<td>3</td>
<td>1</td>
<td>n.s.</td>
</tr>
<tr>
<td>Allergic heredity</td>
<td>27</td>
<td>24</td>
<td>n.s.</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>15</td>
<td>14</td>
<td>n.s.</td>
</tr>
<tr>
<td>Parents’ education (113/120 answered these questions):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>compulsory school</td>
<td>2</td>
<td>1</td>
<td>n.s.</td>
</tr>
<tr>
<td>grammar school</td>
<td>46</td>
<td>36</td>
<td>n.s.</td>
</tr>
<tr>
<td>university degree</td>
<td>11</td>
<td>17</td>
<td>n.s.</td>
</tr>
<tr>
<td>Parents’ work:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>manual worker</td>
<td>29</td>
<td>21</td>
<td>n.s.</td>
</tr>
<tr>
<td>civil servant</td>
<td>19</td>
<td>17</td>
<td>n.s.</td>
</tr>
<tr>
<td>self-employed</td>
<td>5</td>
<td>3</td>
<td>n.s.</td>
</tr>
<tr>
<td>student/unemployed</td>
<td>6</td>
<td>4</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

All families were evaluated after six months. At the follow-up after 18 months 91% in the IG and 86% in the CG participated. One family had moved away, three did not show up. One
girl was diagnosed with cystic fibrosis, another girl with ciliary dysfunction and finally the parents of one girl in the intervention group did not participate in any of the group sessions. The follow-up rate for the adherence study between 12 and 18 months was 85%.

6.2.1 The group meetings
In 81% one or both parents in a family attended the first 3 group meetings and on an average 68% of the parents participated in these discussions. Only 39% attended the fourth meeting after 6 months. There were no significant differences between the participation of fathers and mothers.

We also performed an evaluation of the parent’s opinion on the value of these meetings and there were no differences depending on which nurse or doctor who led the group meetings.

6.2.2 Adherence – the parents view
The parents responded to a WQ on their view on issues important for adherence (see table 13). There were no differences initially between the IG and the CG, but after 6 months the parents in the IG had significantly more negative answers to the questions “Is there any uncertainty about the medication of your child?”, and more positive answers to the questions “Did you/your child get a good advice on how to live in order to avoid asthma symptoms?” and “Do you consider the positive effects of your child’s medicine to be greater than the negative ones?”. After 18 months the significant differences remained concerning the first two questions. For all the other questions there was a tendency for more positive answers in the IG both after 6 and 18 months.

6.2.3 Adherence – Ratings on a visual analogue scale
The parents’ and the physicians’ rating of adherence on a visual analogue scale (VAS) are reported in table 6.
Table 6. Doctors’ and parents’ rating on a visual analogue scale (VAS) of childrens’ adherence.
Per cent of children in different regions of the VAS-scale. 0 = very good adherence, 100 = very poor adherence.

<table>
<thead>
<tr>
<th>VAS 0-100</th>
<th>Doctor’s estimation</th>
<th>Parents’ estimation</th>
</tr>
</thead>
<tbody>
<tr>
<td>At inclusion &lt; 10</td>
<td>26</td>
<td>80</td>
</tr>
<tr>
<td>At inclusion 0-50</td>
<td>57</td>
<td>18</td>
</tr>
<tr>
<td>At inclusion &gt; 50</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>After 6 months &lt;10</td>
<td>50</td>
<td>66</td>
</tr>
<tr>
<td>After 6 months 10-50</td>
<td>41</td>
<td>25</td>
</tr>
<tr>
<td>After 6 months &gt;50</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>After 18 months&lt;10</td>
<td>57</td>
<td>71</td>
</tr>
<tr>
<td>After 18 months 10-50</td>
<td>39</td>
<td>21</td>
</tr>
<tr>
<td>After 18 months &gt;50</td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

6.2.4 Adherence – verified and according to parents
The adherence study between 12 and 18 months revealed that there was a difference between the verified adherence and the adherence reported by the parents in the diaries concerning children in the CG in contrast to children in the IG (table 7). The verified adherence was significantly poorer in the CG with one third of the children showing adherence below index 50 which is generally considered a limit for acceptable adherence.
Table 7. Adherence for all children between 12 and 18 months after study start

A  According to the parents:

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>50-150</th>
<th>&lt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group</td>
<td>93</td>
<td>92%</td>
<td>4%</td>
</tr>
<tr>
<td>Control group</td>
<td>89</td>
<td>85%</td>
<td>10%</td>
</tr>
<tr>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

B  Verified adherence:

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>50-150</th>
<th>&lt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group</td>
<td>94</td>
<td>88%</td>
<td>8%</td>
</tr>
<tr>
<td>Control group</td>
<td>72</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>p=0.06</td>
<td>n.s.</td>
<td>p=0.015</td>
<td></td>
</tr>
</tbody>
</table>

6.2.5 The burden of asthma

A global estimation of their children’s asthma was done by the parents with the help of a VAS. In this scale 0 meant no problems and 100 very severe asthma. After 6 months the value was around 30 and after 18 months 22 with no change in the CG and a non-significant trend for better results in the IG (p = 0.08). Between 12 – 18 months from inclusion three children were hospitalized for a total of seven days and there were 0.3 emergency visits / child with no differences between the IG and CG. During this period the parents in the CG reported 3.9 exacerbation days / child, while the IG reported 1.1 days / child (p = 0.05). The use of ICS is reported in table 8, showing that the proportion of children in the CG using relatively high doses of ICS had increased significantly after 18 months.

Table 8. Treatment with inhalation of ≥ 0.4 mg budesonide / day

<table>
<thead>
<tr>
<th></th>
<th>At inclusion</th>
<th>18 months</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group</td>
<td>16%</td>
<td>31%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Control group</td>
<td>11%</td>
<td>59%</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Table 9 reveals that there was a significant reduction in the number of children with persistent asthma in the IG after 18 months.

Table 9. Classification of asthma severity: Asthma symptoms >2 days/week

<table>
<thead>
<tr>
<th></th>
<th>At inclusion</th>
<th>After</th>
<th>18 months</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group</td>
<td>59%</td>
<td>7%</td>
<td>p=0.03</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>71%</td>
<td>29%</td>
<td>n.s.</td>
<td>p=0.008</td>
</tr>
</tbody>
</table>

There is a correlation between adherence and days missed from day care centre as 21% of the children with an adherence index >50 had more than 3 sick days while the figure for children with adherence ≤50 was 57% (p < 0.05).

An economic evaluation was calculated on the assumption that each day home from day care centre because of a child’s asthma meant 1 day away from work for one parent (82% of the mothers worked outside the home). The parents in the IG had to stay at home 2.8 days less per child than the parents in the CG during these 6 months which resulted in 73 days saved altogether. Assuming that the salaries for the health personnel are comparable to the parents and that the parents participation in the group meetings are exchangeable with other reasons for taking a day free from work in the interest of the child (which is permitted in Sweden) the gain for society was 59.5 days, as the health personnel spent 13.5 days carrying out the intervention.

6.3 PAPER IV

The response rate for the PACQLQ was initially 95% and after 18 months 82% with 105 of the initial 119 parents remaining in the study. The analysis of this data was performed from a gender perspective but also for intervention outcome.

We found no significant differences in the three indices at inclusion, six or 18 months for mothers and fathers. On the other hand there were clear differences initially between the genders on individual questions (table 9). The mothers were more bothered by the children interfering with their job or house work (p = 0.007) and they were awakened more often during the night because of the child’s asthma (p = 0.02). They also felt more helpless and frightened when the child had asthma symptoms (p = 0.03). The fathers had (non-significantly) lower scores on the questions of being concerned about their child’s performance of daily activities, whether they were overprotective or were worried about their child being able to lead a normal life.

As a group the mothers had a significant improvement in the activity index after 6 months (p = 0.04) and both genders had very significant improvements after 18 months compared to inclusion. After 18 months 71% (range 54-94) of the mothers and 68% (range 60-78) of the fathers had answered the questions with the highest score i.e. seven. The only question that had a lower score was the one about feeling angry that the child had asthma.

Only the mothers in the IG had improvements in MID indices after 6 months (table 11). These improvements were significant concerning emotional index (p < 0.001) and overall index (p = 0.03).

On individual questions there were significant improvements for the mothers in the IG on the one concerning interference with the job situation (p < 0.001) as well as concerning feeling helpless or frightened (p = 0.009) and being woken at night (p = 0.01).
**Table 10. Paediatric Caregivers’ Quality of Life Questionnaire: Mothers and fathers answers to specific questions at inclusion**

<table>
<thead>
<tr>
<th>Question</th>
<th>Mothers</th>
<th>Fathers</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During the past week…</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. How often did you feel helpless or frightened when your child experienced cough, wheeze or breathlessness?</td>
<td>4.80 (1.73)</td>
<td>5.38 (1.33)</td>
<td>p=0.03</td>
</tr>
<tr>
<td>2. How often did your family need to change plans because of your child’s asthma?</td>
<td>5.59 (1.61)</td>
<td>5.69 (1.44)</td>
<td>n.s.</td>
</tr>
<tr>
<td>3. How often did you feel frustrated or impatient because your child was irritable due to asthma?</td>
<td>6.17 (1.13)</td>
<td>6.41 (0.95)</td>
<td>n.s.</td>
</tr>
<tr>
<td>4. How often did your child’s asthma interfere with your job or work around the house?</td>
<td>5.41 (1.88)</td>
<td>5.96 (1.44)</td>
<td>p=0.007</td>
</tr>
<tr>
<td>5. How often did you feel upset because of your child’s cough, wheeze or breathlessness?</td>
<td>5.42 (1.67)</td>
<td>5.63 (1.60)</td>
<td>n.s.</td>
</tr>
<tr>
<td>6. How often did you have sleepless nights because of your child’s asthma?</td>
<td>4.92 (1.72)</td>
<td>5.43 (1.43)</td>
<td>n.s.</td>
</tr>
<tr>
<td>7. How often were you bothered because your child’s asthma interfered with family relationships?</td>
<td>6.36 (1.21)</td>
<td>6.59 (0.80)</td>
<td>n.s.</td>
</tr>
<tr>
<td>8. How often were you awakened during the night because of your child’s asthma?</td>
<td>4.51 (1.74)</td>
<td>5.16 (1.47)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>9. How often did you feel angry that your child has asthma?</td>
<td>6.36 (1.16)</td>
<td>6.41 (1.16)</td>
<td>n.s.</td>
</tr>
<tr>
<td>10. How worried or concerned were you about your child’s performance of normal daily activities?</td>
<td>5.92 (1.10)</td>
<td>5.80 (1.17)</td>
<td>n.s.</td>
</tr>
<tr>
<td>11. How worried or concerned were you about your child’s asthma medications and side effects?</td>
<td>5.29 (1.58)</td>
<td>5.50 (1.38)</td>
<td>n.s.</td>
</tr>
<tr>
<td>12. How worried or concerned were you about being overprotective of your child?</td>
<td>6.32 (0.95)</td>
<td>6.02 (1.26)</td>
<td>n.s.</td>
</tr>
<tr>
<td>13. How worried or concerned were you about your child being able to lead a normal life?</td>
<td>5.68 (1.44)</td>
<td>5.63 (1.45)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
Table 11. Comparison of gender aspects of change in PACQLQ-index between intervention and control group; after 6 months.

<table>
<thead>
<tr>
<th></th>
<th>Mothers (Activity)</th>
<th>Mothers (Emotional)</th>
<th>Mothers (Overall)</th>
<th>Fathers (Activity)</th>
<th>Fathers (Emotional)</th>
<th>Fathers (Overall)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>Activity</td>
<td>0.85</td>
<td>0.31</td>
<td>-0.04</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>0.67</td>
<td>0.18</td>
<td>0.16</td>
<td>0.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>0.72</td>
<td>0.23</td>
<td>0.08</td>
<td>0.26</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Specific Questions:

<table>
<thead>
<tr>
<th>Question</th>
<th>Mothers</th>
<th>Control</th>
<th>Fathers</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 1</td>
<td>1.16</td>
<td>0.71</td>
<td>0.08</td>
<td>0.50</td>
</tr>
<tr>
<td>Question 4</td>
<td>0.69</td>
<td>0.14</td>
<td>0.07</td>
<td>0.07</td>
</tr>
<tr>
<td>Question 8</td>
<td>1.18</td>
<td>0.60</td>
<td>-0.19</td>
<td>0.81</td>
</tr>
</tbody>
</table>

6.4 PAPER V

The investigation after 6 years had a follow-up rate of 90% with an even distribution between the IG (91%) and the CG (89%).

6.4.1 General results

Of the 54 children (age range 6.7-12.5 years), 29% had no current signs of asthma, 43% exhibited persistent and 28% intermittent asthma. According to the background data 46% now had furry pets at home and 19% of the parents were smokers. The children were slightly overweight and half of them had a confirmed allergy. Forty-three per cent of them had experienced some side-effects of the asthma medication, mostly well-known side effects of the short acting beta-2-agonist (SABA). The burden of the asthma disease on the individual and the healthcare system had been minimal during the 4.5 years since the last follow-up investigation was performed. Only two children had been hospitalized and the emergency visits had been 0.14/year/child. During the last year they had been absent from school due to asthma 1.3 days/child. One third of the children had used ICS < 25% of the time during the previous 4.5 years and 19% had used ICS > 75% of the time. Their lung functions were within normal range (table 12).
Table 12. General results and pulmonary function for the intervention and control groups

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=25</td>
<td>p-value</td>
</tr>
<tr>
<td>Adherence: mean VAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>according to the doctor:</td>
<td>4.6 (4.2)</td>
<td>22.4 (21.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>according to the parents:</td>
<td>8.4 (15.7)</td>
<td>16.4 (24.2)</td>
<td>n.s.</td>
</tr>
<tr>
<td>ACQ score:</td>
<td>0.25 (0.35)</td>
<td>0.34 (0.57)</td>
<td>n.s.</td>
</tr>
<tr>
<td>ECP value microg/l:</td>
<td>19.1 (21.6)</td>
<td>16.3 (14.6)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Phadiatop kU/l:</td>
<td>11.3 (14.0)</td>
<td>15.8 (14.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Eosinophil percent:</td>
<td>6.6 (5.9)</td>
<td>5.4 (4.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Exhaled NO (FENO) (ppb)</td>
<td>31.2 (29.7)</td>
<td>17.2 (10.7)</td>
<td>0.05</td>
</tr>
<tr>
<td>FEV1 (% of the predicted)</td>
<td>98.1 (13.2)</td>
<td>97.4 (21.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>FEV1-reversibility (%)</td>
<td>6.7 (9.4)</td>
<td>5.0 (5.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dry air test (% decrease)</td>
<td>8.6 (9.0)</td>
<td>4.3 (3.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>MEF50 (% of the predicted)</td>
<td>99.4 (22.8)</td>
<td>101.2 (20.2)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Side-effects of medication (%)</td>
<td>41</td>
<td>44</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

100 on the VAS scale indicates no adherence and 0 very good adherence.

The values presented are means (SD)

6.4.2 The results of the IG compared to the CG

Comparison of the IG and the CG showed that adherence, in the doctor’s estimation was better in the IG (table 12), difference=17.8 (95% CI = 26.2 to 9.3) but also that the FENO was significantly higher in the IG, difference=14.0 (95% CI = 0.3 to 27.8) as well as the fall in FEV1 following provocation with dry air =4.3% (95% CI = 0.6 to 8.0).

The rise in pet ownership was 5% in the case of the IG compared to 22% in the CG. The burden of asthma was generally higher in the CG and the difference was significant for number of consultations with a nurse (p =0.007).

The QoL was better for the parents and children in the IG and became significantly so for mothers with respect to emotional index (p =0.05), and overall index (p = 0.04) and for fathers regarding the question concerning worries about side-effects of the medication (p = 0.05).

More children in the IG could manage by taking ICS < 25% of the time during the last year (p = 0.05) and there was no child with severe asthma in this group, compared to 3 in the CG (p = 0.06).

Summarizing the positive answers to the questions relevant to adherence in table 13 depicts a more favorable outcome for the IG (p < 0.001).
Three patients in the IG and none in the CG were considered by the parents as free from asthma but had to start ICS after the examination and likewise, six patients in the IG and two in the CG, who were using only SABA as needed, reinstituted ICS due to the clinical history and lung function tests. The difference between the groups concerning this aspect was significant (p < 0.001). In five of these cases it was only the children’s answers to the PAQLQ that gave a hint that they required ICS as the parents did not identify that their children had problems. Combining positive responses to the questions about chest tightness and difficulties in taking a deep breath identified all the 11 children who needed renewed treatment with ICS.

**Table 13.** Parents’ answers to questions important for adherence aspects.

<table>
<thead>
<tr>
<th>Percentage of parents responding yes to the following questions:</th>
<th>Intervention group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=25</td>
</tr>
<tr>
<td>Does your child take the medication as advised?</td>
<td>82</td>
<td>64</td>
</tr>
<tr>
<td>Did you/your child receive good advice on how to avoid asthma symptoms?</td>
<td>100</td>
<td>88</td>
</tr>
<tr>
<td>Did you/your child follow this advice?</td>
<td>89</td>
<td>68</td>
</tr>
<tr>
<td>Do you consider the positive effects of your child’s medication to be greater than the negative effects?</td>
<td>93</td>
<td>88</td>
</tr>
</tbody>
</table>

6.4.3 **Diagnosis of asthma before or after 2 years of age**

Twenty-eight of the children were diagnosed with asthma after 2 years of age. They exhibited persistent asthma more often than the 26 children who were younger than 2 years at diagnosis (p = 0.006). The time between the first sign of asthma and initiation of ICS was 8.7 months compared to 3.2 months for the younger children (p = 0.007). In addition, the ICS treatment was more intense for the older children (p = 0.009) and according to their parents, their asthma was more severe (p = 0.05).

The QoL of life for the mothers of the older children was worse with respect both to the emotional (p = 0.03) and overall index (p = 0.03) and furthermore, the mean ECP value was higher (p = 0.007) and they were more overweight (p = 0.05). On the other hand, the adherence of the older children was better, according to the parents (p = 0.04).
7 DISCUSSION

The discussion is divided into two main parts: firstly methodological considerations and secondly interpretations and implications of the findings. Each part is further analysed according to the five papers respectively with discussions of different themes.

7.1 PAPERS I AND II: METHODOLOGICAL CONSIDERATIONS

7.1.1 Prevalence and incidence

Two of the epidemiological studies in paper I and II are based on a retrospective longitudinal, register study of medical records and cover all children 0-6 years of age in 1998 (and all children 1-6 years, in 1999) in a specific region who were seen because of asthma during one year. All the out-patient clinics had computerized medical records and each visit was given a diagnosis code which enabled prevalence estimations.

In practice this was a cross-sectional study given the period prevalence of asthma in the population over the course of one year. Therefore it is possible to compare this prevalence figure with the prevalence found in the cross-sectional study performed with the help of a WQ in early 2000. An obvious loss in precision with this comparison is that the medical register study does not cover the first two months of year 2000.

The medical records in the children’s hospital covering this time period were not computerized but all visits with relevant diagnoses could be identified and thus the out-patient visits and the admittances to the hospital during the years of interest could be estimated.

There is a risk as many doctors were involved in diagnosing the children and hence, wrong classification might have occurred. This is of course a potential risk with the data delivered from the GPs as well. As 86% of the children with an asthma diagnosis were controlled by paediatricians and thus further evaluated, the risk for miss-classification is small.

The calculation of the incidence during 1998 was based on the presumption that every child with a new asthma diagnosis was reported, but afterwards it turned out that in some centres there had been a misunderstanding and some children were reported as newly diagnosed when they visited the clinic for the first time, despite having received the diagnosis earlier.

This is an obvious bias of unknown magnitude and could in part explain the rather high figure (2.2%) found in our study compared to other studies (61).

7.1.2 The DBH WQ

The DBH study covering the whole county of Värmland with 14 077 children aged 1-6 years had a response rate of 79%. We performed the medical study in the southern and more urban part of Värmland where 6 295 of the children lived. The response rate in this part was 75%
which is acceptable and should give good precision. An analysis of the medical records to find the prevalence of asthma among the non-responders revealed that this was not significantly different from the prevalence according to the DBH WQ or to the prevalence in the medical records of those who answered the WQ. This confirms that the WQ is valid as a prevalence estimator.

7.1.3 The complementary WQ
The complementary WQ, distributed to those who were asthmatics in 1999 either according to the medical records and/or the DBH WQ, can be regarded as a hypothesis-generating study. It has a qualitative approach as our intention was to find possible explanations for the discrepancies between the results of the two methods used to define the prevalence of asthma. Therefore the problem with recall bias (as this WQ was answered in year 2003) is not that great as the exact percentage of responses to the different questions is less important than the proportions between the different groups. The positive side to sending out the WQ in 2003 was that we received data on the further development of the children’s asthma for comparison. The response rate to this WQ is rather good considering the fact that it was distributed several years after the initial investigation.

7.2 PAPERS III – V: METHODOLOGICAL CONSIDERATIONS

The intervention study can be classified as a prospective, randomized treatment study with per protocol design but at the same time it is also a cohort study where children selected from a population on the grounds of a high risk for developing persistent asthma are followed for six years. The strength of the randomized treatment study, and with the cohort study as well, is that very few of the potential participants declined inclusion (6/66) and that the follow-up rate is high (90%). Furthermore, neither the background data, nor the outcome for the children who did not participate differed much from the children in the study which means that we can give a realistic picture of asthma development in this cohort of children.

The weakness of the study is the relatively low number of participants which potentially could result in less precision. As was described earlier (see Methods and Subjects) the reason that we decided to stop inclusion at 60 was that more participants would take over two years to recruit according to our estimations and that this could result in practical difficulties in keeping the same treatment protocol etc. We also had a power estimation concerning the WQ on QOL saying that this number would give a power of >80% (176).

Another weakness is that the intervention was not blind to the participants or the investigators. One solution to this problem would be to have the control group in another clinic. This however, would introduce another problem, as different clinics may have
different traditions on how to inform their patients and parents. To blind the participants is practically impossible in a setting like this and would be experienced as artificial by both staff and families. We considered it important to have the same doctors and nurses providing the ordinary management of the asthma for comparison.

The WQs used are validated and have been used in many other clinical studies (176) (178) (182) with the exception of the ACQ test that is only validated for adults (183) (184). According to a personal communication (E. Juniper) a pilot study has shown that this questionnaire is also possible to use in school children if the questions are answered together with the parents as we did in our investigation.

Potential confounders such as different socio-economic or educational backgrounds of the parents in the IG and CG have been studied with the help of a new WQ to the parents concerning these factors. No significant differences were found concerning these aspects (see table 5 in Results). There was a significant difference in pet ownership between the groups from the start. It is hard to see that this could influence the results of the study and, anyway, this difference was eliminated at the follow up.

7.3 PAPERS I AND II: INTERPRETATIONS AND IMPLICATIONS OF FINDINGS

7.3.1 The prevalence of asthma

We found a prevalence of asthma in pre-school children of just below 5% in our medical record study covering 1998-1999. This is in accordance with a similar study from Italy (57) but significantly lower than the prevalence of nearly 6% found in the WQ investigation in the same area in 1999 and lower than the prevalence of 7% at 4 years noted in a prospective study from Sweden (85) and of 11% at 7 years of age ever having been diagnosed with asthma in yet another Swedish investigation using medical records (185). A similar prevalence to ours is reported from Germany (84), while WQ estimations from England and Australia found a substantially higher prevalence of asthma at around 20% in pre-school children (25) (42) (63).

There is one Swedish study showing a definite rise in prevalence in school-children up to 1991 (89) and one from Great Britain in pre-school children demonstrating the same trend during the nineties (25) in pre-school children. Our relatively low figure in the medical records study might be an example of the new trend noticed in several European countries of a stagnation or even decline in prevalence (70). There is, however, no earlier Swedish study that compared prevalence on two different occasions in pre-school children. As the figure was the same in 1998 and 1999 (and also in Italy) the method used seems to be valid in spite
of difficulties with the definition of the asthma diagnosis in these age groups, and the most probable explanation is that a study based on medical records gives a lower prevalence than an investigation using a WQ. This is probably due to the fact that many patients who feel well do not visit their physician every year and thus are not registered.

### 7.3.2 Comparison of different ways of measuring prevalence

The diagnosis of asthma is obviously difficult and uncertain during the first 2 years due to problems in defining the disease and a high remission rate (33) (35), but then stabilizes during the following years according to our results both in the medical records and in the WQ study. If we used clinically diagnosed asthma registered in medical records as the reference point a validation of the DBH WQ revealed a relatively high and, at least for children aged over two, constant sensitivity and specificity, but the positive predictive value was low.

In our first paper we present a method for the analyzing procedure that has seldom been applied before and in our second paper we present a unique method for comparing two methods of prevalence estimation (medical records and WQ) using the personal identification number of each patient. A similar comparison of the different prevalence figures has been performed earlier in adults in Sweden but they used another method to identify the clinical asthma prevalence (58). They found that the prevalence in the medical records was less than half that reported in the WQ and concluded that under-diagnosis of asthma is common by physicians.

According to our study, however, paediatricians seem to be more alert to diagnosing asthma among their patients. The individual patient identified by the different methods was however the same in only half of the cases. Including non-responders with asthma the DBH WQ identified only 54% of the children with medical records of asthma and gave simultaneously a 40% false positive rate of diagnosis. An analysis of the purchase of asthma medication in the USA gave similar findings (56). Only 35% of those children reported by their parents as being asthmatics were associated with the purchase of asthma medication and 45% of those whose parents had purchased such medication were not described as having asthma.

The conclusion of that study was that relying on parental reports may lead to underestimation of the prevalence of serious asthma. This is also in agreement with our present results where only 2/3 of the parents of the children at high risk for persistent asthma answered the DBH questionnaire. This reflects a major drawback with WQ studies, namely that the parents of children with severe diseases are often involved in studies and tend not to answer other questionnaires to the same extend as parents of healthy children.

The question about doctor’s diagnosed asthma gives the highest value of the Youden’s index (0.744), i.e. is the most relevant question if one wishes to find patients with asthma of clinical importance and is in accordance with the literature (64) (65) (66). The question about
“wheezing ever” has a higher score (0.723) in our study than the question concerning “wheezing during the last 12 months” (0.704), and the question about “coughing during the night” has a much lower value (0.209) as expected.

7.3.3 The complementary WQ

The answers to the complementary WQ gave indications as to why the parents had answered the DBH WQ the way that they did. The parents in the false negative group obviously thought that their children exhibited very mild respiratory problems in 1999 and were not aware that their child had been diagnosed with asthma. In the case of the false positive group other mechanisms seem to have been operating. These children could have been prescribed asthma medication earlier, which their parents continued to give them, without consulting a doctor. Some patients treat themselves with medications prescribed earlier or even to relatives or friends. This is one important reason for under-diagnosis of asthma in connection with analysis of medical records. Furthermore, the DBH WQ question about doctor’s diagnosed asthma did not specify whether the diagnosis was current or ever asthma. This fact can partly explain the difference between the two methods of prevalence measurements as many parents probably interpreted the question as ever. However, in some cases the parents might have misunderstood long-standing cough as asthma and thus there is a risk of overestimating the diagnosis.

7.3.4 Estimation of children in need of asthma treatment

The majority of children in the congruent group, as well as those in the non-responders group with asthma, were treated with SABA and ICS and probably had asthma. Our conclusion was that those requiring treatment with ICS constitute a core group of asthmatic children and even if there probably is a certain amount of over-treatment with SABA, most children receiving these drugs (and especially those who had seen a doctor for wheezing) could be labelled as asthmatics. This is the reason for suggesting that at least 40% of the false negative and the false positive groups and 80% of the congruent group and the non-responders were actually asthmatics needing treatment. This adds up to 271 children altogether, or 4.4% (95% CI= 3.9-4.9) of the total study population. As 44 of these (belonging to the false positive group) were not identified in the medical records this explains why assessment of the prevalence of asthma based on the DBH WQ appears to be adequate as these 44 practically compensate for the 50 children in the false negative group.

If one speculates that among the 1599 children whose parents did not answer the WQ there were probably a number receiving anti-asthmatic treatment who had not visited a doctor during 1999, and if we add these to the 271 children above, we could end up very close to the prevalence figure found in the medical records.
As noted above (see papers I and II: Methodological considerations) our incidence was about double that noticed in studies with school-children, but similar to findings in a study with children 0-7 years of age (86). This is probably due to many preschoolers diagnosed with asthma growing out of their symptoms within a couple of years.

7.3.5 The burden of asthma

The issue of the burden of asthma is discussed in the papers I and II from the point of view of visits to an out-patient clinic and admittances to the hospital but we do not cover the total health care use for other problems than asthma by the asthmatic children. A study from USA found that asthmatic children had a high utilisation rate due to multiple visits for otitis, sinusitis and allergic rhinitis (26) (102).

In the county of Värmland a paediatrician is supposed to see pre-school children with asthma at least once and traditionally most children with asthma are followed by paediatricians working in outpatient clinics (167). After children had been hospitalised with their first asthma episode they were in most cases referred to and followed by a paediatrician in the outpatient clinic, with good continuity. The GPs diagnosed relatively few young children with asthma and only 1/3 of the patients who were given the diagnosis for the first time by a GP were referred to a paediatrician. In spite of this, 94% of the asthmatic children had been examined by a paediatrician as they had been hospitalized at least once, or had been to the emergency clinic.

We have noticed that the admittance rate has decreased during the last 10 years and nowadays very few school-children are hospitalized due to asthma (103). The average duration of the hospital stay of just over one day was very low compared to other studies (103) (186) and the readmission rate probably will rise if the durations are further reduced. Children living a long distance from the hospital stayed longer for safety reasons. The rate of first admissions and readmissions are the same as that reported from Norway concerning this age group (103). The relatively low admittance rate is probably due to a more widespread use of ICS as an investigation revealed that admittance rate was 9/1000/y in a community were 11% were on maintenance therapy while the rate was 3/1000/y in another were 33% had ICS (187). Most often the first admission to the hospital is in connection with the debut of the asthma symptoms and for the majority this first admission is also the last; probably due to better follow up and treatment than before (106) (186).

The frequency of visits to out-patient clinics was relatively constant throughout the pre-school years, probably reflecting the unchanging prevalence of asthma in children 2 years of age and older, documented in both the DBH WQ and the medical records study. In contrast to this, the rate of hospital admissions is very high during the first years of life and practically reduced to zero by six years of age, in agreement with other studies (63) (103) .
Around one third of young children with asthma require many outpatient clinic visits and a few need several hospital admissions and this is the same proportion of asthmatics as those who were characterised as having a high risk for persistent disease in our study and, likewise, the same figure has been found in follow-up studies (35) (188). Together with local traditions and parental knowledge about the disease the admission and readmission rate is the net result of prevalence, disease severity and quality of care in the community.

7.4 PAPERS III-V: INTERPRETATIONS AND IMPLICATIONS OF FINDINGS

The issue of the burden of asthma on the individual families and the health care system is discussed in all these papers, but from different perspectives. In paper III the intervention study is followed for 18 months and the effect of asthma on the children’s lives is reported in the form of medication requirement, the need to stay home from day care centre, and the need for hospitalization and emergency visits. In paper IV the effect on the QoL for parents is investigated and, finally, in paper V we try to summon up what has happened during a 6 year follow-up period.

7.4.1 The intervention study

The recruitment period for the intervention study was shorter than expected due to a relatively high incidence rate. The follow-up rate of around 90%, after both 18 months and six years, is good and enables us to draw conclusions. The background data revealed that the education level was lower than expected compared to the mean in Sweden and our part of the country (189). The proportion living in own houses is higher than in general, but normal for our region. It is interesting to compare this socio-economic background with reports from the United States which also find that the asthma prevalence and morbidity is inversely related to income in all racial/ethnic groups (125). One factor associated with participating in validation studies is high socioeconomic status of the family and, thus, there are selection biases involved in studies that need close cooperation with the families involved (190). The attendance of the first three group discussions was acceptable but less than 40% participated in the fourth meeting and thus we think that the effects of the intervention were conveyed during the initial meetings. It is when the parents are emotionally involved and even perhaps a little shocked, that they are most susceptible to information (191). Consequently we now have decided to use only three meetings in close connection to diagnosing the child in our treatment plan for asthmatic children.
7.4.2 The burden of asthma

The parents graded the global effects of their children’s asthma around 25 on a 100 point VAS during the period 6-18 months after inclusion with no differences between the IG and CG. This relatively low rating of asthma related problems is probably due to their children having low numbers of hospitalizations and emergency visits. There was a significant difference between groups concerning persistent asthma and the decrease in the severity of the asthma symptoms was significant only in the IG.

During the last 6 months before the follow-up the children in the IG had only ¼ of the exacerbation days of the children in the CG, in spite of the fact that 60% of the children in the latter group were said to use high doses of ICS compared to 30% in the IG.

The economic calculation presented in the results section, based on the lower number of exacerbation days, probably underestimates the effect of the intervention as we only had data for the last 6 months of the study period. Since we only have three meetings now, our costs are reduced giving a larger saving.

7.4.3 Adherence issues

The aim of the intervention study was primarily to improve adherence. Here we can conclude that we succeeded. The parents view on issues important for adherence was significantly better among the parents in the IG and most importantly the verified adherence was better and significantly so for those considered to have poor adherence. It is interesting to notice that even the mean adherence index in the CG is better than in most studies with different types of interventions, for example one using the same adherence index (192). This means that conventional care with individual information and education and a written action plan can have a relatively good effect if the patients come for regular follow-ups.

The adherence noted by the parents either in the diaries or on the VAS differs much from the verified adherence and initially also from the adherence estimated by the doctors on a VAS. Both tend to underestimate the problem of poor adherence. After 6 months the ratings on the VAS had converged and there were no significant differences between the IG and CG except that the doctors’ rating of very good adherence after 18 months was in favor of the IG (p = 0.02).

The finding of higher doses of ICS in the CG mentioned above is probably a result of these parents denying that they do not follow the prescription. The reluctance to admit non-adherence can lead to the doctors prescribing higher ICS doses as they tend to attribute the inadequacy of treatment to a poor effect of the ICS instead of recognizing the patients’ non-adherence (4).

Obviously, the doctors in our study had very low expectations concerning the adherence at inclusion while the parents exaggerated the way they gave ICS to their children, something that is well-known from literature (132). As the parents and the doctors got to know each
other better the parents gave more accurate reports and after 18 months their estimation was even more realistic than the doctors’ according to the results of the objective adherence measurements performed. This underlines the importance of a long-term, stable continuity in patient - physician relations.

7.4.4 Gender aspects on QoL

Regarding the burden of asthma as presented by the parents in response to the PACQLQ in paper IV we can conclude that this WQ can be used independently by mothers and fathers as the answers concerning the main indices did not differ. This is also the conclusion in another Swedish study (193). The original validation studies of this WQ were performed with very few fathers as responders (194) (195).

Still, it was interesting to see that the answers to individual questions could differ significantly between the genders at inclusion. Mothers were generally more disturbed both concerning the job situation and by being awakened during the night, and they were also more emotionally influenced as they felt more helpless and frightened. These differences had leveled out after 6 months and after 18 months the values were close to 6.5 on 7 grade scale.

When evaluating answers to this WQ you must take into consideration when the test is performed as there is an obvious ceiling effect when the parents are experienced and the children are well treated (196) (197). The gender difference noted in the responses at inclusion reflects the increased strain on mothers when their child gets asthma shown in previous studies (198), especially in young mothers and in single-parent families (194) (199). We could see that mothers seemed to be preoccupied with and took responsibility for the here-and-now situation while fathers tended to be more concerned about the long-time consequences of the chronic disease. Fathers in Sweden today are expected to participate much more actively in their children's everyday life than was the case for previous generations. According to a recent investigation they have the intention to take their responsibility, but half of the fathers stated that they did not have sufficient time for the child (200).

Perhaps the most interesting finding in this study was that only the mothers in the IG had significant improvements in all indices and especially on the key questions after 6 months. The fathers in the IG had no changes while the fathers in the CG slept even better, so the difference on this question became clinically relevant. Obviously the mothers in the IG felt more secure and confident and our interpretation is that the fathers in the IG took more responsibility for the well-being of their children and the treatment of the asthma. We suggest that the equalization of the parental roles in the IG is one possible explanation for the improved medication in this group which in turn led to fewer exacerbations.
7.4.5 The follow-up study

There are many important lessons to draw from the results of the 6-year follow-up presented in paper V. One is that children receiving the usual care and treatment of asthma in Sweden today, such as the children in our CG, have a very good prognosis with respect to preservation of lung function. The burden of asthma has changed, exacerbations and emergency visits are few in comparison with other reports (124) and hospitalization is rare. However, 70% of the children are still classified as asthmatics after six years which underlines the importance of good initial care and further treatment and follow-up for children who are at risk of developing persistent asthma (47).

As a group the children who declined to enter the intervention study differed somewhat from the participants as they were younger, most of them had a confirmed allergy and none had furred pets at home. Their young age probably played a role in the parent’s decision not to participate, as the investigation included several extra blood tests as well as SPT. The children in this group seemed to have the same outcome as the study group but as the number was small no statistical comparisons were performed.

7.4.6 Differences between the IG and the CG

There were still differences in favour of the children in the IG compared to the CG. The outcome was consistently better in almost all respects and became statistically significant for several of the parameters registered, such as estimated adherence according to the doctor, parents’ answers to questions of relevance for adherence, use of lower ICS-doses, need for consultations with the nurse and above all for the QoL of the parents.

On the other hand there were some drawbacks to our intervention since 28% of the children in the IG needed renewed administration of ICS after the examination versus 8% in the CG. Obviously the parents in the IG underestimated the severity of their children’s asthma symptoms and the conclusion we must draw is that our program for initial support may cause the parents to feel so secure that they do not recognize the recurrence of asthma. In order to prevent this we have to schedule follow-ups even after the symptoms appear to have disappeared.

Is the better QoL of the parents in the IG due to their parents underestimating their children’s asthma symptoms? In order to answer this we analyzed the results when excluding the 11 children that had had to reinstitute ICS. We found that the overall index of the mothers decreased so the difference to the mothers in the CG was no longer significant (P=0.06). On the other hand the difference between the fathers rose from p=0.11 to p=0.056. Our conclusion is that the difference in QoL is real. However, the difference in the number of children who could manage with ICS < 25% of the time disappears if we eliminate these 11 children.
7.4.7 It is important to talk with the children alone

Moreover, we learnt that it is important to talk to the children separately when they have reached the school-age since they tend not to tell the whole story in the presence of their parents, probably in an attempt to not trouble them. In many cases it was only the children’s answers to the PAQLQ that revealed that the child was in need of ICS, something that was later confirmed by the evaluation of the lung function and a thorough examination. The importance of listening to what children with chronic diseases have to say, to get a truer picture of their situation, has been stressed both with adolescent asthma (53) and in other chronic diseases like cerebral palsy (201), juvenile chronic arthritis and diabetes (98). However, the answers to the ACQ were of no help in this respect.

7.4.8 Further findings of interest

Children who were diagnosed before two years of age had a better prognosis, perhaps due to the fact that they had ICS introduced much earlier than the older children. Another explanation could be that the younger children had less severe asthma disease.

Intermittent ICS treatment, governed by the early use of relatively high doses of ICS in case of a respiratory infection or signs of an exacerbation, had been practiced by 80% of our children with a good outcome as far as we could find.

Nearly half of the children had experienced some side-effects of the medication and 1/6 had reported neuropsychological changes when they were on high doses of ICS which were reversible when the doses were tapered (202).

7.4.9 A national survey of hospital admittances with asthma

In our region we now have incorporated the first three group discussions in our routine management of newly diagnosed asthma in the pre-school ages with a high risk for persistent asthma. A recent survey of paediatric healthcare in Sweden from 2004 revealed that our region has the lowest hospital admittance rate for asthma in children older than two years of age in the country (203). The number of hospital admittances varied from 18/10 000 children/year in Jämtland to 3 in Värmland with a mean of 9 as in Kronoberg. It cannot be explained by better economic resources or more/less hospital beds or lower prevalence of asthma as these are average for the country (Paper I). I have performed an analysis, based on figures from Apoteket AB (the national pharmacy), of the prescriptions of ICS to children (table 14) in the different parts of Sweden during the same year as the hospital admittances were measured. The result was that the amount of prescribed ICS varied widely in different parts of the country (from 1.29 to 3.50 DDD/child) and also that there was no relationship between the amount of ICS that has been delivered from the pharmacy and the rate of hospital admittances because of asthma. This is probably explained by different adherence
rates analogous to our finding that children in the CG had higher doses of ICS, but in reality they did not actually use it to the same degree as the children in the IG.

My conclusion is that this survey speaks in favour of our way of managing newly detected asthma with initial intense support and information.

**Table 14.**
Inhaled Corticosteroids: Defined daily doses in relation to number of children 0-16 years of age living in the region 2004.

<table>
<thead>
<tr>
<th>Region</th>
<th>DDD/children 0-16 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Västerbotten</td>
<td>3.50</td>
</tr>
<tr>
<td>2. Dalarna</td>
<td>3.09</td>
</tr>
<tr>
<td>3. Uppsala</td>
<td>2.57</td>
</tr>
<tr>
<td>4. Norrbotten</td>
<td>2.48</td>
</tr>
<tr>
<td>5. Jönköping</td>
<td>2.24</td>
</tr>
<tr>
<td>6. Jämtland</td>
<td>2.23</td>
</tr>
<tr>
<td>7. Stockholm</td>
<td>2.21</td>
</tr>
<tr>
<td>8. Södermanland</td>
<td>2.06</td>
</tr>
<tr>
<td>9. Skåne</td>
<td>2.05</td>
</tr>
<tr>
<td>9. Västernorrland</td>
<td>2.05</td>
</tr>
<tr>
<td>10. Blekinge</td>
<td>1.99</td>
</tr>
<tr>
<td>11. Kronoberg</td>
<td>1.92</td>
</tr>
<tr>
<td>12. Värmland</td>
<td>1.87</td>
</tr>
<tr>
<td>13. Gävleborg</td>
<td>1.84</td>
</tr>
<tr>
<td>14. Östergötland</td>
<td>1.78</td>
</tr>
<tr>
<td>15. Västra Götaland</td>
<td>1.76</td>
</tr>
<tr>
<td>16. Gotland</td>
<td>1.71</td>
</tr>
<tr>
<td>17. Halland</td>
<td>1.69</td>
</tr>
<tr>
<td>18. Kalmar</td>
<td>1.58</td>
</tr>
<tr>
<td>19. Västmanland</td>
<td>1.42</td>
</tr>
<tr>
<td>20. Örebro</td>
<td>1.29</td>
</tr>
<tr>
<td>An average for Sweden</td>
<td>2.07</td>
</tr>
</tbody>
</table>
8 CONCLUSIONS

Compared to doctor diagnosed asthma registered in medical records the ISAAC questionnaire gives an acceptable prevalence estimate for children older than 2 years of age, although in half of the cases the individual child is not identified.
Extra support and information in the form of group discussions for parents of children with newly diagnosed asthma improves adherence, decreases the risk of exacerbations during the first years and contributes to a better quality of life for the parents during the coming six years. It also saves society money.
The mother takes a greater responsibility for the well-being of the child with asthma than the father does. Group discussions probably result in an equalization of the parents’ roles in handling their child’s asthma.
To get a better understanding of the severity of asthma it is important to talk with school-children alone and not rely completely on what the parents say.
Most children with a high risk for persistent asthma can be successfully treated with intermittent ICS.
It is important to have scheduled follow-up appointments after the termination of ICS treatment as the relapse rate is high.
Today, children with asthma should not have to be hospitalized (with the exception of the first wheezing episode) provided that they receive adequate information, support and treatment.
9 SAMMANFATTNING PÅ SVENSKA

Astma är den vanligaste kroniska sjukdomen bland barn och den kan påtagligt påverka både barnens och föräldrarnas livskvalitet. Under de senaste decennierna har astmasjukdomen ökat i de flesta länder men det finns studier som tyder på att prevalensen (hur många i befolkningen som vid en vid en viss tidpunkt har sjukdomen) visat en tendens att stabiliseras de senaste åren. Orsakerna till ökningen respektive stabiliseringen är oklar. För att mäta prevalensen har man vanligen använt sig av befolkningsbaserade frågeformulär som validerats med hjälp av kliniska undersökningar av ett urval. En annan metod är att studera journaldata och registrera läkardiagnosticerad astma. En jämförelse mellan dessa båda metoder att uppskatta vanligheten av astma inom en region har aldrig genomförts när det gäller barn. Målsättningen med våra första två undersökningar var dels att fastslå hur ofta diagnosen astma sattes av läkare i södra Värmland, dels att jämföra denna prevalens med den vi fick fram i en enkät till samtliga föräldrar till barn yngre än 7 år i samma område. Vi ville också undersöka hur mycket astmasjukdomen belastade sjukvården i form av läkarbesök och sjukhusinläggningar. Förutsättningen för att genomföra dessa studier var att samtliga allmän- och barnläkarinläggningar hade datoriserade journaldata och att vi hade tillgång till Barnungdomsmedicinska klinikens arkivdata.

Dålig följsamhet till råd om medicinering och hur man bör leva för att undvika symptom är ett av de största problemen när det gäller behandlingen av kroniska sjukdomar i allmänhet och astma i synnerhet. Vanligen ligger följsamheten under 50 % och det har visat sig att allmän upplysning om sjukdomen och utdelande av skriftliga råd har dålig effekt om man följer upp patienterna under en längre tid. Vi ville genomföra en undersökning där vi jämförde vanligt omhändertagande av förskolebarn som just fått astmadiagnos och som hade ökad risk att få bestående astmabesvär med en intervention i form av diskussioner med 4 föräldrar i grupp i nära anslutning till att diagnosen hade satts. Mötena skulle innehålla ren information om astmasjukdomen men då huvudsakligen i form av att läkaren/sköterskan besvarade frågor från föräldrarna. Metoden avsåg också att utgå från föräldrarnas uppfattning av vad astmasjukdomen innebär och att de kunde lära av varandras erfarenheter om hur man kan hantera omhändertagandet. Vi avsåg också att, med hjälp av närvaron av en kurator vid några möten, fänga upp den oro som vi misstänkte att föräldrarna kände och ge dem aktivt stöd i hur man kan hantera denna. En målsättning var att få papporna engagerade i omhändertagandet av astmasjukdomen. Avsikten var att följa upp barnen under flera år. De metoder vi använt oss av vid dessa undersökningar har varit studier av journaldata, analyser av olika enkätsexperter beträffande bakgrundsfaktorer, andningsbesvär, astmadiagnos och livskvalitet. Vidare har vi undersökt barnen kliniskt, tagit laboratorieprov och genomfört olika analyser av lungfunktionen.
Resultat:

**Studie 1. Astmaprevalens och belastning på sjukvården 1998.**

Av 9410 barn i åldrarna 0-6 år visade sig 4,5 % ha fått astmadiagnos av en läkare. Uppföljningen av dessa barn skedde i 8/10 fall inom öppenvården. Knappt 1/3 av nyupptäckta fall av astma uppfyllde kriterier som tydde på att de hade hög risk att få behålla sjukdomen upp i vuxen ålder. Om man jämförde förhållanden med 1988 hade inläggningarna (och fr.a. återinläggningarna) på sjuhus p.g.a. astma minskat.

**Studie 2. Jämförelse mellan kliniskt diagnosticerad astma med föräldrars uppfattning av astmadiagnos via en enkät.**

Enkäten besvarades av 75 % av föräldrarna och där uppgavs att 5,9 % av barnen fått astmadiagnos av en läkare. En parallell journalstudie fann att 4,9 % fått diagnosen. Med hjälp av ett nytt frågeformulär till dem som vi antingen via journaldata funnit ha fått astmadiagnos eller som föräldrarna angav att de fått diagnosen astma uppskattade vi att 4,4 % av barnen var i behov av medicinering p.g.a. astma. Om vi utgick från att journaldiagnos var den rätta hade enkäten en sensitivitet (förmåga att identifiera de sjuka) på 77 % och en specificitet (förmåga utesluta de friska) på 97,5 %. I åldersgruppen 1-2 år var sensitiviteten endast 22 %. Enkäten identifierade 54 % av de barn som hade journaldiagnos samtidigt som 40 % av dem som enligt enkäten hade astmadiagnos inte hade diagnosen enligt journal.

**Studie 3. Resultat av gruppdiskussioner med föräldrar till nydiagnosticerade astmabarn.**

I denna prospektiva studie av 60 barn i åldrarna 3 månader - 6 år var efter 18 månader 88 % möjliga att utvärdera. De 32 föräldrapar som randomiserades till interventionsgruppen (IG) hade 70 procents närvaro i de 3 första träffarna men endast 39 % i mötet efter 6 månader. Det var lika många pappor och mammor som deltog. Föräldrarnas syn på frågor angående följsamhet förändrades i högre utsträckning i positiv riktning i IG jämfört med kontrollgruppen (KG). Den uppmätta följsamheten mellan 12 och 18 månader var också signifikant bättre i IG där medelvärdet var 94 och endast åtta procent hade dålig följsamhet (< 50) jämfört med att 30 % i KG hade dålig följsamhet. Barnen i IG hade också påtagligt färre dagar då de fick stanna hemma från daghem/skola p.g.a. astma under samma period jämfört med KG (1,1 dagar jämfört med 3,9). Om man räknade ut hur många fler dagar föräldrarna i KG fick stanna hemma för att ta hand om astmasjukt barn och jämförde med hur många arbetsdagar personalen använde för gruppsamtalen fann man att samhället gjorde en ekonomisk vinst med vår intervention.

**Studie 4. En analys av hur mammor och pappor besvarar en enkät angående livskvalitet vid astma hos barn.**

Papporna och mammorna besvarade separat ett frågeformulär angående livskvalitet hos föräldrar till barn med astma (E. Juniper’s PACQLQ) vid 3 tillfällen, dels då barnen gick med i studien, dels efter 6 månader (då föräldrarna i IG deltagit i 4 träffar), dels efter 18 månader.
Formuläret har 13 frågor och svaren sammanställdes till ett index angående effekter av astman på aktiviteter, ett index angående emotionella aspekter och slutligen ett totalindex omfattande alla frågor. När det gällde dessa övergripande index fanns inga könsskillnader vid något tillfälle. Däremot var mödrarna vid första frågetillfället mycket mer störda på natten, de kände sig mer oroade och hjälplösa och barnens astma störde deras yrkesliv i mycket högre grad än vad fäderna uppgav. Efter 6 månader hade mammorna i IG förbättrat alla sina index signifikant, däremot hade inte mammorna i KG några betydelsefulla förbättringar. Papporna hade inga signifikanta förbättringar och papporna i IG hade i jämförelse med papporna i KG t.o.m. en påtaglig försämring när det gäller frågan angående nattsömn. Efter 18 månader fanns det inga skillnader och samtliga svar låg nära det mest positiva svarsalternativet.

Studie 5. Resultatet av en uppföljning efter 6 år.

Vid denna uppföljning kunde 90 % av de ursprungliga deltagarna undersökas. Vi fann att knappt en tredjedel inte längre hade några tecken till astma, 28 % hade intermittent astma och 43 % hade astma med kontinuerliga besvär. Det fanns fortfarande påvisbara skillnader mellan IG och KG. Barnen i IG hade klarat sig med lägre doser av inhalerat kortison, de hade haft färre kontakter med sjuksköterska och ingen i denna grupp hade svårastma jämfört med 3 i KG. Föräldrarna i IG hade förbättrat en mer positiv syn på följsamhetsfrågor och de hade en högre livskvalitet. Fler barn i IG jämfört med i KG behövde återinsätta kortisonbehandling i samband med uppföljningen. Detta behov framkom bl.a. genom frågor direkt till barnen. Olika undersökningar av lungfunktionen visade normala resultat. Intermittent användning av kortisoninhalationer hade praktiserats av 81 % av alla barn. Barnen hade varit väldigt lite sjuka de senaste 4,5 åren och endast 2 barn hade behövt läggas in 1 dag var p.g.a. astma. Hälften av barnen hade diagnosticerats före 2 års ålder och de hade en bättre prognos än de som var äldre när de gick in i studien.

Slutsatser

Den enkät som besvarades av föräldrarna gav en acceptabel, om än något högre, prevalenssiffra jämfört med en baserad på journaldata, åtminstone för barn äldre än 2 år. Frågorna är tidigare bara validerade för äldre barn och en klassisk validering med klinisk undersökning av fall och kontroller borde genomföras beträffande förskolebarn. Diagnosen astma i denna ålder är svår att fastställa eftersom många barn har övergående astmaliknande symptom i samband med förkyllningar. Detta kan vara en förklaring till att de barn som identifierades med våra två metoder bara i hälfsten av fallen stämde överens. Vår prevalens är något lägre än den som andra har funnit för något äldre barn i Sverige och motsäger inte att den tidigare ökningen av astmaprevalensen även i Sverige har stagnerat. Liksom andra visat kan de flesta astmabarn nu med framgång behandlas inom den öppna vården med inhalation av kortison och behovet av inläggningar på sjukhus har nästan eliminerats från ett eventuellt initialt vårdtillfälle i samband med att de får diagnosen.
Vår undersökning tyder på att det kan vara väsentligt att tidigt diagnosticera astma och sätta in anti-inflammatorisk kortisonbehandling där så är motiverat. I majoriteten av fallen förefaller det vara tillräckligt med intermittent behandling enligt de riktlinjer vi praktiserat i denna studie. En kliniskt viktig lärdom är att det är väsentligt att inte nöja sig med att fråga föräldrarna utan att också vända sig direkt till barnen. De kan då ge en annorlunda och troligen sannare bild av hur mycket besvär astman orsakat.

Vår metod med intensiv information och stöd i gruppförråder vars barn nyligen fällt diagnosen astma visade sig ha en mycket god och bestående effekt både på synen på att följsamhet är viktig och på den faktiska uppmätta följsamheten. Sannolikt kan det vara ett resultat av detta att barnen i IG hade mindre sjuklighet vid 18-månaderskontrollen. Vi fann också att mammorna i IG fick en mycket bättre livskvalitet efter gruppundervisningen.

Papporna i IG tog oftare hand om barnen på nätterna och därmed visade de troligen ett större ansvar för barnets situation. Den ökade jämnheten mellan könen och samstämmigheten i synen på hur man skulle sköta astman i IG kan vara en rimlig förklaring till hur effekten av gruppmötena uppstod. Efter 6 år kunde vi se en klart högre livskvalitet hos föräldrarna i IG. Barnen hade haft lägre sjukvårdskonsumtion och lägre kortisondoser. En trolig negativ effekt av vår intervention var att föräldrarna i IG vid 6-årsuppföljningen i högre omfattning inte uppmärksammade att deras barn var i behov av kortisonbehandling. Detta tolkar vi som att de kanske blivit alltför trygga i sina inställning till hur man sköter sjukdomen vilket måste uppmärksammas i det fortsatta arbetet med samtalsgrupper. Vi har nu infört metoden med föräldragrupper som rutin och i enlighet med resultatena av vår undersökning nöjer oss med 3 mötestillfällen. Uppföljningen av de barn som får sin medicinering utsatt måste förbättras och föräldrarna skall uppmuntras att återkomma om barnen återfår sina astmasymptom. Vid den första sammanställningen av vårdtillfällen för astmabarn äldre än 2 år som genomfördes i Sverige 2004 hade Karlstad barnklinik de lägsta siffrorna i landet. Kanske kan detta vara en värdemätare på vårt nya arbetssätt?
I wish to express my warmest gratitude to all those who have supported me in this project. I would especially like to thank all the children and the parents participating in these studies. In particular, I would like to thank:
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12 APPENDIX

Underlag för de fyra gruppdiskussioner som ingick i interventionsstudien (Structure of the four group discussions with parents):

Träff 1, leds av sjuksköterska och läkare

Tema: Presentation och diskussion om astma – definition och egna ”bilder”.

· Presentation av gruppmedlemmarna.
· Presentation av familjer, barn och respektive sjukdomshistoria.
· Vad tänkte du på och vad kände du, när du fick diagnosen astma? Vad är astma för dig?
· ”Hinkmodellen”: Det är inte säkert att det som får symtom att utlösas är den viktigaste faktorn.
· Låta föräldrarna pröva ”sugrörsmetod”, dvs. tre sugrör initialt därefter plocka bort ett i taget.
· Medicinering
· Ärfiltighet
· Berätta om anatomin och vad som händer med hjälp av modeller och bilder.
· Hur informerades den förälder som ev. inte var med vid läkarbesöket om diagnosen? Släktingar och äldre bekanta med astma?
· Betona att det är angeläget att båda föräldrarna är med i fortsättningen.

Träff 2, sjuksköterskor och kurator

Tema: Astmans påverkan på familjen – övriga syskon

· Är det något oklart beträffande vad som togs upp vid förra träffen?
· Vad tänkte ni på när ni gick hem?
· Oro inför framtiden
· Påverkan på sociala livet
· Gränsdragningsproblematik
· Saneringsdiskussion
· Ta upp miljöfaktorer – allergiutveckling
· Rökning
· Besök hos släktingar och vänner – förebyggande aspekter.
· Diskussion om ev. statligt vårdbidrag, intygsfrågor.
Träff 3, sjuksköterska, läkare och kurator

Tema: Framtiden

· Prognos – hur brukar det bli?
· Vad kan man göra för att främja en positiv utveckling?
· Ta upp att fysisk träning är ett sätt att förbättra prognosen.
· Åter ta upp problematiken kring balansgången mellan överbeskydd och uppgivenhet.
· Diskutera ”kortisonskräck” och dess biverkningar.
· Diskutera släktingars och goda vänners tendens att komma med ”goda råd”.
· Kurator kan gärna ställa ”dumma frågor”, dvs. frågor som man misstänker att föräldrarna inte vågar ställa för att ”avslöja sig”.
· Ev. oklarheter kring medicinering och sjukdomsorsaker.
· Utvärdering av de träffar som varit och förslag till förbättringar.
· Egna tankar inför framtiden.

Träff 4, sjuksköterska, läkare och kurator

Tema: Erfarenheter och framtidsfrågor

· Gå laget runt och höra hur barnen mått, vad som hänt.
· Ta upp ev. nyheter på området sedan sist, tidningsartiklar etc.
· Ev. oklarheter kring medicinering, sjukdomsorsaker.
· Utvärdering av de träffar som varit och förslag till förbättringar.
· Egna tankar inför framtiden.
13 ERRATA

In the paper “The burden of asthma as reflected by the prevalence defined by doctor’s diagnosis and the use of health care services by pre-school children in a Swedish region” the word “cumulative” should be deleted on page 1247, line 2, left column. On line 5, sixty-six should be exchanged with 58 and on line 21 it should be 0.1 visits/1000 children 0-6 y of age/y. The references 12, 13 and 14 are omitted after the first sentence in the discussion on page 1248.

In the paper “Comparison of clinically diagnosed asthma with parental assessment of children’s asthma in a questionnaire” table 5 should be exchanged with the corrected table (with the number 4) in the Results part of this thesis. On page 4 under “Discussion”, line 7 from the bottom, 45% should be 41%.

In the paper “Group discussions with parents have long-term positive effects on the management of asthma with good cost-benefit” 2.1 should be 1.1 in the abstract and on line 4 in the 4th paragraph under the head” The burden of asthma” on page 606. On line 5 in the first paragraph under the same head p should be = 0.08. In the 6th paragraph, line 3 and 5, “moderate” should be interposed before “persistent”.

Under the head “Economic calculation” on the same page 1.8 should be 2.8 and 31 should be 26. On line 8 the days saved should be 73 (not 56) and consequently 42.5 should be replaced with 59.5 as on page 607, 8 lines from the bottom.

On page 605, 10 lines from the bottom left column “girl” should be replaced by “boy”.

Page 603 under “Outcome measures”: The classification according to GINA guidelines should be intermittent; mild-, moderate-, severe persistent.

In the paper “A gender perspective on parents’ answers to a questionnaire on children’s asthma” the words “in-hospital days” on page 1 and 6 should be changed to “hospital admittances”. Reference to “16” in the 4th paragraph on page 559 should be “17”.

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