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Organisation of Asthma in Primary Care, Quality of Life and Sex-related Aspects in Asthma Outcomes

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Abstract

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Objectives: To investigate the organisation of asthma care in primary care and evaluate outcomes for patients attending primary care centres with and without asthma clinics. Other objectives were to study the association between quality of life and asthma control in patients in primary care and to analyse sex differences regarding asthma outcomes related to menopausal status.

Material and methods: Cross-sectional surveys and a patient record study.

Results: Of all the primary health care centres, 77% had a spirometer and 53% an asthma clinic. At centres with asthma clinics 77% of the patients reported sufficient knowledge of asthma as compared with 65% at centres without asthma clinics ($p<0.001$). With more time allocated for the nurse, 44% of patients achieved asthma control as compared with 27% at asthma clinics with less time ($p<0.003$). Patients using short-acting beta-2 agonists more than twice in the last week had clinically significant lower MiniAQLQ scores (5.17 versus 5.91). This finding also held for night awakenings during the previous week (4.42 versus 5.86), courses of oral corticosteroids (5.26 versus 5.64) and reported emergency consultations during the last six months (4.85 versus 5.71). Premenopausal women had significantly lower total MiniAQLQ scores than men in the same age group (5.44 versus 5.89, $p<0.001$), while no difference was found between postmenopausal women and men of similar ages. The adjusted odds for premenopausal women for asthma exacerbations was 2.0 (95%CI 1.22-3.43) as compared with men in the same age group. No differences were found when comparing postmenopausal women with men of similar ages.

Conclusions: Half the primary health care centres had an asthma clinic and the majority had access to a spirometer. Patients at primary health care centres with asthma clinics reported better knowledge of their disease, and asthma control is more often achieved if the nurse is allocated more time. Achieving asthma control is associated with better quality of life in patients in primary care. Premenopausal women had lower quality of life and less often asthma control than men of the same ages, while no corresponding difference was found between postmenopausal women and men of similar ages.

Keywords: Asthma, Primary Health Care, Cross-Sectional Studies, Quality of Health Care, Asthma clinic, Spirometer, Asthma management, Knowledge, Outcome Assessment, Control, Symptoms, Quality of Life, Sex, Menopause, Sex Hormones

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Original papers

This thesis is based upon the following publications:

- PAPER I Lisspers K, Ställberg, B, Hasselgren M, Johansson G, Svärdsudd K. Organisation of asthma care in primary health care in Mid-Sweden. *Prim Care Respir J* 2005 Jun;14(3):147-53. Epub 2005 Apr 14.*
- PAPER II Lisspers K, Ställberg, B, Hasselgren M, Johansson G, Svärdsudd K. Primary health care centres with asthma clinics: effects on patients' knowledge and asthma control. Submitted.
- PAPER III Lisspers K, Ställberg, B, Hasselgren M, Johansson G, Svärdsudd K. Quality of life and measures of asthma control in primary health care. *J Asthma* 2007 Nov;44(9):747-51.*
- PAPER IV Lisspers K, Ställberg, B, Janson C, Johansson G, Svärdsudd K. Sex-related differences regarding quality of life and asthma control in Swedish asthma patients. Submitted.

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Contents

Foreword.....	7
Introduction.....	9
Asthma bronchiale.....	9
Definition, prevalence, mortality and health economics	9
Expressions and influencing factors	10
Diagnosis and classification	11
Guidelines, treatment goals and morbidity	12
Management and treatment.....	14
Organisation for asthma in primary care – asthma clinics.....	16
Quality of life – generic and disease-specific instruments	17
Sex-related differences	18
Aims.....	20
Material and methods.....	21
Asthma in Middle Sweden - the AIM-study (paper I-III)	21
Paper I.....	21
Papers II and III	22
The Praxis study asthma/COPD (paper IV)	22
Paper IV	23
Statistics	23
Results.....	25
Paper I	25
Data from the Praxis-study	27
Paper II	27
Paper III.....	31
Paper IV	33
Discussion.....	36
Methodological considerations.....	36
Study design	36
Selection	36
Questionnaires and patient records	37
Response rate – non-responders	38
Analysis of the effect of non-responders	38

Discussions of main results	38
Organisation for asthma in primary care	38
Asthma outcomes in relation to asthma clinics	40
Quality of life and asthma control	42
Sex-related differences	44
Concluding remarks	47
Swedish summary	48
Acknowledgements	50
References	52
Appendix 1	62
Appendix 2	63

Abbreviations

ACT	Asthma Control Test
AIM	Asthma in Middle Sweden
AQLQ	Asthma Quality of Life Questionnaire
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
FEV ₁	Forced Expiratory Volume in one second
FVC	Forced Vital Capacity
GINA	Global Initiative for Asthma
GP	General Practitioner
ICS	Inhaled Corticosteroid
IgE	Immunoglobulin, class E
IPCRG	International Primary Care Respiratory Group
LABA	Long-acting beta2-agonist
MiniAQLQ	Mini Asthma Quality of Life Questionnaire
PEF	Peak Expiratory Flow
PHCC	Primary Health Care Centre
SAS	Statistical Analysis System
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
VC	Vital Capacity
WHO	World Health Organisation

Foreword

When I decided to become a general practitioner I realized I had to be well initiated in the major diseases in primary care. One of these is asthma, and I felt my knowledge about this disease, and its treatment was not good enough to be able to manage the patients well. I therefore asked to be given extra field experience at the Department of Allergy and Pulmonary Medicine of Falun. Here, with inspiration from my colleagues, I became aware of how interesting and complex a disease asthma is, and how it involves a broad spectrum of issues ranging from immunology to environment.

As a GP my main concern has of course been the well-being of the patients. Although there was already good asthma medication available when I started to work, my patients still suffered from symptoms of the disease, which limited their lives and emergency consultations at the primary health care centre were common. The diagnostic tools in primary care were limited to stethoscopes and peak flow meters and there was a need for spirometry. It was also clear that more knowledge and training for the patients about the disease was needed, about what to avoid and how to inhale and dose their medication. Here, an asthma clinic with a nurse at the primary health care centre became an option for educating and training the patients and for spirometry. But, what about the patients in their everyday lives? How were they doing, did they profit from having access to the asthma clinic? Did they improve in well-being, symptoms, knowledge and in relation to their asthma exacerbations? What could we do to improve our management of patients with asthma? These were my first questions at the local level, and they then became research issues at the regional level in the AIM-study evaluating the organisation for primary care and how patients experienced their asthma regarding symptoms and quality of life. In the Praxis-study this continued, and came to including secondary care, with the main aim of relating the care actually given to the published guidelines. Some questions were answered, but the research also raised new questions. One is about the sex-related differences in asthma of which I was not previously aware.

As a practising GP at the primary health care centre in Gagnef, I notice that a great deal remains to be done to improve care for these patients. They form a large and diverse group with varying needs, and it is a challenge to find new ways to develop the care for them.

Introduction

Asthma bronchiale

Definition, prevalence, mortality and health economics

Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements are engaged. The chronic inflammation is associated with variable airway hyperresponsiveness that leads to episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or early in the morning [1].

The disease affects more and more many peoples' lives and has become more common in both children and adults around the world over recent decades [2-5]. There are estimates that about 5% of the world population has asthma. In Swedish epidemiological studies in the sixties and seventies the prevalence of adult asthma was estimated at 2-3% [6]. Later studies demonstrated an increase to 5% in the eighties, 6-8% in the nineties, while data from the latest studies in Sweden indicates an increase to about 7-10% [6-8]. The prevalence is highest among young adults, owing to high incidence among children and youths [9, 10]. Recent data suggests that the prevalence is levelling off [11, 12]. Asthma is twice as common among males before puberty when it becomes more common in females [13]. After 50 years the incidence in men approaches that of women [14]. There are several theories as to why asthma prevalence has increased so rapidly, for example the hygiene hypothesis [15, 16], but there is today no clear explanation of the aetiology of asthma.

According to estimates by WHO in the early 2000s, 180,000 persons die annually of asthma and the rates are increasing [17]. The mortality rate in Sweden is 200 persons per year, in the age range 5-35 it is about 3-5 per year [18].

The cost of asthma is considerable, both in terms of direct medical costs and indirect costs [4]. In a Swedish study from 2007 the average annual cost for asthma in the age groups between 25 and 56 years was estimated to SEK 15,919 per person, where the direct costs constituted about a third of the total costs. The severity of the disease and older ages are factors related to increased costs. The total cost of asthma in the whole population is approximately SEK 7.4 billion [19].

Expressions and influencing factors

Asthma is a heterogeneous and multifactor disease that varies in expression over time within one individual and between individuals. Some patients are very little affected by their asthma, while in others the disease has a great impact on their lives.

Many factors can influence the development and appearance of asthma, both individual factors such as genetic factors, sex and obesity, and environmental factors such as allergens, infections, smoking habits, occupational sensitizers, air pollution and diets [1].

There is a hereditary component in asthma, and studies have shown that multiple genes may be involved in the pathogenesis [20, 21]. The differences in asthma prevalence over the life span suggest that reproductive hormones influence the development and severity of asthma [22]. Obesity is also a risk factor for asthma [23, 24].

There is a close relationship between allergic sensitivity and development of asthma, with a two to six times higher risk of developing asthma if a person is sensitized to an allergen [25-27]. Allergic asthma in Sweden is especially associated with indoor allergens such as furry animals, and cat allergy is a risk factor for asthma [25, 28]. Allergens, to which the individual is sensitized, may cause asthma exacerbations at exposure. Rhinitis, both allergic and non-allergic, is an important risk factor for asthma [6, 29].

Asthma is the most common occupational disorder in industrialized countries, constituting about 10% of asthma in adults of working age [30]. Tobacco smoke accelerates the decline in lung function in individuals with asthma, increases asthma severity and makes patients less responsive to medical treatment [31, 32]. Air pollution may give rise to asthma exacerbations, but the role of air pollution in the development of asthma is unclear [33, 34].

Infections may be a risk factor [35], although there are also indications that some infections can protect against development of asthma [34, 36, 37]. Viral infections are also well known to exacerbate an already existing asthma [38].

The relationship between the effects of breast-feeding and the development of asthma has been extensively studied, and data indicates that breast-feeding could be protective [39]. The indoor environment is of importance concerning the development of asthma and passive smoking and damage caused by damp are risk factors for asthma among children [26, 27, 40]. It has also been claimed that frequent consumption of processed foods and too little use of foods high in antioxidants may have contributed to the increase in the prevalence in asthma and allergies [41].

Low socio-economic status is associated with higher asthma prevalence both among children and adults [42, 43].

Diagnosis and classification

The basis of the diagnostics for asthma, as for most illnesses, is the patient's medical history. The family history of asthma and allergy is important to consider. Common symptoms are episodic breathlessness, often related to exercise, wheezing, coughing and chest tightness. Typical for asthma is also the variability of the disease, sensitivity to non-specific irritants and worsening in connection with exercise and at night.

Since the asthma symptoms vary, physical examination of the lungs may be normal, but wheezing confirms airflow limitation. In patients with a more severe exacerbation there may be cyanosis, tachypné, tachycardia and use of accessory muscles of the chest.

Lung function measurement and demonstration of reversibility improves the probability of an asthma diagnosis. There are two commonly used ways of measuring lung function, peak expiratory flow (PEF) and spirometry.

PEF meters are simple to handle and patients can use them at home. With a PEF meter it is possible to measure reversibility, which is defined as an improvement of 60 l/minute or 20% after inhalation with a bronchodilator [44]. Another way of using the PEF meter as a diagnostic tool is to measure the diurnal variation in PEF, where a variation of 20% is regarded as diagnostic for asthma [45].

Spirometry is the preferred method for measuring lung function to ascertain an asthma diagnosis. The important variables are forced vital capacity (FVC), vital capacity (VC) and forced expiratory volume in one second (FEV₁), where reversibility (increase after inhalation of bronchodilator) of 12 % or more and 200 ml or more is regarded as significant [46]. Owing to the variability of asthma, patients will not always have reversible lung function. Especially younger patients, patients with mild asthma and patients on asthma treatment may have normal spirometry. To perform spirometry in a reliable way, the user has to be well-informed about how to handle and calibrate the spirometer and how to instruct the patients. Studies have shown that spirometries performed in primary care satisfy quality parameters if the staff has sufficient training [47].

When assessing an asthma diagnosis, it is also important to know whether the patient has an atopy, as the association between asthma and allergy is strong. Atopy is diagnosed mainly using two methods: skin prick tests and measurement of serum specific IgE. Skin prick tests used to be the most frequently used method, but measurement of serum specific IgE has in evaluations proven to be of equal validity [48].

When asthma is suspected but lung function is normal, measurements of airway responsiveness may be helpful in establishing the asthma diagnosis. Several methods are available, such as, methacholine, histamine, mannitol, dry air, and exercise. These methods are rarely used in primary care, possibly with the exception for exercise. Exhaled nitric oxide is used to measure

airway inflammation in asthma, but has yet not been evaluated prospectively for diagnosing asthma [49].

International guidelines [50] have previously recommended that asthma before treatment is classified into intermittent, mild persistent, moderate persistent or severe persistent based on assessment of symptoms, lung function measurement, use of reliever medication and physical limitations. Classification of asthma by severity may be useful when decisions are made about initial management. However, in recent guidelines, classification is made with regard both to the severity of the underlying disease and responsiveness to treatment [1].

With regard to the earlier GINA-classification of the severity of asthma, half of the population has intermittent asthma and half has persistent asthma. Among the patients with persistent asthma, 1/3 have been estimated to have mild persistent, 1/3 moderate and 1/3 severe persistent asthma [51].

Guidelines, treatment goals and morbidity

The first international guidelines for managing asthma were published in 1992, and the Global Initiative for Asthma (GINA) was started in 1993, with the aim of reducing chronic disability and premature deaths, and allowing patients with asthma to lead productive and fulfilling lives. The GINA guidelines have since undergone annual updates.

Clinical guidelines seek to summarise information and offer evidence-based recommendations to guide clinicians in daily practice. One concern is that the evidence on which guidelines are based rarely comes from primary care. Therefore, the International Primary Care Respiratory Group (IPCRG) published guidelines for the diagnosis and management of chronic respiratory diseases in different general practice settings globally in 2006.

The treatment goals of asthma management are [1]:

- achieve and maintain control of symptoms,
- maintain normal activity levels, including exercise,
- maintain pulmonary function as close to normal as possible,
- prevent asthma exacerbations,
- avoid adverse effects from asthma medications,
- prevent asthma mortality.

The 2006 GINA guidelines contained an important change in the approach to asthma management, placing the emphasis on assessing, treating, and monitoring patients based on level of asthma control rather than asthma severity. The clinical signs of asthma and lung function should be assessed. The levels of control are: controlled, partly controlled and uncontrolled. This classification is consensus-based and has not yet been validated. Asthma control as defined by GINA is summarised in figure 1 (adopted from GINA).

Levels of asthma control according to the Global Initiative for Asthma (GINA).			
Characteristic	Controlled (All of the following)	Partly controlled (Any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV₁)‡	Normal	<80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	One in any week†

FEV₁ = forced expiratory volume in 1 second; PEF = peak expiratory flow

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

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

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

Figure 1. Levels of asthma control according to the Global Initiative for Asthma (GINA)

In the IPCRG guidelines the differential diagnosis of chronic respiratory diseases are described using a symptom-based approach, as this is how patients present their illness in primary care. The guidelines also include questionnaires and diagnoses guides by age groups, treatment goals and pharmacologic therapy for asthma and allergic rhinitis.

The National Board of Health and Welfare in Sweden produced guidelines for the management of asthma and chronic obstructive pulmonary disease (COPD) in 2004. These guidelines include recommendations and quality indicators for asthma and COPD.

The Swedish Medical Products Agency publishes treatment recommendations about asthma on a regular basis [52].

The different asthma guidelines have still not been fully implemented and asthma morbidity remains unacceptably high. Most patients do not achieve the goals of asthma management and patients' perception of asthma control differ from actual control [53, 54].

In the AIRE-study in 1999, forty-six percent of the patients reported daytime symptoms and 30% asthma-related sleep disturbances at least once a week. During the last year, 25% reported an unscheduled urgent care visit and 10% one or more emergency room visits.

In the 2001 ALMA-study in Sweden, 16% of asthmatics reported symptoms occurring every day during the previous month. Nocturnal symptoms at least twice per week were reported by 19%. The vast majority classified their disease as mild or very mild, although the majority also reported frequent symptoms. There are probably various reasons for this, including patients' lack of knowledge and awareness of the positive effects of asthma medication on asthma symptoms, as well as other factors such as psychological repression, unwillingness to accept the disease, or depressive and anxiety disorders, all of which could have an impact on morbidity [55-58]. Clinical guidelines may not have been wholly accepted and implemented in primary care [59]. Acceptance could be improved if guidelines in general were simpler and more flexible [60]. The development of regional guidelines would also provide more practical solutions for asthma care and account for factors, such as social or economic that might influence patients' choices of and adherence to therapy [61]. Implementation of guidelines is a challenge and there are some positive examples in Finland, where there is strong commitment to the concept of self-management of asthma [62].

Management and treatment

Considering the diverse expressions of asthma, patients' knowledge of what affects their disease and how it should be treated is essential, as are the demands for the quality of the care given. Good quality of care implies that the demands in terms of diagnostic reliability are high and that the treatment is accurate with continuous evaluations and follow-ups [58]. The concept of

good quality also comprises the possibility for the patients to attain sufficient knowledge of the disease and of how to use adequate treatment for the purpose of gaining optimal asthma control and quality of life [63].

One of the key points in the 2007 GINA guidelines is that effective management of asthma requires a partnership between the patient and his or her health care professionals. In this perspective, the importance of patients' understanding of asthma symptoms, treatment goals and the significance of asthma control is a key. For the health care professional it is essential to comprehend the most important issues from the patient's perspective.

In the IPCRG guidelines some components of asthma management are stressed:

- education and advice,
- monitoring control through assessment of symptoms and medication use,
- establishing individual plans for managing exacerbations,
- facilitating smoking cessation.

Treatment of asthma includes avoidance of trigger factors that can cause asthma symptoms and exacerbations. Patients need to be aware of these "triggers" including allergens, viral infections, pollutants and drugs and know how to treat their asthma if exposed.

Pharmacological asthma treatment is defined in five steps:

Step 1: Short-acting beta2-agonist as needed

Step 2: Inhaled corticosteroids and short-acting beta2-agonist as needed

Step 3: Inhaled corticosteroids with addition of long-acting beta2-agonist or antileukotrien

Step 4: Inhaled corticosteroids with addition of long-acting beta2-agonist and antileukotrien

Step 5: As step 4 and additional medication with oral steroids or anti-IgE

When patients are on treatment, determination of asthma control is suggested, referring to control of the manifestations of the disease, where the aim is to reach optimum control [1]. After achievement of asthma control, continuous monitoring is essential to establish the lowest step and dose of treatment necessary. An Asthma Control Test (ACT) with five questions can be used as a tool for evaluating the level of asthma control [64, 65]. It is important to bear in mind that asthma manifestations vary and treatment may need to be adjusted periodically. Considering that asthma treatment intensity may vary over time, patients need to be as well-informed as possible about their disease and treatment. Thus, individual treatment plans are important and helpful.

Although the aim of asthma management is asthma control, some patients suffer from asthma exacerbations from time to time, and have to make emergency visits. The treatment of an exacerbation includes inhalation with short-acting bronchodilators and in many cases a course of oral steroids. If a bacterial respiratory infection is suspected, antibiotics may be added.

Organisation for asthma in primary care – asthma clinics

In Sweden as in many other countries, asthma is a disease mainly managed in primary care [66, 67]. Consequently, the organisation for asthma care in primary care is of high importance.

Many patients with asthma remain undiagnosed [68-70], and one of the tasks for primary care is to find these patients through accurate investigations. Easy access to spirometry at the Primary Health Care Centre (PHCC) is essential, as spirometry is necessary when evaluating a patient with possible asthma [71]. Other requirements regarding equipment are pulse oxymeters to evaluate patients' oxygen saturation, and nebulisers to administer medication at exacerbations.

All general practitioners (GPs) need to have good knowledge about asthma diagnostics, including spirometry interpretation, and management and treatment of asthma. Considering the fact that the manifestations of the disease are variable, affected by various trigger-factors and that the treatment requires knowledge of inhalation techniques, education of the patient is an important aspect of management [1]. One option for improving the quality of patient care is to have an asthma clinic at the primary health care centre, with a nurse who has a special interest in and knowledge about asthma, allergies and COPD. The nurse cooperates with all the physicians. One of the physicians is responsible for the clinic.

Asthma clinics in primary care were first established in the United Kingdom in the 1980s [72] and several other countries followed the example. The first clinics in Sweden opened during the late 1980s. In the 1990s there was an extension of clinics depending on interest at the primary health care centre, but without national recommendations or economic benefits.

To ensure the quality of the clinics, criteria for a complete asthma clinic were established by the Swedish Respiratory Group in Primary Care in 1998. These criteria were:

1. nurse trained in asthma management and treatment,
2. general practitioner responsible for the asthma clinic,
3. access to a spirometer in the clinic,
4. investigations according to guidelines,
5. patient education according to guidelines,
6. scheduled surgery for the asthma nurse,
7. a minimum of 0.5 hours per week per 1,000 inhabitants allocated for the asthma nurse.

As an effect of the establishment of asthma clinics, patients with Chronic Obstructive Pulmonary Disease (COPD) have also more frequently been taken care of at the clinics, which are now called asthma/COPD clinics. Owing to this broader assignment and the increasing demand for education of the asthma/COPD nurse, the criteria were revised in 2008, with demands for university education for the nurse and increased time allocated for the asthma clinic [73].

In the guidelines published by the Swedish National Board of Health and Welfare in 2004 asthma clinics and access to spirometers were established as good quality indicators for the organisation of asthma in primary care.

Evaluation of asthma clinics may be a demanding task, because there are methodological difficulties associated with performing randomised studies with a control group. There are also differences between the organisation and financial systems of medical care in different countries, which makes it difficult to compare results.

Quality of life – generic and disease-specific instruments

Health-related quality of life has during recent years come to be seen as an important outcome, since the influence of the disease on everyday living is such an important factor for the patients [74]. Quality of life can be defined as a uniquely personal perception, the way an individual patient feels about his/her health status and/or non-medical aspects of life [75].

Another proposed definition is: “the functional effects of an illness and its consequent therapy upon a patient, as perceived by the patient” [76].

Some quality of life instruments are generic, others disease-specific. A generic instrument can be used in relation to all health conditions and to compare quality of life of patients with different diseases with healthy subjects and patients suffering from different diseases. One of the most well-known and widely used generic instruments is the SF-36 [77], a self-administered questionnaire, with 36 questions including eight dimensions.

Disease-specific instruments focus on the aspects of health status relevant to a specific disease or condition. They have been developed to give insight into the patient’s experience of symptoms, functional impairments and the physical, psychological and social impacts of the disease.

When managing chronic diseases like asthma, measurements of quality of life have an especially important function, as the patient’s own experience of the disease provides important information for treatment decisions. The requirements of an asthma specific quality of life questionnaire are that it includes the physical and emotional changes that patients experience as most important. It should also be sensitive to small but clinically important changes for the patient. To ensure a good response rate it should also be short and simple to answer and have good validity, *i.e.* measures what is

expected. Another property is good reliability, that the chance for random errors is small.

One of the most commonly used and acknowledged quality of life instruments for asthma is the Asthma Quality of Life Questionnaire [78, 79]. When the instrument was developed the requirements were that it should measure the functional impairments most important to adult patients with asthma, covering physical and emotional functioning. It should also be reliable, *i.e.* reproducible when the clinical state is stable, and able to discriminate between patients with various levels of impairment. Other requirements were that it should be responsive, *i.e.* sensitive to changes important to the patient even if those changes were small. The questionnaire should also be valid, *i.e.* actually measure quality of life in asthma [79]. It consists of 32 questions including four domains: symptoms (12 items), activity limitations (11 items), emotional function (5 items) and environmental stimuli (4 items). Several independent evaluations have demonstrated that the instrument is sensitive to small but clinically important changes within the individual and has good reliability and validity [80-82].

The MiniAQLQ questionnaire was developed for larger clinical trials and surveys [83]. The demands on this questionnaire were that it should be similar to the AQLQ, but short and easy to complete. The MiniAQLQ includes 15 questions; 5 in the symptom domain, 4 about activity limitations, 3 about emotional function and 3 about environmental stimuli. Patients are asked to recall how they had experienced their situation during the last two weeks on a scale ranging from 1 to 7, where 1 means maximum impairment and 7 no impairment. The mean of the total sum and of each domain is calculated. To be clinically relevant, meaningful to the patient, the difference should be at least 0.5 points [84]. Comparing evaluations of the AQLQ and MiniAQLQ have shown that although the MiniAQLQ does not have the precision of the larger questionnaire it is satisfactory, especially in larger surveys [83]. The MiniAQLQ has been validated in patients 17 years and older but has also been used in studies with younger patients (personal communication Juniper, EF).

Sex-related differences

Sex-related differences in the clinical manifestations of airway disease occur throughout the human life span and are related to biological and socio-cultural factors [14]. As mentioned above, asthma is more prevalent among boys, but after puberty it becomes more common in females.

Several studies have demonstrated that women have poorer outcomes in asthma than men regarding symptoms, asthma exacerbations and quality of life [85-87]. If this reflects different biological, psycho-social or cultural distinctions between men and women is unclear. It could also be an effect of different management of the sexes by the health care system.

The biological sex differences in relation to asthma include genetic, pulmonary, and immunological factors. There is compelling evidence that sex hormones could be major determinants of the biological sex differences [88]. About 30% to 40% of females with asthma report worsening of their asthma during the perimenstrual period [89, 90], and studies suggest that menstruation may trigger severe asthma exacerbations in women with poorly controlled asthma [91]. Oestrogen replacement therapy has been shown to impair patients' asthma [22, 92], but has also been associated with improved lung function [93]. Oral contraceptives have been associated both with a higher prevalence of asthma, and with no significant relation to the prevalence [94]. A meta-analysis regarding asthma exacerbations during pregnancy demonstrated that exacerbations of asthma requiring medical interventions occurred in about 20% of women, with approximately 6% of women being admitted to hospital [95].

Awareness of these sex-related differences is important for the clinical practice regarding treatment and management as well as for research.

Aims

The aims of the study were:

- to analyse the organisation of asthma in primary care, access to spirometers, prevalence of nurse-based asthma clinics, and the fulfilment of national criteria for asthma clinics,
- to evaluate outcomes with special reference to knowledge, asthma control and quality of life in younger asthma patients attending primary health care centres with and without nurse-based asthma clinics,
- to analyse the association between asthma control and health-related quality of life in a cross-sectional study of younger asthma patients in primary care,
- to analyse asthma outcomes, *i.e.* asthma control, quality of life and asthma management, with special reference to sex and menopausal status.

Material and methods

Asthma in Middle Sweden - the AIM-study (paper I-III)

The AIM-study is a cross-sectional study in two steps. In the first part, performed in 2000 and with a follow-up in 2002, the organisation of asthma in primary care was investigated. The second part, conducted in 2001, was a survey with patients 15-45 years attending 42 randomly sampled primary health care centres (PHCCs) that participated in the first part of the study.

The study was performed in the Uppsala-Örebro region, which has a population of 1.9 million, *i.e.*, 22% of the Swedish population. The region consists of seven counties with rural areas, towns and cities, but none with more than 200,000 inhabitants. At the time of the study the region was served by 240 PHCCs, with catchment areas ranging from 1,000 to 20,500 residents.

Paediatric out-patient clinics were also included in the first part of the AIM-study, where one clinic in each county was randomly sampled. In the second part patients at the out-patient clinics 15-18 years old were randomly sampled. These data were not used in this thesis.

Paper I

A questionnaire (appendix 1) was sent to the 240 PHCCs and 238 responded. The questions concerned the number of GPs appointed, the size of the catchment area, access to a spirometer and whether there was an asthma clinic at the centre. PHCCs with asthma clinics answered additional questions about the criteria for asthma clinics.

According to the fulfilment of the seven criteria for a primary care-based asthma clinic [96] PHCCs were divided in three groups: complete asthma clinics (all criteria fulfilled), incomplete asthma clinics (some but not all criteria fulfilled) and PHCCs with no asthma clinic.

To enable comparison of the organisation and access to an asthma clinic in relation to the size of the catchment area, PHCCs were classified as small (less than 3,000 residents), medium-sized (3,000-7,999 residents), large (8,000-11,999 residents) or very large (12,000 residents or more).

A follow up, concerning the use of spirometry in primary care, was performed in 2002. This questionnaire was sent to 217 PHCCs with more than

3,000 residents in the catchment area assuming that smaller PHCCs would not have the resources to have a spirometer. 82% returned this questionnaire.

Papers II and III

Both papers included patients from the AIM-study. The base of the second part of the AIM-study consisted of patients from the PHCCs participating in the first survey. In this part, 45 PHCCs were excluded owing to small catchment areas, lack of computerized medical records or interest in participating in the study. The remaining 193 PHCCs were stratified into groups according to the organisation for asthma management and size of catchment area. A proportional random sample of 42 PHCCs was drawn from these strata; 14 with a complete asthma clinic, 14 with non-complete and 14 with no asthma clinic.

Each of the 42 PHCCs generated a list of all patients with asthma diagnoses attending the PHCC during the previous 18 months. Samples of patients 15 to 45 years were drawn from these lists generating a total of 1,477 patients.

The survey included two questionnaires, one constructed by the authors (appendix 2) returned by 1,133 (77%) of the patients and the other the disease-specific quality of life questionnaire, MiniAQLQ, returned by 1,098 (74%) patients.

Four questions in the first questionnaire concerned the attainment of treatment goals; use of less than three doses of short-acting beta-2 agonists per week, no night awakenings, emergency consultations or courses of oral steroids attributable to asthma. Asthma control in this study was defined as the fulfilment of all four of these treatment goals.

The MiniAQLQ includes 15 questions, grouped into four domains: “activity limitations,” “symptoms,” “emotional function,” and “environmental stimuli.” Patients responded on a scale from 1 to 7 and the mean score of each of the four domains and the overall score were calculated. A difference in the mean of 0.5 was regarded as clinically relevant.

The Praxis study asthma/COPD (paper IV)

The Praxis study is a cross-sectional study including both questionnaire and patient records in both primary and secondary care in the same region as the AIM study. The study was intended to investigate whether the guidelines for asthma and COPD produced by the Swedish National Board of Health and Welfare in 2004 were followed by the health care professionals. The organisation and management of asthma and COPD care were examined in 2005 at 56 PHCCs, 8 randomly sampled in each of the 7 counties, and 14 out-patient clinics, 2 sampled from each county, at hospitals with departments of pul-

monary/internal medicine. This was followed by a patient survey sent to randomly sampled patients, 18-75 years with asthma or COPD from these centres. After permission was obtained from the patients, patients records from 2000-2003 (four years) were examined in a structured way. Two nurses at the research centre scrutinized all records and extracted data into a structured data form with continuous supervision and double-checking by the researchers.

Paper IV

The centres/hospitals participating in the first part of the study were asked to generate lists of all patients with a physician's diagnosis of asthma who had attended the centre/hospital during the last four years. From these lists, random samples of 22 patients from each primary health care centre and 35 patients from each out-patient clinic in the age range 18-75 were drawn. This generated a total of 1,226 patients from primary care and 499 from hospitals.

A questionnaire including data about demographics, symptoms, asthma medication, allergy testing, self-assessed disease severity, and quality of life (MiniAQLQ), was sent to the patients in both primary and secondary care, and was returned by 1,228 (71%).

In the questionnaire patients were also asked whether or not they were willing to provide a written permission to have their records examined, and 98% answered affirmatively. Patients records from 2000-2003 were examined in a structured way with data collected into a computerized form.

The level of medication in patients was defined in steps according to the GINA guidelines [1]. Four questions concerned asthma control: use of less than three doses of short-acting beta2-agonists per week, no night awakenings, emergency visits and courses of oral steroids. Lung function data were obtained from the patient records. An asthma exacerbation was defined as an emergency visit or a course of oral steroids.

One of the main objects of this study was to analyse outcomes in pre- and postmenopausal women. With reference to data from an earlier study (97), a subgroup analysis was performed in this study, where men and women ≤ 46 years were classified as the younger group and men and women ≥ 53 years as the older group.

Statistics

Data were analysed with the SPSS (version 12.0 and 13.0) and SAS (version 6.12 and 9.1) statistical programme packages. Summary statistics such as medians, means, proportions and measures of dispersion were computed using standard parametric methods. Simple differences between groups in continuous data were tested with Student's t-test or analysis of variance, and

differences in proportions with the chi-square test. Multiple linear regression (standard least square analysis) with backward elimination of non-significant variables was used for multivariate analyses of variables influencing MiniAQLQ total and domain score. Linear regression was also used to compute adjusted mean scores and to construct the regression surface in Figure 4.

Multiple logistic regression was used for analyse of variables influencing asthma control, which provided an odds ratio and a 95% confidence interval.

Only two-tailed tests were used. P-values less than 5% were considered to indicate a statistical significance. The confidence intervals presented for mean values and proportions were 95%. A difference between groups in the quality of life scores of 0.5 units or more has been claimed to be clinically significant.

Results

Paper I

Of all the PHCCs 77% (182) had access to a spirometer and each centre performed an average of 13 (median 10) spirometries per month. The mean number of spirometries per 1,000 inhabitants and year in the region was 19 (95%CI 14.9-23.6), (Figure 2).

125 (53%) of the PHCCs had asthma clinics. Of all 238 PHCCs 16% had a complete asthma clinic, 37% an incomplete clinic and 47% no asthma clinic. The extent to which the asthma clinics fulfilled the criteria for a complete asthma clinic is shown in Table 1. The most common criteria not fulfilled were, time allocation for the asthma nurse, a scheduled asthma nurse surgery and a specially appointed GP responsible for the asthma clinic.

Of the entire population in the region, 17% had access to a complete asthma clinic, 42% to an incomplete asthma clinic and 41% had no asthma clinic access. The larger the centre, the greater the probability of its having an asthma clinic ($p<0.05$).

The time allocation for the asthma nurse ranged from 0 to 2.1 hours per week per 1,000 inhabitants in the catchment area with a median of 0.42 and a mean of 0.53 hours (95%CI 0.45-0.62). At the complete asthma clinics the time varied from 0.5 to 2.1, with a mean of 1.0 hour (95%CI 0.90-1.20).

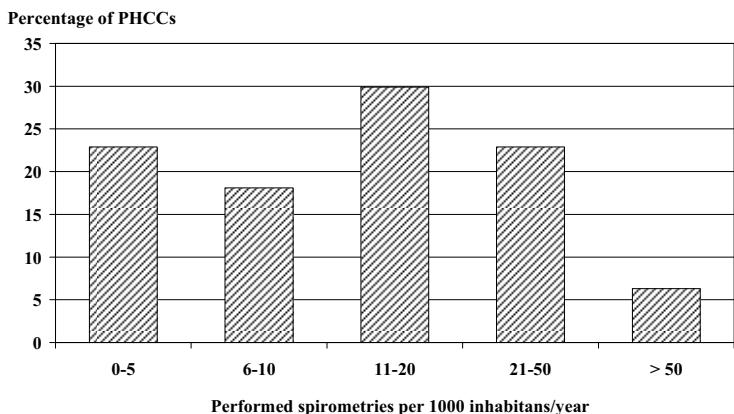


Figure 2. Distribution (%) of primary health care centres according to number of performed spirometries per 1,000 inhabitants yearly

Table 1. Primary health care centres reporting asthma clinics in the questionnaire and number of fulfilled and missing criteria for a complete asthma clinic according to the Swedish Respiratory Group in Primary Care recommendations

No. of fulfilled criteria	Missing criteria for a complete asthma clinic											
	Asthma clinics		Access to spirometer	Time criterion	Scheduled nurse surgery	Patient education	Patient investigations	Trained nurse	Responsible GP			
	n	%	n	n	n	n	n	n	n			
1	1	0.8	0	1	1	1	1	1	1			
2	0	0	0	0	0	0	0	0	0			
3	4	3.2	2	4	4	2	2	0	2			
4	9	7.2	0	9	9	4	0	1	4			
5	35	28.0	1	33	24	1	1	0	8			
6	38	30.4	0	25	8	0	0	0	5			
7	38	30.4	0	0	0	0	0	0	0			
Total	125	100.0	3	72	46	8	4	2	20			

Table 2. *The organisation for asthma at primary health care centres in Mid-Sweden in 2001 and 2005*

	AIM-study			Praxis-study		
	n= 238			n=56		
	n	mean or %	95%CI	n	mean or %	95%CI
Asthma clinics	125	53	46-59	36	64	51-76
Complete asthma clinics	38	16	12-21	17	30	20-43
Hours per 1000 residents in catchment area/week		0.53	0.45-0.62		0.84	0.64-1.04
Access to spirometer	182	77	71-81	52	93	83-97
GP responsible for asthma clinic	107	86	78-91	27	75	59-86
Scheduled nurse surgery	80	64	55-72	28	78	62-88

Data from the Praxis-study

In a follow-up study of the organisation for asthma and COPD in 2005 in the same region, the Praxis-study, involving 56 PHCCs, 93% of the PHCCs had a spirometer and 30% had a complete and 34% an incomplete asthma clinic.

The time allocation for the asthma nurse ranged from 0.1 to 2.6 hours per week and 1,000 inhabitants in the catchment area with a mean of 0.84 (95%CI 0.64-1.04). At the complete asthma clinics the time varied from 0.6 to 2.6 hours, with a mean of 1.1 (95%CI 0.82-1.40).

Table 2 illustrates data from the AIM- and Praxis-studies regarding the organisation for asthma at the PHCCs.

Paper II

In the AIM-study, 399 (35%) of the patients had access to a complete asthma clinic, 398 (35%) to an incomplete asthma clinic and 339 (30%) of the patients had no asthma clinic at their PHCC (Table 3). At the PHCCs with complete asthma clinics 193 (50%) patients and at the incomplete asthma clinics 136 (35%) patients reported they had had an appointment with the asthma nurse during the last year. Allergies, scheduled appointments and medication at a higher treatment step were more common at PHCCs with asthma clinics.

Sufficient knowledge of the disease was reported more frequently by patients at PHCCs with complete (82%) than by patients at PHCCs with incomplete asthma clinics (73%) and with no asthma clinics (65%). Patients at PHCCs with asthma clinics were also more aware of how to adjust their

Table 3. Patient characteristics at primary health care centres with complete, incomplete and no asthma clinics

	Complete asthma clinics		Incomplete asthma clinics		No asthma clinic		p
	n	% or mean	n	% or mean	n	% or mean	
Number (women)	399	(58.9)	398	(63.5)	339	(57.5)	
Age (mean)		30.1		30.2		30.7	ns
Visit asthma nurse the last year	193	50.4	136	35.1	64	19.8	<0.001
Reported allergies	318	82.8	334	85.9	254	78.4	0.03
Current smokers	61	15.6	65	16.5	50	14.9	ns
Medication							0.01
Step 1 ^{a)}	89	23.1	92	23.4	140	31.1	
Step 2 ^{b)}	148	38.3	172	43.8	136	40.7	
Step 3 ^{c)}	149	38.6	129	32.8	94	28.1	
Scheduled appointments the last year	179	48.5	170	45.9	105	32.5	<0.001
Sick leave last six months	72	19.7	77	21.3	77	24.8	ns

^{a)} only beta2-agonist

^{b)} inhaled corticosteroid (ICS) regularly or periodically

^{c)} ICS + long-acting beta2-agonist or ICS + antileukotrien

Table 4. *Patients' statements about their knowledge of asthma, inhalation techniques, use of peak flow meters and how to adjust medication at variations of the asthma disease. Comparisons between complete, incomplete and no asthma clinics*

	Complete asthma clinics		Incomplete asthma clinics		No asthma clinic		p
	n	%	n	%	n	%	
Knowledge of asthma	315	81.0	289	73.2	217	64.6	<0.001
Education about inhalation techniques	363	93.3	350	91.9	287	87.2	0.014
Peak flow measurements	131	33.2	102	26.1	72	21.5	0.002
Adjustment of medication at infections	236	60.4	210	53.2	151	45.3	<0.001
Adjustment of medication at more symptoms	293	75.1	298	75.4	220	65.5	0.003
Adjustment of medication according to peak flow	210	68.9	184	62.6	107	53.0	0.001

medication at variations of asthma attributable to worsening or infection (Table 4).

The odds for obtaining asthma control for patients stating they had knowledge about the disease was 1.5 (95%CI 1.1-2.0) adjusted for age, sex and primary health care centres with and without asthma clinics. The relationship between knowledge and the number of achieved treatment goals is illustrated in figure 3. Patients with knowledge about the disease and those who had received education about inhalation techniques had higher quality of life scores ($p<0.001$ and $p=0.006$) than patients with insufficient knowledge and lack of education about inhalation techniques.

Patients who had an appointment with the asthma nurse had shorter history of asthma, medication at a higher step and were more knowledgeable about asthma and adjustment of their medication. They more often reported emergency visits, less often achieved asthma control and had lower quality of life than patients who had not attended asthma clinics.

Table 5 demonstrates and compares data for patients at asthma clinics with more time allocated for the nurse (>one hour/1,000 inhabitants /week) and those with less time for appointments with the asthma nurse. Patients at asthma clinics with more time allocated were, compared to patients at asthma clinics with less time, more knowledgeable about how to change their medication at infections, 73% as compared with 58% ($p=0.009$) and expressed more sufficient knowledge about asthma, 39% as compared with 27% ($p=0.03$). Patients at asthma clinics with more time allocated also more frequently obtained asthma control, 44% as compared with 27% ($p=0.003$), but there were no differences in quality of life measures.

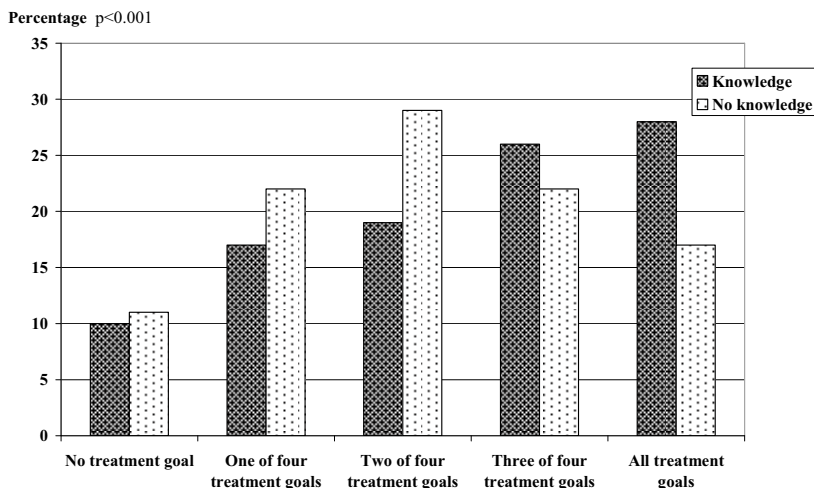


Figure 3. Relationship between patient-reported knowledge (in percent of the total number of patients in the study population) of asthma and achievement of treatment goals 0-4. Treatment goals are defined as: use of less than three doses of short-acting beta2-agonist per week, no night awakenings, no emergency consultations and no use of oral steroids

Table 5. Comparison of patients who had attended the asthma clinic during the last year. Time for the nurse is expressed as hours per week/1000 inhabitants in the catchment area of the primary health care centre

	One hour or more		Less than one hour		p
	n	%	n	%	
Patients (% women)	104	67.3	225	59.1	
Age, mean		29.6		28.6	
Allergies	92	90.2	177	80.5	0.03
Daily smokers	14	13.6	36	16.1	ns
Medication					ns
Step 1 ^{a)}	18	17.5	40	17.9	
Step 2 ^{b)}	37	35.9	98	43.8	
Step 3 ^{c)}	48	46.6	86	38.4	
Change medication at infections	75	72.8	129	57.8	0.009
Change medication at more symptoms	86	83.5	176	78.9	ns
Change medication according to peak flow	70	78.7	117	68.0	ns
Sufficient knowledge	40	39.2	61	27.4	0.032
Asthma control ^{d)}	45	43.7	61	27.4	0.003

^{a)} only beta2-agonist

^{b)} inhaled corticosteroid (ICS) regularly or periodically

^{c)} ICS + long-acting beta2-agonist or ICS + antileukotrien

^{d)} defined as use of short-acting beta2-agonist less than three doses per week, no night awakenings, emergency visits or courses of oral steroids

Paper III

Six hundred and eighty-two of the patients (60%) were women, with a mean age of 31 years (table 6). Two thirds of the patients had an asthma history of more than 5 years and 80% reported atopy. Ten percent of the men and 20% of the women were daily smokers.

Table 6. *Characteristics of the study population*

	Men			Women			p
	n	mean or %	SD ¹⁾	n	mean or %	SD ¹⁾	
Number	451	39.8		682	60.2		
Age, years		30.1	8.9		30.5	9.4	ns
Years with asthma, %							ns
< 1 year	35	7.8		43	6.4		
1-5 years	117	26.2		199	29.7		
> 5 years	294	65.9		429	63.9		
Atopy, %	358	81.9		548	83.0		ns
Daily smokers, %	43	9.6		133	19.7		<0.0001
Occupational status, %							<0.0001
full-time + students	392	88.3		409	61.4		
part-time	17	3.8		142	21.3		
unemployed	22	5.0		37	5.6		
Other ²⁾	13	2.9		78	11.7		
Sick leave last 6 months, %							ns
never	349	80.6		461	76.5		
once	46	10.6		63	10.4		
twice	15	3.5		30	5.0		
more than twice	23	5.3		49	8.1		
Short-acting beta2-agonist ³⁾ , %	208	47.0		316	46.8		ns
Night awakenings ⁴⁾ , %							<0.005
never	336	78.5		462	68.6		
once	46	10.7		94	14.0		
several times	46	10.7		117	17.4		
Emergency consultations ⁵⁾ , %							<0.0001
never	364	81.3		483	71.7		
once	60	13.4		105	15.6		
twice	12	2.7		45	6.7		
more than twice	12	2.7		41	6.1		
Oral steroids ⁵⁾ , %							<0.0001
never	402	89.3		553	81.9		
once	21	4.7		69	10.2		
twice	10	2.2		33	4.9		
more than twice	9	2.0		17	2.5		

¹⁾ standard deviation ²⁾ includes patients on parental leave and disability pensioners

³⁾ more than twice during the last week ⁴⁾ owing to asthma during the last week

⁵⁾ during the last six months

Table 7. Mean values of domains and overall MiniAQLQ scores according to parameters of asthma control. The overall scores are adjusted for age, sex, sick leave, occupation and knowledge of the asthma disease

	Symptom score	Activity score	Emotion score	Environment score	Overall score (\pm SD) ¹⁾	p
Short-acting beta2-agonist ²⁾						<0.0001
no	5.79	6.14	5.87	5.83	5.91 (0.92)	
yes	4.85	5.58	5.01	5.33	5.17 (0.92)	
Night awakenings ³⁾						<0.0001
never	5.76	6.11	5.75	5.81	5.86 (0.85)	
once	4.63	5.60	5.09	5.31	5.12 (0.84)	
several times	3.92	4.84	4.36	4.76	4.42 (0.89)	
Emergency consultations ⁴⁾						<0.0001
never	5.51	6.00	5.64	5.73	5.71 (0.96)	
once	5.02	5.60	5.00	5.21	5.21 (0.94)	
twice	4.91	5.64	4.88	5.42	5.20 (0.96)	
more than twice	4.60	5.18	4.70	4.97	4.85 (1.00)	
Oral steroids ⁴⁾						<0.0001
never	5.46	5.94	5.55	5.65	5.64 (0.96)	
once	4.78	5.52	5.02	5.44	5.16 (0.98)	
twice and more	5.01	5.65	5.14	5.29	5.26 (0.98)	

¹⁾ standard deviation

²⁾ more than twice during the last week

³⁾ owing to asthma during the last week

⁴⁾ during the last six months

Almost half of the patients had used short-acting beta2-agonists more than twice during the last week, and 21% of the men and 31% of the women had experienced night awakenings due to asthma. During the last 6 months, 19% of the men and 28% of the women had emergency consultations and 9% of the men and 18% of the women had taken oral steroids owing to asthma exacerbations.

The MiniAQLQ scores were higher for men (5.66) than for women (5.44) ($p=0.001$) and decreased with age, smoking and sick leave periods during the last six months. The scores increased with extent of employment and level of perceived knowledge about asthma.

The MiniAQLQ scores were lower for patients who had used short-acting beta2-agonists more than twice during the last week and for those who had been prescribed a course of oral steroids during the last six months. The scores decreased in relation to the number of night awakenings during the last week and emergency consultations during the last six months (table 7).

The combined influence of the variables, use of short-acting beta2-agonists, night awakenings and emergency consultations on the overall MiniAQLQ score after adjustment for the influence of sex, smoking habits,

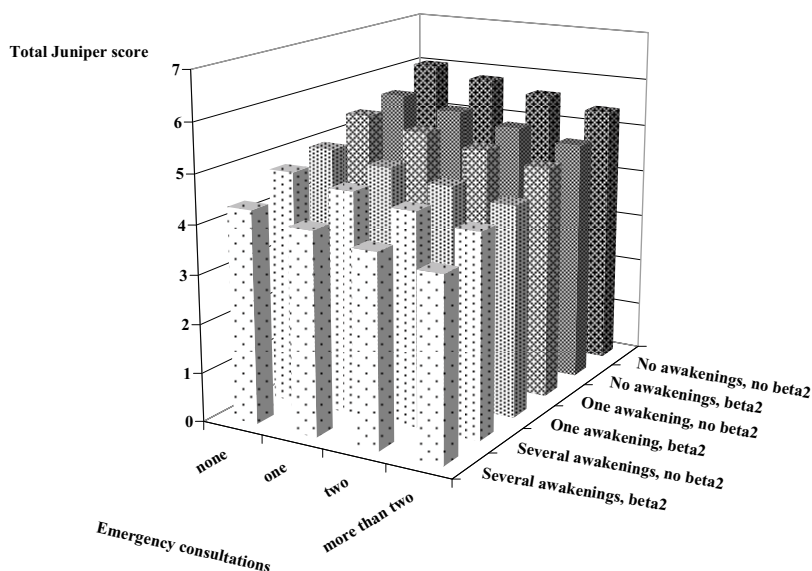


Figure 4. Combined influence of the variables use of short-acting beta2-agonists, night awakenings and emergency consultations on overall MiniAQLQ score

sick leave and occupational status is displayed in figure 4. The mean overall score was 3.70 among patients using beta2-agonists more than twice during the last week, having several night awakenings and more than two emergency consultations, as compared with 6.03 for those not using beta2-agonists and having no night awakenings and emergency consultations.

Paper IV

The majority of the patients from the Praxis-study (60%) were women, and they were more often daily smokers than men, 13% as compared with 7% ($p=0.004$). There were no sex differences in mean FEV₁ % of predicted value before bronchodilatation, medication for asthma or patient-assessed level of severity.

One third of the patients had received their asthma diagnosis during the study period 2000-2003, and 40% of these at an emergency visit. There were no sex differences in the diagnostic measures. Regular control for asthma was similar, but women more often than men received a written self-management plan, 26% compared to 19% ($p=0.02$).

Table 8. Sex differences in patients ≤ 46 years and ≥ 53 years. Short-acting beta2-agonist more than twice during the last week, night awakenings attributable to asthma during the last two weeks, and asthma exacerbations during the last six months

	≤ 46 years				≥ 53 years			
	women		men		women		men	
	n	mean or %	n	mean or %	p	n	mean or %	p
Number	275		178			354		240
Age (mean)		33		34	ns		63	63
Daily smoking	45	16	7	4	<0.001	30	9	18
Depression	27	10	7	4	0.027	43	12	12
BMI (mean)		25		26	ns		27	27
Sick leave (working/studying) ^{a)}	44	19	13	8	0.003	30	19	14
FEV ₁ in % of predicted prebronchodilatation	72	91	52	93	ns	114	81	93
Medication					0.004			ns
Step 1 ^{b)}	68	25	67	39		55	16	35
Step 2 ^{c)}	63	23	42	24		86	25	57
Step 3 ^{d)}	141	52	65	37		201	59	146
Short-acting beta2-agonist	126	46	77	44	ns	191	55	132
Night awakenings	78	29	34	19	0.034	116	33	76
Asthma exacerbation	78	29	30	17	0.005	117	33	76
Quality of life (score) ^{e)}		5.44		5.89	<0.001		5.04	5.10

^{a)} due to asthma during the last six months

^{b)} only beta2-agonist

^{c)} inhaled corticosteroid (ICS) regularly or periodically

^{d)} ICS + long-acting beta2-agonist or ICS + antileukotrien

^{e)} adjusted mean (age, education, smoking, BMI, allergy, depression) of total score of MiniAQLQ

In Table 8 women and men were compared in the age range when women are pre- and postmenopausal. The cut off levels were ≤ 46 years (younger group) and ≥ 53 years (older group). In the younger group, women were more often daily smokers than men, 16% versus 4% ($p<0.001$). Depression and sick leave were more common in women in both age groups.

Women in the younger group had medication at higher steps than men ($p=0.004$), whereas there were no differences in the older group.

Younger women reported more night awakenings ($p=0.034$) and asthma exacerbations ($p=0.005$), but there were no differences in the use of short-acting beta2-agonists in comparison with younger men. In the older age group there were no sex differences in these asthma control parameters.

Multivariate logistic regression analysis showed that the odds for younger women as compared to younger men of having night awakenings was 1.6 (95%CI 1.00-2.68) and for asthma exacerbations 2.0 (95%CI 1.22-3.43) adjusted for age, smoking, education and BMI. Daily smoking and lower education were independently associated with night awakenings, while higher age and lower education were associated with asthma exacerbations.

In the younger group, women had both significant and clinically relevant lower quality of life than men, 5.44 compared with 5.89 ($p<0.001$), whereas there was no difference in the older group. Lower education and higher BMI were independently associated with lower quality of life. The quality of life scores regarding domains, and the total scores for the younger and older age groups with respect to sex are displayed in figure 5. There were significant differences between the sexes for all variables in the younger group but not in the older group.

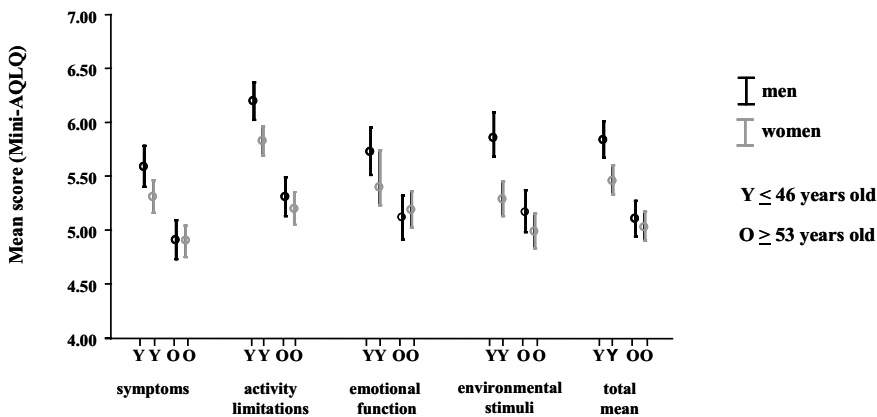


Figure 5. Quality of life scores regarding mean and 95% confidence intervals for the domains and total score in men and women in the younger (≤ 46 years) and older (≥ 53 years) group respectively

Discussion

Methodological considerations

Study design

Both the AIM-study and Praxis-study are cross-sectional studies, and the latter also includes a patient record study.

A cross-sectional study enables description of the relationship between diseases (or other health-related states) and other factors of interest in a specified population at a particular time. It is not possible to establish causal relationships or to obtain reliable perspectives on the natural history of a disease like asthma in a cross-sectional study.

For our aims in the AIM- and Praxis-studies a cross-sectional study was considered suitable to measure the frequency of conditions concerning the asthma disease and to demonstrate associations.

Selection

Other demands on a cross-sectional study are that it should be performed in representative samples of the population if the generalizations from the findings are to have validity.

In Paper I there was no selection of the PHCCs as all centres in the area were asked to participate in order to obtain a complete picture of the organisation of asthma care in the region. The aim of Paper II was to evaluate outcomes for patients with and without access to asthma clinics. In this part, PHCCs with small catchment areas had to be excluded as they were too small to have asthma clinics. Other PHCCs, a total of 45, were excluded owing to lack of computerized records and lack of interest. The remaining 193 PHCCs were then stratified into groups according to organisation of asthma care and size. A proportional random sample of 42 PHCCs was drawn from these strata, 14 in each group. In this way it was possible to measure differences between complete and incomplete asthma clinics, and the stratification according to size was done to make the PHCCs more comparable. With this selection, there is a predominance of PHCCs with asthma clinics in this study, which may result in better outcomes for the patients. To adjust for this, and to be able to generalize the results to the population in the

area, the results in Paper III were weighted with regard to the sampling proportion. There were no differences in the main outcomes after the weighting.

One bias in the AIM-study is that only patients who had attended the PHCC during the last 18 months were sampled, which could imply that fewer patients with mild asthma participated in the study. Another selection bias with this method is that all patients attending a PHCC do not receive a recorded diagnosis, as the physician may neglect to state a diagnosis in the records. Some patients with milder asthma may also receive their prescriptions without having an appointment with the physician. The population in the AIM-study was young, 15-45 years, and the results can only be generalized to young adult asthma patients in primary care.

In the first part of the Praxis-study, PHCCs and outpatient clinics at hospitals were stratified with regard to the seven counties to enable comparison between them.

Patients were then randomly selected from diagnosis lists of the patients that had attended the PHCCs and out-patient clinics at hospitals with pulmonary/internal medicine departments during four years, 2000-2003. This period was chosen to be able to obtain “baseline data” about asthma patients in the region before the guidelines from the National Board of Health and Welfare, published in 2004, were implemented. The main aim of the Praxis-study was to compare the actually care given in the region with the guidelines.

The study population in the Praxis-study covers a broad age span, 18-75 years, and it should be possible to generalize the findings to the population of adult asthma patients in primary and secondary care in Sweden.

The questionnaire in the Praxis-study did not include data about menstrual status, oral contraceptives, oestrogen substitution, or laboratory data regarding hormonal status. Therefore the age limits of the subgroups in Paper IV regarding menopausal status were set according to results from a previous study [97]. These cut-off limits can be questioned, but the results remained unchanged after testing other cut-offs close to age 50 years.

Questionnaires and patient records

Both studies used the quality of life questionnaire MiniAQLQ, which is well validated and used in many studies.

The MiniAQLQ, with 15 questions, does not have the precision of the AQLQ with 32 questions, but is a satisfactory quality of life instrument especially in larger surveys. In these large studies it was used for practical reasons, with the intention of obtaining a good response rate.

One questionnaire in the AIM-study and one in the Praxis-study was constructed by the researchers to include questions about demographics, symptoms, medication, contact with the health care system and knowledge about

the disease. Most of these questions have previously been used in other large surveys [53].

To obtain as good validity as possible in the patient record study, we aimed to interpret and extract data from the records in a highly structured way. All records were collected at the research centre, where two nurses scrutinized them and extracted relevant data from all records into a structured data form. This was performed with continuous supervision and double-checking by the researchers.

Response rate – non-responders

Both studies had high response rates, which together with the random sampling of patients, increases the probability that the study populations are representative of the patient population with asthma in the region.

An analysis of the non-responders was made in the AIM-study. A telephone interview was performed with 104 non-responders (27% of the non-responding sample), of whom 70 (67%) were willing to be interviewed by telephone. In these interviews an abbreviated form of the disease oriented questionnaire was used. In addition, some variables such as age and sex were known for 90% of the 104 non-responders. There were no differences between responders and non-responders regarding age, sex, duration of asthma, pollen allergy, use of rescue medication and not picking up prescribed medication owing to the cost.

Analyses of responders and non-responders in the Praxis-study showed no differences in response rate between the sexes, and there were no differences in response rate between the sexes in the younger and older subgroups in Paper IV.

Analysis of the effect of non-responders

When analysing the results of one of the main outcomes in the AIM-study, the total mean of the quality of life score, we received a mean for the responders (n=1098) of 5.52 with a SD of 1.12. The mean of the non-responders (n=379), calculating an extreme situation with ± 5 SEM, changed 0.04 points in either direction. Our interpretation is that this difference did not change the results or the conclusions of the study.

Discussions of main results

Organisation for asthma in primary care

Today asthma is mainly managed in primary care [7, 66], which makes high demands on the organisation and content of care. The quality requirements

and indicators for diagnostics, treatment and management of asthma have also been expressed in national and international guidelines [1, 52, 74, 98]. The quality indicators for primary care include access to spirometer and an asthma/COPD clinic.

Diagnostic tools such as spirometers were quite rare at PHCCs 10-15 years ago, as were asthma clinics. According to the results in Paper I, which was almost a complete mapping of the PHCCs in the region in 2000, 77% had spirometers. In another Swedish study from 2000 in the county of Stockholm, 58% had access to a spirometer [99], which could be explained by greater access to pulmonary function laboratories and hospitals in Stockholm. From an international perspective these proportions were high. In a UK study of 209 randomly sampled GPs, 59% had access to a spirometer [100], and in a Canadian study of 268 family physicians in Ontario, 40% reported access to a spirometer (personal communication D'Urzo A, Toronto, Canada).

In the Praxis-study in 2005, performed in the same region as the AIM-study, the proportion had increased to 93%. Approximately the same level, 96%, was demonstrated in a study of 173 PHCCs in western Sweden at the same time [101]. In another study performed in Sweden during 2005, the SYMPATI-study [102], 99% of the 111 PHCCs had access to a spirometer, and in a study from the county of Östergötland in 2006, all 42 PHCCs had spirometers [103]. In a Spanish study of 50 PHCCs in 2005, the proportions were similar to the results in the Praxis-study, 91% [104].

These percentages indicate that the access to spirometers in primary care is increasing rapidly, although the difference in the frequency of using spirometry may affect the quality. Good, sufficient training of the staff performing spirometry is essential to obtain high-quality data, as has been emphasised in several studies [47, 71]. One fifth of the PHCCs in the AIM-study performed only 0-2 spirometries per month, and in the Spanish study from 2005 22% of the PHCCs never used their spirometers, and only 2 centres performed between 10 and 20 tests per week. In the study from western Sweden, approximately 90% of the PHCCs reported that they used their spirometers every week.

In the AIM-study, the mean number of spirometries performed per 1,000 inhabitants and year in the whole region was 19. According to the guidelines produced by The Swedish National Board of Health and Welfare in 2004, the optimum number of spirometries per PHCC has been estimated to at least 60. Only 6% of the PHCCs in the AIM-study reached more than 50. This issue was not investigated in the Praxis-study. Important explanations for the discrepancy between the recommended and actual levels might include lack of staff time and insufficient knowledge among the GPs regarding the importance of spirometry.

More than half, 53%, of the PHCCs in Paper I had an asthma clinic, but according to the national criteria for asthma clinics only one out of three was

complete, *i.e.* fulfilled all seven criteria. The main shortcoming was that too little time was allocated for the nurse, and there was great variation among the centres in this respect. One recent Swedish study focused on the question of sufficient time allocation for the asthma nurse and found that this is an important factor in providing good quality asthma management [105]. The conclusion was that at least one hour per week per 1,000 inhabitants is necessary to provide good care for asthma and COPD patients. Only 17% of the asthma clinics in the AIM-study reached these goals. The other two most common reasons for incompleteness were absence of a scheduled surgery and absence of a GP responsible for the clinic.

Another important aspect of an asthma clinic is that the nurse is well educated to provide good quality care and patient training. There is no national recommended minimal standard level of education for the nurse, and for this reason we made no evaluation of the asthma nurse training in Paper I. However, according to the international guidelines [1, 106], patients education is a priority activity.

The conclusions of Paper I are that 77% of the centres had a spirometer and 53% had an asthma clinic. Most of the incomplete asthma clinics had the structural prerequisites to become complete, such as a spirometer and a trained asthma nurse according to national recommendations in Sweden. The most common limiting factors were related to time allocation for the asthma nurse. Later studies show that access to spirometers and asthma/COPD clinics is increasing.

During year 2008, new national criteria for an asthma/COPD clinic will be published. The background is that the requirements for education of the nurse have been elevated to the university level and the need for even more time allocated for the asthma clinics, since they now also include patients with COPD [73].

Asthma outcomes in relation to asthma clinics

The issue in Paper II was whether access to asthma clinics improves patients' outcomes with respect to knowledge, asthma control and quality of life.

The results revealed that patients at PHCCs with asthma clinics had more scheduled appointments, medication at a higher step (*i.e.* ICS more regularly), were more well-informed about the disease and about how to change it when their condition worsened than patients at PHCCs without asthma clinics. However, they still did not have better asthma control or higher quality of life. One explanation might be that the quality of care at the asthma clinics is generally too low to influence these outcomes. From Paper I we know that there is great variation in the time allocated for the asthma nurse. Sufficient time is important to achieve good quality, as was recently demon-

strated in a Swedish study where at least one hour per 1,000 inhabitants and week was proposed [105].

The odds for patients who reported that they had knowledge about asthma versus patients lacking this knowledge to achieve asthma control was 1.5 (95%CI 1.1-2.0), after adjustment for age, sex and organisation for asthma. This underlines the importance of good quality education with self-management plans and recognition of the special needs of the patients to empower them to have full control over their disease, which is emphasised in the guidelines [1].

When studying the effects on outcomes in relation to the allocated time for the asthma nurse, the cut-off level of one hour or more per 1,000 inhabitants/week was chosen, as less time seemed to be insufficient [105]. Patients who had attended asthma clinics with more time for the asthma nurse reported sufficient knowledge and asthma control more frequently. More time for the nurse increases the possibilities for each patient to have sufficient time for education and special needs, which may enable patients to become more aware of the signs and symptoms of the disease and possible improvements [107-110]. It also enables the nurse to create individual self-management plans together with the patient, including adjustment of medication in different situations, which may result in more adequate treatment and enhanced asthma control [111-113]. In Sweden, time allocation for the asthma nurse is a problem at most PHCCs [105, 114], which undoubtedly influences the quality of the work performed at the clinics.

There are several possible objections concerning the method used in this study. A cross-sectional study gives a description of the state of the disease and outcomes at one time, but it is not possible to follow progress. We used patient questionnaires only, no examination of the patients or objective measurements of lung function. In this case, a randomised controlled trial with the intervention of the asthma clinic concept would have been preferable, but difficult to perform in an unobjectionable way owing to difficulties in avoiding bias even in a randomised study [72]. Only patients who had attended the PHCCs during the last 18 months participated. This could have resulted in a bias towards more severe and newly diagnosed patients, as patients with milder disease may attend the PHCC less often. When asked in the questionnaire, only half of the patients stated that they had seen the asthma nurse during the last year. There was no information on whether the patient had attended the asthma clinic previously, such information could have influenced the results. The structure of the asthma clinic was known, but not the contents of the asthma nurses' work.

National guidelines in Sweden [98] recommend asthma clinics in primary care, but few studies have presented positive outcomes. One Swedish study evaluating patients before and after intervention from an asthma nurse demonstrated improvements in asthma control [115], but there are few well-designed randomised controlled trials evaluating asthma clinics. In a Coch-

rane analysis from 2002 [72], only one study satisfied the criteria for inclusion [116]. This study demonstrated that patients at asthma clinics had fewer night awakenings and more often used peak flow meters. In one study published after the Cochrane report, patients had fewer emergency visits after follow ups by both GP and nurse [117], while another did not show higher quality of life in the patients attending the asthma clinic [118].

Quality of life and asthma control

Disease-specific instruments for measuring quality of life have been developed and validated, and are generally available [78, 79, 83], but health-related quality of life in asthma patients has not often been used as a main outcome in studies evaluating asthma treatment and management in primary care [74, 119]. Guidelines emphasise the achievement of asthma control, but most patients do not achieve these goals [53, 120], and patients' perceptions of asthma control differ from actual control [54, 120]. Reasons for this may include lack of knowledge and awareness of the positive effects of asthma medication on asthma symptoms, as well as other factors such as psychological repression, unwillingness to accept the disease or depressive and anxiety disorders [55, 56, 121]. The correlation between asthma control and quality of life is controversial. Some studies have demonstrated a positive association between achievement of asthma control and improvements in asthma-specific quality of life [63, 122], while other studies have shown only a weak correlation between asthma symptoms, frequent use of rescue medication and asthma-specific quality of life [123, 124].

The results from Paper III indicate a strong association between asthma control and asthma-specific quality of life (see figure 3). The quality of life scores decreased in relation to number of night awakenings, emergency visits, and whether or not patients had taken a course of oral steroids or used short-acting beta2-agonists more than twice during the last week. In multivariate analysis, when adjusting for sex, smoking habits, sick leave and occupational status, the total score for patients with asthma control was 6.03 as compared with 3.70 for patients who were not controlled. In a population based study published in 2008 with the aim of analysing the relationship between health related quality of life and asthma severity, the AQLQ scores decreased in relation to number of asthma attacks and nocturnal symptoms, as well as whether or not patients had made emergency visits the last year [125]. A prospective study in 2007 including 987 patients from the TENOR study concluded that asthma control remains a strong predictor of health related quality of life even when underlying differences in severity classification are taken into account [126]. The GOAL study, published in 2007, found a strong correlation between asthma control and quality of life, and that near to normal health-related quality of life can be achieved when treatment aims for total control of asthma [127]. This implies that the achieve-

ment of treatment goals is important for patients' well being, an important point to be aware of when monitoring asthma patients at the clinic. Another aspect is that quality of life is a distinct component of health status, capturing the patient's perspective and experience of the disease, and should be measured in clinical practice and used as an outcome measure [124, 128]. To obtain a complete picture of a patient's health status, health-related quality of life need to be measured together with the conventional clinical indices [129, 130].

According to a study concerning validation and usefulness of questionnaires for patient-reported outcomes in asthma [128], the clinician's ratings correlated poorly with changes in quality of life scores and pulmonary function tests. Considering this, brief quality of life questionnaires could be valuable in the management of patients in the clinical practice. The MiniAQLQ has not yet been validated for such use.

Given the fact that the study population was young, mean age 30, expectations should be high regarding quality of life. In a recent study [131] a score of six or more has been proposed as indicating that the asthma has little impact on patients' quality of life. In this study only 43% of the patients had a score of six or more. This may be attributable to undertreatment, non-compliance or insufficient patient education. Alternatively, the score six or more may be too high.

Women had less adequate asthma control and lower quality of life scores than men although there were no sex differences of clinical relevance regarding quality of life. The patients in the AIM-study were 15-45 and the results are similar to those found in the Praxis-study (Paper IV) in patients 46 and younger but not in patients 53 and older. Several other studies have shown that women experience greater impairment in health related quality of life than men at similar asthma severity [125, 130]. Other reasons for the differences could be a sex-related difference in evaluating and answering the MiniAQLQ, where women may be more likely to perceive symptoms of asthma and loss of control [132]. It could also be that men in general accept or repress their symptoms more and seek less medical care than women [133].

Self-reported perceived knowledge of the disease was an indicator of higher quality of life in the AIM-study, showing that education is important in asthma management and provides patients with more self-assurance and ability to control the disease, as described in other studies [63, 134]. This was also demonstrated recently in a study using a specific instrument measuring perceived control of asthma [135]. A useful way of improving this essential aspect of asthma management could be to have a well-trained nurse at asthma clinics [115].

Management of asthma should aim to achieve the best possible control for patients, as it is important to their well being. Health-related quality of life is an outcome that should also be considered in the clinical evaluation, as it

describes patients' perspectives of the influence of the disease on their lives and therefore add information to conventional clinical outcomes.

Sex-related differences

Sex-related differences in asthma prevalence over the life is a familiar concept. Before puberty, boys dominate, with an increase in the incidence of asthma in women until menopause, when it becomes equal between women and men [136, 137]. The reasons have not yet been fully explored, but one proposed theory is the influence of sex hormones on the development of asthma and asthma severity [22, 88, 92, 138]. There are studies suggesting that female sex hormones and the menstrual cycle phase influence respiratory function, with a worsening of asthma during pregnancy and the perimenstrual period [95, 139-141].

Several studies have demonstrated that women generally have poorer outcomes in asthma than men, considering symptoms, emergency visits and quality of life [85-87, 136]. It is unclear whether this difference reflects biological, psychosocial or cultural distinctions between men and women.

The aim of the study presented in Paper IV was to analyse whether there are sex-related differences that could be related to menopausal status regarding asthma control, quality of life and asthma management.

The selection of the population for this study, including patients in both primary and secondary care, ensures that the whole range of asthma severity is represented. The response rate was high, 71%, and analysis of non-responders showed no differences in response rate between the sexes in the younger and older groups. The broad age range in the study, 18-75 years, made it possible to compare a younger group with premenopausal women, and an older group with postmenopausal women. The cut-offs were set at ≤ 46 years and ≥ 53 years, in accordance with previous studies [97, 142].

The results in this study demonstrate that women have poorer asthma control and quality of life during the premenopausal period, but after menopause there are no sex-related differences regarding these outcomes. There were no sex-related differences in asthma management, except for the fact that women more frequently received written asthma management plans.

As mentioned above, women in the AIM-study, with younger asthma patients of 15-45 years, had lower quality of life than men, and also poorer asthma control regarding night awakenings, emergency visits and courses of oral steroids [143]. These results were similar to the results in the younger group, 18-46 years, in the Praxis-study. In a study from 2006 including 1,351 patients 18-50 years old, in which asthma control was assessed with the Asthma Control Test, smoking, female sex and BMI over 30 were independently associated with inadequate asthma control [144]. In another study from 1998 analysing quality of life in asthma patients 15-55 years old men reported significantly higher quality of life than women [136].

Despite having lower quality of life and less often asthma control as compared to men in the same ages premenopausal women used more medication for their asthma. There might be several reasons for this. In this study we found that younger women were more frequently smokers, and daily smoking was associated with night awakenings owing to asthma symptoms. As smoking has been reported to decrease the effects of inhaled corticosteroids [31, 145, 146], this could influence the effects of treatment.

Another factor that could influence quality of life is depression, which was more common in women in all ages in our study. However, there were only sex-related differences with lower quality of life for women in the younger group, where the women were premenopausal. Although the younger women had significantly lower quality of life than the men, there were no sex-related differences in lung function indicating, as in previous studies [79, 119], that the association between lung function and quality of life is weak.

The relationship between female sex hormones and severity of asthma, asthma worsening and exacerbations have been analysed in several studies [87, 95, 139]. Some studies suggest that an increase in airway hyperresponsiveness related to the luteal phase of the menstrual cycle could be the reason for premenstrual exacerbations, which are common and estimated to affect about 40% of women with asthma. The influence of oestrogen replacement therapy on asthma development has also been studied, and found to worsen the patient's asthma [22, 92, 147] but also to be associated with improved lung function [93]. Oral contraceptives have both been associated with higher prevalence of asthma, and shown no significant relation to the prevalence [94]. In this study there was no possibility to control for these factors as the survey did not include questions about menstrual status, oral contraceptives and hormone replacement therapy. Increased levels of oestrogen in the obese could be one explanation for the relationship between female obesity and a higher risk of developing asthma [148]. We also found that obese (BMI > 30) premenopausal women in our study had clinically relevantly lower quality of life than obese men in the same age group. Another study found that men had lower quality of life than women with increasing BMI [149]. Some studies imply that the sex differences are more related to differences in response to a disease than to differences in the asthma disease [136].

The subdivision into younger and older age groups in this study was made with reference to previous studies [97, 142], but our chosen cut-off age could be questioned. However, the results in this study remained the same even when we set other cut offs around the age of fifty (data not shown).

One weakness of this study was that the questionnaire was sent to the patients in 2005 while the records were analysed from 2000-2003. This may have the effect for some patients that their asthma situation was different in 2005 than indicated by the data in the patient records from a few years ear-

lier. As mentioned above, there were no questions about the hormonal status in the survey, which would have given important information when classifying the patients as pre- or postmenopausal. Patients were selected from diagnosis-lists based on physicians' diagnosis of asthma in the records, without considering the results of lung function tests such as spirometry.

The results from this study indicate that there are sex-related differences in asthma outcomes at the ages when women are premenopausal. One theory regarding these differences is that they are attributable to the influence of female sex hormones on the asthma disease.

For a clinician, it is important to be aware that the hormonal status of premenopausal women may influence their asthma regarding both control and quality of life. There is a need for further clinical research studies regarding the relationship between female sex hormones and asthma outcomes.

Many studies have demonstrated that there are sex-related differences in asthma outcomes, possibly attributable to sex hormones. In the future, this should be considered in the guidelines for asthma.

Concluding remarks

- The organisation for asthma in primary care is improving, with more frequent spirometers and complete asthma clinics, but all patients do not yet have access to high quality asthma management.
- One of the main tasks for asthma clinics in primary care is education - more well-informed patients have better asthma control and quality of life.
- Patients have better asthma control at asthma clinics with more time allocated for the asthma nurse.
- Health-related quality of life, *i.e.* the patient's perspective on the influence of the illness on his/her life, is an important additional outcome in asthma, with a strong association to asthma control.
- A validated quality of life questionnaire for clinical practice would enable clinicians to obtain an understanding of this aspect of the disease and to evaluate treatment in a more comprehensive way.
- There are sex-related differences in asthma outcomes among younger patients. The influence of female sex hormones on asthma has not yet been fully investigated, and needs more research attention.

Swedish summary

Avhandlingens syften har varit att analysera och utvärdera organisationen för astma samt relationen mellan livskvalitet och astmakontroll för patienter i primärvården. Ett ytterligare syfte har varit att analysera könsskillnader vad gäller utfallsmåttan astmakontroll och livskvalitet för astma och dess relation till menopaus.

Studiematerialet baseras på två tvärsnittsstudier i Uppsala-Örebro regionen. Den första, AIM-studien hade två delar, en enkät angående organisationen för astma år 2000 och en patientenkät år 2001. Praxis-studien, som genomfördes år 2005 innehöll en patientenkät samt journalstudier på dessa patienter under åren 2000-2003. Patientenkäterna innehöll frågor angående bakgrundsdata, medicinering, symtom och sjukvårdskontakter samt en sjukdomsspecifik livskvalitetsenkät, MiniAQLQ.

Resultaten visade att 77% av vårdcentralerna hade spirometer och 53% astmamottagning. På vårdcentraler med astmamottagning angav 77% av patienterna att de hade tillräckliga kunskaper om astma jämfört med 65% på vårdcentraler utan astmamottagning ($p < 0.001$). Om astmasköterskan hade en timme eller mer per 1000 innevånare och vecka för mottagningen uppnådde 44% av patienterna astmakontroll, jämfört med 27% om mottagningen hade mindre tid ($p = 0.003$). Patienter som medicinerat med kortverkande beta2-agonister mer än två gånger senaste veckan hade kliniskt signifikant lägre livskvalitet (5.17 jämfört med 5.91). Dessa resultat gällde också för patienter som vaknat senaste veckan på grund av astma (4.42 jämfört med 5.86), fått kortisonkur (5.26 jämfört med 5.64) och de som angav akutbesök på grund av astma senaste halvåret (4.85 jämfört med 5.71). Premenopausala kvinnor hade signifikant lägre livskvalitet än män i samma ålder, medan postmenopausala kvinnor inte uppvisade någon skillnad jämfört med män i samma ålder. Oddsens var 2.0 (justerat för ålder, rökning, BMI, utbildning) för premenopausala kvinnor att ha astmaexacerbationer jämfört med män i samma ålder. Inga skillnader kunde påvisas mellan postmenopausala kvinnor och män i samma ålder.

Studierna visade sammanfattningsvis att hälften av vårdcentralerna hade en astmamottagning och majoriteten en spirometer. Patienter på vårdcentraler med astmamottagning angav att de hade tillräcklig kunskap om astma i större utsträckning än patienter på vårdcentraler utan astmamottagning. Andelen patienter som uppnådde astmakontroll var större om astmamottagning-

en hade mer tid. Att uppnå målen för astmakontroll är relaterat till högre livskvalitet hos patienter i primärvården. Premenopausala kvinnor hade sämre astmakontroll och lägre livskvalitet än män i samma ålder, medan inga skillnader kunde påvisas mellan postmenopausala kvinnor och män i samma ålder.

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Appendix 1

Questionnaire about organisation of asthma care (translated from Swedish).

1. How many full-time GP-positions are there at your centre?
How many GP's are appointed?
2. How many inhabitants are there in your catchment area?
3. Are patients with asthma investigated and treated at your clinic?
Yes ☐ No ☐ Don't know ☐
4. Is your clinic equipped with a spirometer?
Yes ☐ No ☐ Don't know ☐
5. Does your centre have an asthma clinic?
Yes ☐ No ☐ Don't know ☐

- If your answer to question 5 is yes, please answer questions 6-11
- If your answer to question 5 is no, the questionnaire is completed.

6. For how many years have your centre had an asthma clinic?
Less than 1 year ☐ 1-3 years ☐ More than 3 years ☐
7. How many hours are weekly allocated for the asthma clinic?
8. Does the asthma clinic have a specially trained nurse?
Yes ☐ No ☐ Don't know ☐
9. Does the clinic have a GP responsible for the asthma clinic?
Yes ☐ No ☐ Don't know ☐
10. Does the asthma nurse have a scheduled surgery?
Yes, every week ☐ Yes, now and then ☐ No ☐ Don't know ☐
11. Does the asthma nurse perform structured investigations with peak flow measurements, peak flow diary and calculations of variability and reversibility at the asthma clinic?
Yes ☐ No ☐ Don't know ☐
12. Does the asthma nurse educate the patient about asthma, medication, treatment plans and prevention.
Yes, often ☐ Yes, now and then ☐ No ☐ Don't know ☐

Appendix 2

English condensed version of “Questions about your asthma”. Answers were mostly multiple choice but sometimes open answers were required. Typical choices were “Yes”, “No” and “Don’t know” if not otherwise specified. Abbreviations used: Inhaled corticosteroids (ICS), short- and long acting beta2-agonist (SABA) and (LABA).

Background data

1. What is your age and gender? ____ years Female/Male
2. How many years have you had asthma? < 1 year, 1-5 years, > 5years
3. What is your main occupation? – full-, part-time or domestic worker, unemployed, student or other specified alternative?
4. Do you smoke daily?

Symptoms

5. Do you get asthma/ rhinitis symptoms from pollen (birch, grass or mugwort) or to furred animals (cat, dog or horse)?
6. Have you woken up due to cough, wheeze or shortness of breath in the last week?
7. Have you made emergency/unscheduled urgent care visits to hospital, primary care or paediatric care due to asthma in the last six months? If yes: once, twice, > two times.
8. Have you been hospitalised due to asthma in the last six months?
9. Have been home from work or studies due to asthma in the last six months? If yes: once, twice, > two times. If yes, nr. of days?

Medication – answers if not otherwise specified - regularly, periodically or not at all.

10. Have you used SABA due to asthma symptoms more than twice in the last week?
11. Have you used ICS the last six months?
12. Have you used LABA the last six months?
13. Have you used leukotrien antagonist the last six months?
14. Have you used systemic corticosteroids due to asthma exacerbation the last six months? If yes, specify how many times.
15. Have you used homeopathic drugs, zone therapy or acupuncture the last six months?
16. Have you renounced to pick up your prescribed asthma medication due to costs in the last year?

Medical care

17. Do you go to annual follow-ups for your asthma?
18. Do you know which doctor is responsible for your asthma treatment?
19. Do you use a peak flow meter? often, sometimes, seldom or never
20. Have you ever received instructions on how to inhale your medication?

Knowledge – answers “Yes absolutely”, “Yes partially” and “No”.

21. Do you know how to change your medicating at: infections, more asthma symptoms, deteriorated peak flow value?
22. Do you consider yourself to have sufficient knowledge of your asthma disease?

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