

Quality of life in adolescents with asthma, during the transition period from child to adult

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Abstract

Aim: The present investigation was designed to evaluate the health-related quality of life (HRQOL) of adolescents with asthma between the age of 16 and 21, when they are transferred from paediatric to adult care.

Methods: In this prospective study, 156 teenagers (69 females) with asthma were screened employing spirometry, a histamine challenge, skin prick test for allergy and filled out the 'Living with Asthma Questionnaire' both at the time of entry into the study and after 2 and 5 years of follow-up. An exercise test and questions concerning regular performed exercise were carried out at baseline and 5 years later.

Results: At all three time-points, the HRQOL of the men was generally better than that of the women. At the same time, the HRQOL of both genders was significantly better, both in terms of the overall scores ($P < 0.001$) as well as the scores for most of the individual domains, in connection with the 5-year follow-up. The young women who exercised regularly at the time of their entry exhibited better HRQOL at this time than those who did not ($P < 0.001$), whereas regular exercise had no impact on the HRQOL of the young men. The women with severe asthma demonstrated a poorer HRQOL than those suffering from mild-to-moderate asthma.

Conclusion: The HRQOL of adolescents with asthma improves with age. The pronounced positive correlation between regular exercise and HRQOL in female adolescents with asthma revealed here deserves special attention in the care of young women and deserves further exploration.

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Key words

adolescents – asthma – physical exercise – quality of life – transition

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Authorship

Kerstin Sundell has participated in the design of the study, conducted the analyses and wrote the manuscript. Sten Erik Bergström, Gunilla Hedlin and Alf Tunsäter have participated in the design of the study and were involved writing the manuscript. Britt-Marie Ygge has participated in writing the manuscript.

Ethics

The study was approved by the Ethics Committee at Huddinge University Hospital and informed consent, based on oral and written information, was received from both the patients involved and their parents.

Conflicts of interest

Kerstin Sundell has lectured for and sits for advisory boards for Merck Sharp & Dohme (Sweden) AB. She has no personal shares in the company. Sten-Erik Bergström has lectured for Merck Sharp & Dohme (Sweden) AB. He has no personal shares in the company. Alf Tunsäter has produced written documents and/or lectured for and/or sits on advisory boards for AstraZeneca, Glaxo SmithKline, Pfizer, Boehringer, Ingelheim, Orion Pharma, Shering Plough, Novartis, MSD, Pharmacia & Upjohn, Draco Läkemedel and AGA/Linde Gas Therapeutics. He has also received research support from AstraZeneca, GlaxoSmithKline, and ScheringPlough. He has no personal shares in any of the companies. Gunilla Hedlin and Britt-Marie Ygge have no conflicts of interest.

Introduction

Asthma, a multifactorial disease characterized by variable airflow obstruction, bronchial hyperresponsiveness (BHR) and inflammation, is one of the most common chronic diseases among teenagers and adolescents and can greatly impair the quality of everyday life. With a prevalence among Swedish teenagers of approximately 7%–10% (depending on the criteria employed) (1), and similar incidences in the Netherlands, New Zealand and the United States (2, 3), adolescent asthma is almost as common as this disease is in young children and more frequent than in adults (2). Previous studies indicate that the ratio of forced expiratory volume in 1 sec on forced vital capacity (FEV₁/FVC) at 35 years of age is significantly lower among individuals who suffer from childhood asthma that persists beyond the age of 16 compared with those with childhood asthma but without symptoms at 35 years of age (4). Furthermore, Strachan as well as Sears has demonstrated that in males the severity of asthma decreases significantly during the progression from childhood to adulthood, whereas females exhibit a tendency to develop more serious asthma during adult life (4, 5).

While the physiological factors that influence one's risk for developing asthma have been examined extensively, the psychological aspects of this condition have been less well characterized (6). In late adolescence important psychological changes occur at the same time as the teenager strives for emancipation and must make decisions of importance for his/her future. Chronic asthma makes considerable demands on an individual's lifestyle requiring continuous adaptation to the schedule of daily medication, regular visits to health care centres and dealing with occasional exacerbations, demands that impose on virtually every aspect of the adolescent's life, including school, meals, sports, work, travel and dating. It is not surprising that low self-esteem and social dependence, which may in themselves render effective asthma management more difficult, are more common among adolescents with a chronic disease than among their healthy peers (7).

Since few studies concerning the health-related quality of life (HRQOL) of asthmatic adolescents between the age of 16 and 20 have appeared, the present investigation focused on this 5-year period during which transferral from paediatric to adult care occurs and most teenagers leave home to begin a more independent life. Our hypothesis was that asthma has a deleterious effect on daily activities such as work, school, social/leisure activities and on mental health in these adolescents. We also examined possible differ-

ences between boys and girls in this respect, changes over time during this period; and possible correlations between HRQOL and atopy, bronchial hyperresponsiveness, lung function and regular physical exercise. Finally, we compared the HRQOL of asthmatic adolescents receiving care at a hospital-based asthma/allergy clinic compared with those followed up in the primary care organization.

Materials and methods

Conducted at the paediatric asthma/allergy clinic of the Children's Hospital at Huddinge University Hospital (Stockholm, Sweden), this investigation was a part of a more extensive prospective study concerning the development of asthma severity in adolescents and young adults (8).

Subjects

Initially 156 young people, including 69 women and 87 men with asthma, were recruited consecutively from the paediatric asthma/allergy clinic at the Children's Hospital, Huddinge. All subjects fulfilled the American Thoracic Society (ATS) criteria for asthma (9) and had visited our clinic regularly for at least 3 years for treatment of their asthma and, in several cases, other allergies such as allergic rhinitis and eczema. Their mean age at the time of entry into the study was 17.7 years (range 15.9–21.9, median 17.1) with six being older than 20 years of age. Of our subjects, 77% reported receiving regular treatment with inhaled corticosteroids.

Information concerning medication was supplied by the patients themselves and not based on drug prescriptions. Patients inhaling ≥ 600 μ g corticosteroids (budesonide or equivalent) as daily dosage or demonstrating a FEV₁ that was $<80\%$ of the expected despite such inhalation of corticosteroids were designated as suffering from severe asthma, while in the other cases the asthma was considered to be mild-to-moderate (10). The former group was followed up at the adult asthma clinic ($n = 53$), while those with mild-to-moderate asthma were assigned randomly to care at the adult asthma clinic ($n = 51$) or primary care ($n = 46$).

Two of our original patients could not continue to participate because of mental retardation; one was found to have a disease of the chest wall in addition to his asthma; and three declined to continue, so that the final study group included a total of 150 subjects (Table 1). Patients who admitted that they often did

Table 1. Description of our subjects at the time of their entry into the study

Parameter	The entire study population (<i>n</i> = 150)	Those with severe asthma (<i>n</i> = 53)	Those with mild/moderate asthma	
			Treated at a specialized clinic (<i>n</i> = 51)	Receiving primary care (<i>n</i> = 46)
Females (%)	43	35	68	64
Mean age in years	18	18	17	17
Positive skin prick test (%)	89	87	86	96
Regular treatment with inhaled steroids (%)	77	84	75	72
Demonstrating with BHR* (%)	72	75	76	65
Working capacity (%) [†]				
High	58	47	65	60
Medium	24	29	23	28
Low	16	24	14	12
Exercised regularly (%)	57	45	67	63

*Bronchial hyperresponsiveness was defined as a PD₂₀ value for histamine of $\leq 880 \mu\text{g}$.

[†]Based on oxygen uptake (mL/kg/min) and categorization according to the Åstrand scale.

BHR, bronchial hyperresponsiveness.

not take their prescribed drugs and/or who missed more than two consecutive clinical visits (without a reasonable explanation) were considered to demonstrate 'poor adherence to asthma management'.

Study design

All subjects were evaluated with respect to a skin prick test, spirometry, a bronchial challenge with histamine and HRQOL at the time of their entry into the study and in connection with follow-up 2 and 5 years later. An exercise test was also performed at the time of entry and 5 years later. Results of the asthma evaluations have been reported in detail previously (8), brief description is included in this paper.

Test of lung function

For this purpose, a Vitalograph spirometer (Vitalograph, Buckingham, UK) and forced expiration in the standing position without nose clips were employed in accordance with the criteria of the ATS (9).

Test for allergy

The skin prick test was performed with standard dilutions (100 000 BU/mL) of 12 different allergens (*birch*, *timothy grass*, *mugwort*, *cat*, *horse*, *dog*, *dermatophagoides pternyssinus*, *cladosporium*, *alternaria*, *aspergillus fumigatus*, *fish and peanut*) in 50% glycerol (Soluprick, ALK, Hørsholm, Denmark). The reaction was regarded as positive if the diameter of the wheal was ≥ 3 mm.

Bronchial hyperresponsiveness

The bronchial challenge involved inhalation of histamine diphosphate via an automatic inhalation-synchronized jet nebulizer (Spira Elektro 2, Respiratory Care Center, Hämeenlinna, Työkeskus, Finland) (11). The dose of histamine that induced a 20% reduction in FEV₁ (PD₂₀ FEV₁) was determined by linear interpolation from the log dose-response curve.

The exercise test

Aerobic capacity was evaluated on the basis of submaximal exercise on an ergometer cycle (Monark, Exercise AB, Vansbro, Sweden) (12–15). Prior to performing this test, all of the subjects inhaled a β_2 -agonist and warmed up by cycling gently for 10 min in order to prevent an asthmatic reaction and allow determination of working capacity. For those who performed this exercise test, the body mass index (kg/m²) was calculated in the standard manner.

HRQOL

HRQOL was assessed with the 'Living with Asthma Questionnaire', translated with validation into Swedish and adapted to Swedish circumstances (16, 17). This questionnaire encompasses 11 domains including a total of (68 items), i.e. (i) *social and leisure activities*; (ii) *sports*; (iii) *holidays*; (iv) *sleep*; (v) *work and other activities*; (vi) *colds*; (vii) *mobility*; (viii) *effects on others*; (ix) *medication usage*; (x) *sex*; (xi) *dysphoric*

states and attitudes. This instrument also evaluates two cognitive (activities and avoidance) and two emotional factors (distress and preoccupation), as well as compensating for bias (i.e. the tendency to agree with items irrespective of their content).

The subject responded to each statement as 'untrue', 'slightly true' or 'very true', or chose the alternative 'not applicable'. The quality of life in each domain was calculated, according to Hyland, as the sum of the scores for all individual items divided by the number of items, i.e. the mean scores, which were subsequently analysed as continuous variables.

Statistical analyses

The differences in HRQOL between men and women were analysed (for each subject) in connection with the 2- and 5-year follow-ups utilizing the non-parametric Wilcoxon signed ranks test.

Comparison of the various factors (gender, atopy, physical activity, asthma severity and follow-up in primary care or at the specialized outpatient clinic) was carried out with the non-parametric Mann-Whitney test. Possible correlations between HRQOL and lung function and degree of hyperresponsiveness were examined with the Spearman's rho procedure.

In connection with all of these comparisons, a P value of <0.05 was considered to be statistically significant. Finally, adjustment for atopy, physical activity, gender, severity of asthma, treatment with inhaled steroids, smoking habits (active, passive) and adherence to treatment was obtained with a logistic regression model. In all cases, the SPSS statistical package (version 14.0, SPSS Inc, Chicago, IL, USA) was used for analysis.

Results

Atopy, lung function and bronchial hyperresponsiveness at the beginning of the study

As presented previously (8) at the time of their entry into this study, 89% of our subjects were atopic. At this same time-point, reactions to perennial allergens (cat, horse, dog or mite) were observed in 113 patients (76%), and 111 (74%) were allergic to pollen.

The mean FEV₁ was 94.0% (standard deviation 12.9%) of the predicted. In the test for bronchial hyperresponsiveness, the median PD₂₀ value for histamine chloride was 440 µg. Fifty-eight per cent of the subjects demonstrated a high working capacity compared with 20% at the time of the 5-year follow-up (8).

Participating in regular physical activity decreased from 57% at the time of entry into the study (Table 1) to 28% at follow-up.

HRQOL

On all three occasions for evaluation (i.e. at the time of entry and after 2 and 5 years of follow-up), our young female subjects exhibited lower overall mean HRQOL scores than did the young men (Fig. 1A). The scores for the young women were also lower in 6 of the 11 separate domains of HRQOL at the time of entry and after 5 years of follow-up [although not the same domains; (Fig. 1B and C)]. After 2 ($n = 117$) and 5 years ($n = 106$) of follow-up, the mean overall score was higher than at the time of entry for both men and women, which was also the case for some of the individual domains (Fig. 1A, B and C). Moreover, while remaining significant, the differences between the women and men decreased continuously as more time elapsed after their entry into the study (Fig. 1A, B and C).

Young women suffering from severe asthma at the time of entry into our study had a lower overall mean score ($P < 0.05$) than did the women with mild-to-moderate asthma at this same time-point. However, after 5 years of follow-up, all of these differences had disappeared. In the cases of the young men, the severity of asthma exerted no significant impact on the overall mean score.

Regular physical exercise (i.e. running, ball sports, aerobics, etc. ≥ 2 h each week) at the time of entry into the study exerted a significant positive effect on the overall mean HRQOL score for the female subjects at this same time-point, as well as on their scores for 6 of the individual domains and the subdomains reflecting cognitive factors (i.e. activity and avoidance) and the emotional factor disability (Table 2). However, after 5 years of follow-up, these differences were no longer observed whereas a new difference with respect to 'common colds' had appeared. In contrast, in the case of the young men, physical activity had no impact on any aspect of HRQOL at any time (not shown).

There was no correlation between the FEV₁ value (as a percentage of the predicted value) and overall HRQOL throughout the study (data not shown). Neither atopy nor bronchial hyperresponsiveness appeared to exert any impact on HRQOL. The HRQOL's of subjects receiving primary care or care at the specialized asthma clinic were similar (data not shown). The HRQOL, lung function, bronchial responsiveness, working capacity and atopy of the dropouts were the same as for those who completed this study (data not shown).

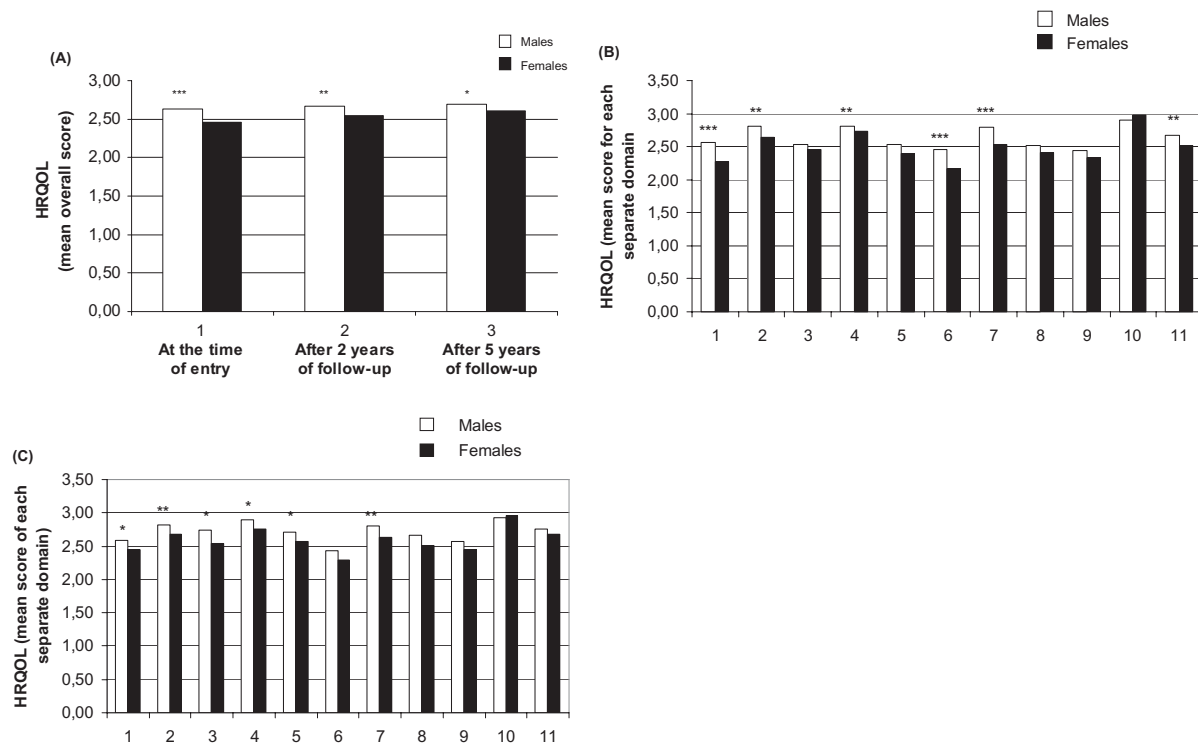


Figure 1. (A) The overall mean health-related quality of life (HRQOL) scores for our male and female subjects at the time of their entry into the study and after 2 and 5 years of follow-up. For a description of the evaluation of HRQOL and calculation of mean scores, see the Materials and methods section. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.005$ in comparison with the corresponding female value, as analysed employing the non-parametric Wilcoxon signed ranks test. (B) The mean scores for the individual domains of HRQOL for our male and female subjects at the time of their entry into the study. For a description of the evaluation of HRQOL and calculation of mean scores, see the Materials and methods section. The individual domains were as follows: 1 = social and leisure activities, 2 = sports, 3 = holidays, 4 = sleep, 5 = work, 6 = common colds, 7 = mobility, 8 = effects on others, 9 = use of medication, 10 = sex, 11 = dysphoric state and attitudes; ** $P < 0.01$, *** $P < 0.005$ in comparison with the corresponding female value, as analysed employing the non-parametric Wilcoxon signed ranks test. (C) The mean scores for the individual domains of HRQOL for our male and female subjects in connection with their 5-year follow-up. For a description of the evaluation of HRQOL and calculation of mean scores, see the Materials and methods section. The individual domains were as follows: 1 = social and leisure activities, 2 = sports, 3 = holidays, 4 = sleep, 5 = work, 6 = common colds, 7 = mobility, 8 = effects on others, 9 = use of medication, 10 = sex, 11 = dysphoric state and attitudes; * $P < 0.05$, ** $P < 0.01$ in comparison with the corresponding female value.

At the time of entry into the study, the major differences described above were not altered by adjusting for atopy, regular exercise, gender, treatment with inhaled steroids, smoking habits (active, passive) and severity of asthma employing to a logistic regression model (data not shown). However, this model did reveal that poor adherence to the recommended asthma treatment was associated with lower HRQOL (odds ratio = 0.29; 95% confidence interval = 0.11–0.73; $P < 0.01$).

Discussion

The transition from dependence to independence during adolescence involves adaption to a multitude of

new social and emotional roles and, at the same time coping with altered bodily functions. Successful experiences during this period are vital to self-esteem and confidence (7) and adolescents with a chronic illness are constantly struggling especially hard for independence, since their illness often keeps them tied physically, emotionally and financially to their families (18).

Our major findings in this study are that adolescent men with asthma exhibit better HRQOL compared with their female peers. Furthermore, we show a positive correlation between regular physical activity and HRQOL among young females when entering the study. Poor adherence to asthma treatment has a negative impact on HRQOL and additionally our results

Table 2. Comparison of the mean score for the overall health-related quality of life (HRQOL) and for the individual domains at the time of entry into the study and after 5 years of follow-up for female subjects who did or did not exercise regularly at the time of entry

Domain	Exercised regularly at the time of entry		<i>P</i> value* (exercised vs did not)	Exercised regularly at the time of the 5-year follow-up		<i>P</i> -value* (exercised vs did not)
	Yes (<i>n</i> = 85)	No (<i>n</i> = 61)		Yes (<i>n</i> = 25)	No (<i>n</i> = 65)	
Overall HRQOL	2.6 (0.05)	2.3 (0.06)	<0.001	2.6 (0.06)	2.6 (0.06)	0.44
Social and leisure activities	2.4 (0.06)	2.1 (0.09)	0.08	2.5 (0.10)	2.4 (0.08)	>0.5
Sports	2.8 (0.06)	2.5 (0.12)	<0.05	2.7 (0.10)	2.7 (0.07)	>0.5
Holidays	2.5 (0.08)	2.4 (0.11)	0.32	2.5 (0.13)	2.6 (0.10)	>0.5
Sleep	2.8 (0.06)	2.6 (0.09)	<0.01	2.8 (0.08)	2.7 (0.11)	>0.5
Work	2.6 (0.07)	2.2 (0.09)	<0.01	2.7 (0.08)	2.5 (0.09)	0.16
Colds	2.2 (0.09)	2.1 (0.08)	0.19	2.5 (0.12)	2.0 (0.11)	<0.01
Mobility	2.7 (0.06)	2.4 (0.08)	<0.01	2.6 (0.13)	2.6 (0.09)	>0.5
Effects on others	2.5 (0.06)	2.4 (0.08)	0.38	2.6 (0.10)	2.5 (0.10)	>0.5
Medication usage	2.4 (0.07)	2.2 (0.09)	<0.05	2.5 (0.12)	2.4 (0.08)	0.27
Sex	3.0 (0.03)	3.0 (0.00)	0.45	3.0 (0.00)	2.9 (0.09)	0.21
Dysphoric states and attitudes	2.6 (0.06)	2.4 (0.06)	<0.05	2.7 (0.07)	2.7 (0.06)	0.78
Activity [†]	2.7 (0.05)	2.4 (0.08)	<0.01	2.7 (0.08)	2.7 (0.07)	0.42
Avoidance [†]	2.5 (0.06)	2.3 (0.07)	<0.05	2.6 (0.08)	2.4 (0.07)	0.25
Disability [†]	2.6 (0.07)	2.5 (0.07)	<0.05	2.7 (0.07)	2.7 (0.06)	0.49
Apprehension [†]	2.4 (0.07)	2.1 (0.07)	0.5	2.4 (0.13)	2.5 (0.10)	>0.5

*As determined by the Mann–Whitney Test.

[†]Subdomains of 'Dysphoric states and attitudes'.

indicate that subjects with mild-to-moderate asthma that received primary or specialized care exhibited similar HRQOL at follow up after 5 years.

Several studies on adults with asthma have revealed a gender difference in HRQOL, including recent reports that even with symptoms of similar severity, women have worse HRQOL than men (19, 20). In this study, we show that adolescent men with asthma exhibit better HRQOL scores on the 'Living with Asthma Questionnaire' than do their female peers, both with respect to the total score and the scores for many of the individual domains.

In general, Kyngas, and co-workers found that low self-esteem and social dependence are more common among adolescents with chronic diseases than among their healthy peers (7). Moreover, in comparison with other chronic conditions, asthmatic children and adolescents appear to more often exhibit psychiatric disorders such as depression as well as emotional and/or behavioural problems (21, 22). This result is consistent with the gender differences among teenagers with other chronic illnesses reported earlier (6, 23). Naleway and Osman report that women more often seek care from a physician for their asthmatic symptoms, even though the frequency of symptoms among men is the same. In these studies, the mean age of the subjects was 33 (24,

25). Among our adolescents, HRQOL improved as they entered adulthood, although the gender difference remained. One possible explanation for the improvement observed here could be improved asthma control as reflected by improved lung function and BHR (8) and/or improved self-confidence with increased independence. With regard to the common question as to whether the HRQOL of children and adolescents suffering from asthma is influenced by the severity of their symptoms, findings to date have been inconsistent (26). Here, adolescent women with severe asthma had a lower HRQOL than those with mild asthma, although no such correlation was observed for the males.

A number of investigations have shown that training programs significantly improve aerobic fitness in children and adolescents with asthma, reducing the frequency of hospitalizations and wheezing, absenteeism from school, the number of consultations with physicians and use of medication, as well as improving HRQOL (27). In our study, we found a positive correlation between regular physical exercise and HRQOL among asthmatic adolescent women, which, however, disappeared as they entered adulthood. Our patients were simply asked whether they exercised regularly and the validity of such a single question approach has been confirmed by Godin and co-workers, as well as by

several other investigators (28–30). The lack of a similar positive effect of regular exercise on the HRQOL of our adolescent men may reflect that these men do not expect asthma to affect their HRQOL and do not consider this condition to be a hinder for physical activity, an attitude of ignoring asthmatic symptoms that might result in under-treatment.

Since both the lung function and HRQOL of our patients with asthma of mild-to-moderate severity remained stable during the 5-year study period, regardless of whether they received specialized treatment or primary care, it would appear that adolescents with such mild-to-moderate asthma can be handled effectively in the primary care system, which also is in line with our results concerning FEV₁, histamine challenge and working capacity (8).

Although the present investigation documents significant observations concerning the HRQOL of adolescents with asthma, some shortcomings must be considered. One is the lack of a healthy control group, which we chose not to include because it would have necessitated the use of a generic instrument for assessing HROQL, rather than our specialized questionnaire that focuses on chronic asthma and is thereby considerably more sensitive for our present purposes. Although most of our study population exhibited bronchial hyperresponsiveness that did not demonstrate any correlation with HRQOL, the number of subjects with impaired lung function was too small to permit any statistical analysis.

An additional limitation is that our follow-up rate was only 69%, which is in line with the rate of follow-up in several others (26, 31) but lower than in other previous prospective studies (32). In investigations on patients living in a large metropolitan area, a higher number of dropouts is probably to be expected. For instance, in their 6-year longitudinal study of risk factors for the development of asthma in children and adolescents living in Copenhagen, Ulrik and Baker reported a follow-up rate of 77% (33).

In contrast to most previous prospective studies concerning adolescent asthma, we have focused here on the effects of this condition on HRQOL during the short but critical period of transition from adolescence to adulthood and transfer from paediatric to adult health care. During this period, a chronic disease such as asthma may exert considerable impact on future life in several ways. Our findings reveal that suffering from asthma in the beginning of this transition (i.e. between the ages of 16 and 19) may have negative consequences for HRQOL, which should not be overlooked.

In summary, the present investigation indicates that suffering from asthma during late adolescence is asso-

ciated with a lower HRQOL for women than for men and that this negative impact on adolescent women is enhanced when the asthmatic symptoms are more severe. The HRQOL of both our male and female patients improved as they grew older and entered adulthood. Moreover, our observation of a positive correlation between regular exercise and the HRQOL of adolescent women with asthma deserves to be explored further. Our results also demonstrate that adolescents with mild-to-moderate asthma can be equally handled in our primary care system. Finally, the negative impact of poor adherence to asthma treatment on HRQOL emphasizes the importance of health care programs that include patient education and support for adolescents with asthma as they are transferred from paediatric to adult health care. This support should include special attention for regular exercise suitable for young women.

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