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► **To cite this version:**

Malgorzata Farnik, Wladyslaw Pierzchala, Grzegorz Brożek, Jan Zejda, Michal Skrzypek. Quality of Life Protocol in the Early Asthma Diagnosis in Children. *Pediatric Pulmonology*, 2010, 45 (11), pp.1095. 10.1002/ppul.21293 . hal-00613784

HAL Id: hal-00613784

<https://hal.science/hal-00613784>

Submitted on 6 Aug 2011

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Quality of Life Protocol in the Early Asthma Diagnosis in Children

Journal:	<i>Pediatric Pulmonology</i>
Manuscript ID:	PPUL-09-0111.R4
Wiley - Manuscript type:	Original Article
Date Submitted by the Author:	05-May-2010
Complete List of Authors:	Farnik, Małgorzata; Silesian University of Medicine, Pneumology Pierchała, Władysław; Silesian University of Medicine, Pneumology Brożek, Grzegorz; Silesian University of Medicine, Epidemiology Zejda, Jan; Silesian University of Medicine, Epidemiology Skrzypek, Michał; Medical University of Silesia, Department of Biostatistics
Keywords:	asthma, quality of life, early diagnosis, child



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3 ***Quality of Life Protocol in the Early Asthma Diagnosis in Children***
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23 **Key words:** asthma, pediatrics, health-related quality of life, early diagnosis
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Abbreviated title: QOL in early asthma diagnosis

Summary

Introduction. Asthma is considered an important problem in children and influences on their everyday functioning. This study was concerned with the impact of asthma on the health related quality of life (HRQOL) of newly recognized pediatric asthma patients and their parents.

Methods. Patients were identified by a general respiratory survey. HRQOL was assessed by self-report measures: disease-specific questionnaire for children, the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and generic for parents - the Quality of Life in Child's Chronic Disease Questionnaire (QLCCDQ).

Results. 29 newly diagnosed asthmatic children aged 7-11 years (mean age = 8.6 SD=1.4) were identified from a population-based respiratory health survey. The most impaired HRQOL domains differed in parents and children. In children, activity limitation was the most impaired; however in parents, emotional functioning and symptom perception domains were most impaired. There were no statistically significant differences in patient and parental HRQOL observed in either the group where symptoms were present or in the group where symptoms were not present. Baseline spirometry showed correlation for FEV₁ %FVC and PAQLQ symptom domain (r=0.42). Exercise test showed correlations between FEV₁% FVC and QLCCDQ emotional domain (r=0.7); MEF_{25-75%} and family roles (r=0.81), as well as social functioning (r=0.81). Activity limitation on the PAQLQ correlated with the MEF_{25-75%} (r=0.44) and PEF (r=0.55).

Conclusions. HRQOL newly recognized children with asthma and their parents does not correlate closely with clinical status. Patient and parental HRQOL should be considered as independent dimensions.

Introduction

The results of International Study of Asthma and Allergies in Childhood (ISAAC) have shown that childhood asthma represents an important public health problem worldwide (1). Previously increasing prevalence of childhood asthma, well documented in many countries (2, 3, 4) can be observed in Eastern Europe over the years 1994–2007 (1, 5, 6, 7). The magnitude of the problem could be underestimated because of underdiagnosis (8). The resulting public health burden justifies the development and implementation of population-based measures. Asthma not only has a profound impact on public health, but also on the everyday lives of individual patients.

A patients' burden of chronic illness cannot be assessed by disease severity; it requires measurement reflecting personal perception. There is an increasing interest in activity limitation, emotional functioning, impact on every-day life due to disease and the implementation of health-related quality of life (HRQOL) questionnaires. Deterioration of HRQOL has been described in children and adults with allergic diseases, such as eczema (9) and rhinitis (10). HRQOL assessment highlights important and troublesome problems experienced by patients with asthma (11,12,13). Children with asthma suffer from activity limitation, emotional problems such frustration, fear and irritation (14). Although HRQOL does not correlate closely with asthma control, it is known that children with very severe asthma tend to have a poorer quality of life than those suffering from mild or moderate condition (15). Parents of children with asthma could be limited in normal daily activities and experience emotional distress (16).

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3 Clinical experience shows that a caregiver's HRQOL and their perception of
4 a child's symptoms are important in diagnosis and control of established asthma (17).
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8 Less is known about the potential impact of disease on HRQOL in newly recognized
9
10 children with asthma which were found as the result of screening programs. It
11
12 remains unknown to what extent such a procedure could be helpful in both early
13
14 assessment of asthma and its impact on patients' and parental quality of life.
15
16

17 We implemented the HRQOL protocol in examination of newly identified
18
19 pediatric asthma patients and their families, participants of a large population-based
20
21 respiratory health survey. The goal of the study was to determine the impact of
22
23 asthma on the health related quality of life of newly recognized pediatric asthma
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25 patients and their parents.
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Materials and Methods

A large population-based respiratory health survey resulted in identification of new pediatric asthma patients. All newly identified children with asthma aged 7-11 years and their parents were involved in HRQOL study. A disease-specific quality-of-life questionnaire was used for the children and a generic questionnaire for parents. Clinical status data was obtained prior to an HRQOL assessment.

Participants

Children were recruited using cluster sampling during a respiratory health survey study in primary schools in Katowice (Southern Poland). 2254 children grades I-IV, in 7 out of 51 schools in the town were invited (17.0% of the town population in the defined age group) for respiratory questionnaire assessment. This was a validated questionnaire, used in The Central European Study of Air Pollution and Respiratory Health (CESAR) [Table 1] and other surveys (22, 23, 24). The response rate was 80.8% (1822 children). Study design is shown in Fig. 1

Figure 1. Study design

Based on the questionnaire results children were categorized into three mutually exclusive groups: "Asthma" (5.4% - diagnosis of asthma established before the survey); "Respiratory Symptoms" (27.9% - no previous diagnosis of asthma and one or more symptoms of persistent cough excluding infections, chest wheezing, dyspnea during the last 12 months), "No Respiratory Symptoms" (66.7% - no previous diagnosis of asthma and no respiratory symptoms during the last 12 months).

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2
3 [Table 1] - Respiratory Questionnaire (examples of questions)
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5
6 Clinical evaluation was proposed to all children in "Asthma"- group and 60%
7
8 samples from groups "Respiratory Symptoms" and "No Respiratory Symptoms", with
9
10 the response rates: 41.4%, 70.8% and 25.6%, respectively. A certified pulmonologist
11
12 (Department of Pneumonology, Medical University of Silesia) examined 415 children.
13
14 The physician was blind to the results of the questionnaire. Diagnostic procedures
15
16 were based on GINA guidelines for childhood asthma (25). Forced expiratory
17
18 volumes were measured according to ERS/ATS recommendations (26). Spirometry
19
20 was considered normal if FEV₁, FVC and PEF values exceeded 80% predicted and if
21
22 FEV₁ %FVC ratio was greater than 75%. If actual values presented predicted values,
23
24 a further challenge test of bronchial hyperresponsiveness, described by Gerald et al
25
26 (27), was used. A sub-maximal exercise test (stepping up and down on a single step
27
28 with metronome rhythm) was followed by spirometry obtained at minutes 3, 5 and 10
29
30 after exercise. An FEV₁ decrease greater than 15% was considered positive for
31
32 asthma. Medical records were provided; additional skin allergy tests and a chest
33
34 radiograph were carried out, where needed.
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41 Clinical assessment of 415 children confirmed 33 previously known and revealed 29
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43 new cases of asthma. All newly identified children with asthma and their parents
44
45 were invited to HRQOL assessment.
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53 HRQOL measurements

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55 Quality of life questionnaires were completed by children with asthma at school in the
56
57 patient's normal psychosocial environment. Parents of newly diagnosed children
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3 with asthma completed HRQOL questionnaire as well at school, before the diagnosis
4
5 was communicated.
6

7 8 *The Paediatric Asthma Quality of Life Questionnaire*

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10 The Paediatric Asthma Quality of Life Questionnaire (PAQLQ), dedicated to children
11
12 aged 7-17 years old, was used as a well-validated and reliable measure of HRQOL in
13
14 childhood asthma. The questionnaire consists of 23 questions, covering symptoms,
15
16 emotional function and limitations of activity. Children were asked to recall their
17
18 experiences over the previous week and responded on a 7- point scale (7 – no
19
20 impairment, 1 – severe impairment). Patients completed the questionnaire with
21
22 physicians experienced in HRQOL research. Interviewer-administration was used to
23
24 avoid parental interference with patient responses.
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28 29 *Quality of Life in a Child's Chronic Disease Questionnaire*

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31 An accompanying questionnaire for parents was devised by the authors, based on
32
33 standard procedure – starting from initial questions (identification of needs, definition
34
35 of operational objectives), tool development, pretesting and final version (format,
36
37 wording) preparation, pilot testing and validation of the questionnaire (19, 20).
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40
41 Quality of Life in a Child's Chronic Disease Questionnaire (QLCCDQ) is concerned
42
43 with daily problems and limitations that concern parents of children with chronic
44
45 disease. QLCCDQ is a self – report measure of parent's HRQOL, only symptoms
46
47 subscale is parent-proxy measure. Most questions concern parents' functioning, only
48
49 the symptom subscale reflects parents' perception of symptoms presence.
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53 QLCCDQ consisted of 15 questions and covered patient-perceived symptoms (e.g
54
55 Did the child show any worrying symptoms?) , emotions (e.g. Have you experienced
56
57 anxiety because of your child's health problems?) and activity limitation in roles
58
59 function: social (e.g. Please indicate how much you have been limited by your child's
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3 disease in listed activities in past two weeks: going to church, cinema, visiting
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5 friends), family roles (e.g. Do you struggle to find time to spend with other family
6
7 members (spouse, another child) because of your child' disease?) and occupational
8
9 members (spouse, another child) because of your child' disease?) and occupational
10
11 (e.g. Please indicate how much you have been limited by your child's disease in work
12
13 related activities in past two weeks).

14
15 The questionnaire required circling a choice from seven responses devised for each
16
17 question, from 1 (most bothered or limited) to 7 (not bothered or limited). All
18
19 questions concerned parental HRQOL of previous two-week period.
20
21

22 23 24 *Psychometric data*

25 26 27 PAQLQ

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29 The instrument is reproducible (ICC =0.95) and has shown ability to detect HRQOL
30
31 changes as a result of treatment (p<0.001). Estimation of reliability in stable asthma
32
33 has shown that it was consistent throughout all domains (ICC: 0.84-0.93).
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36 37 QLCCDQ

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39 Reproducibility based on the weighted kappa coefficients showed an expected level
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41 of agreement. Values of weighed kappa coefficients suggested almost perfect
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43 agreement (0.81-1.0) in case of 8 questions, substantial (0.61-0.8) for 5 questions
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45 and moderate (0.41-0.6) for 2 questions. The reliability of the defined subscales was
46
47 evaluated by means of Cronbach's α . The values of α ranged between 0.74 and
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49 0.94: symptoms: 0.93, emotions: 0.91, family roles: 0.77, social roles: 0.79,
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51 occupational roles: 0.92 and activity limitations in roles function: 0.91.
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57 58 *Child's school grades and absenteeism*

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3 Supplementary data such as school grades and absenteeism (missed school days
4
5 due to asthma symptoms) were provided to determine if there were relationships
6
7 between reported HRQOL and child's functioning at school. It could be expected that
8
9 untreated asthma has an impact on school functioning resulting in children lower
10
11 school grades and missed school days. Polish school grades assessment is based
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13 on 6- point scale: from 1 (Fail) to 6 (Excellent).
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20 The study protocol was approved by the ethics committee (Medical University
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22 of Silesia). Each child admitted to the study had the written consent of a parent.
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27 **Statistical analyses**

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32 The statistical analysis was performed using standard procedures available in
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34 the Statistica 7.1 package and SAS, version 9.2 (SAS Institute Inc., Gary, NC).
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36 Normality of distributions of continuous variables was analyzed using the Shapiro–
37
38 Wilk test. Statistical significance of differences between continuous variables was
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40 analyzed by t-Student test and ANOVA while for data with non-normal distribution, U
41
42 Mann-Whitney and Kruskal-Wallis tests were used. Differences between categorical
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44 variables were examined by the chi-square test. Strength of associations, due to non-
45
46 normal distributions, were measured by Spearman's rank correlation coefficient.
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49 The statistical inferences were based on confidence levels $p < 0.05$. If multiple
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51 comparisons were used statistical significance was lowered according to the
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53 Bonferroni adjustment.
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3 Variables included patient and parental HRQOL assessment, symptoms over the
4
5 previous 12 months, baseline and exercise spirometry, school grades and
6
7 absenteeism.
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10 Correlations between child's and parental HRQOL scores were analyzed. Relations
11
12 between clinical status (symptoms, lung function tests) and HRQOL were examined,
13
14 as well as links between educational markers (school grades and absenteeism) and
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16 patient HRQOL scores. Gender and age effects on HRQOL were also analyzed.
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For Peer Review

Results

Participating children

In children with newly diagnosed asthma (mean age = 8.6 years; SD=1.4 years), classified according to GINA protocol, the disease was either episodic (20 children: 6 boys and 14 girls) or chronic mild (9 children: 4 boys and 5 girls). New diagnoses of asthma were made in 10.9% of children from the “Respiratory Symptoms” group and in 3.6% of children from the “No Respiratory Symptoms” group. All 29 newly diagnosed children with asthma and 21 parents responded to the subsequent HRQOL questionnaire.

[Table 2] - Demographic and asthma severity

Patient and parental HRQOL

HRQOL was assessed for each domain, the subscale mean ranging from 1.0 to 7.0. Lower HRQOL scores reflected greater impact of disease on every-day functioning. Children’s most affected HRQOL domain was limitation of activity. Parents’ impairment was most severe in emotional functioning and perceived symptoms, while less impaired domains included social functioning. Domains and overall HRQOL scores for children and parents appear in the table 3.

[Table 3]. HRQOL - domains and overall scores

Statistically important positive correlations were observed between all PAQLQ subscales, as well as most QLCCDQ subscales [Table 4]. QLCCDQ symptom perception subscale correlated only with parental emotional functioning, while

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3 correlations were found between most subscales describing roles functioning.
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5 Bonferroni correction suggested significance level was $p < 0.0001$.
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9 [Table 4]. PAQLQ and QLCCDLQ subscales Spearman's correlations
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12 13 14 15 16 HRQOL measures and clinical assessment

17 18 *Symptoms*

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20 The differences of mean QLCCDQ and PAQLQ subscales scores between groups of
21
22 symptomatic and nonsymptomatic children over in the past 12 months were
23
24 analyzed. Both for QLCCDQ and PAQLQ the differences in scores did not reach
25
26 statistical significance. Bonferroni correction suggested significance level was $p <$
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31 0.01.
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34 35 *Lung function tests*

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37 Statistically important correlations were found between HRQOL and
38
39 spirometry. Challenge tests were done in 23 of the 29 children – 3 children did not
40
41 obtain reproducible spirometry after exercise, 2 children were wheezing before
42
43 exercise commenced, 1 child refused to cooperate. Baseline FEV₁%FVC and
44
45 symptom domain in children showed a correlation ($r=0.42$), while exercise value
46
47 FEV₁%FVC correlated with emotional domain ($r=0.7$). MEF_{25-75%} correlated with
48
49 QLCCDQ family roles ($r=0.81$) and social functioning ($r=0.81$). PAQLQ activity
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51 limitation was correlated with MEF 25-75% ($r=0.44$) and PEF ($r=0.55$), both obtained
52
53 during the exercise test. All exercise test correlations were based on spirometry
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55 results collected 10 minutes after the challenge test [Table 5].
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[Table 5]. HRQOL scores and lung function - Spearman's correlations

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6 School grades and absenteeism
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8 Higher scores on the symptoms subscale of PAQLQ correlated with better
9 school grades ($r= 0.64$; $p=0.02$) and fewer missed school days ($r= -0.53$; $p=0.02$).
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12 No correlations were observed in parents' HRQOL and missed school days or school
13 marks.
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19 Patient gender and age
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22 Females showed a significantly lower symptom score in comparison to males
23 ($p=0.01$), however this effect was not translated into total PAQLQ scores nor into
24 parents' HRQOL.
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29 The relationship between HRQOL scores and age were not statistically significant.
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Discussion

Our study focused on the implementation of the HRQOL protocol in early diagnosis of childhood asthma. The analysis involved data obtained in children with newly diagnosed asthma and in their parents. Since asthma cases were identified through population-based screening, it is not surprising that all previously undiagnosed cases represented either episodic or mild asthma – children with more advanced disease had been diagnosed on regular basis, via pediatric health care. An important finding of our study is that the profile of HRQOL impairment is different in children with asthma and in their parents. Not only did PAQLQ and QLCCDQ scores not correlate but – in addition – the highest impaired domains differed between children and parents. Symptom perception and emotional functioning appeared to be the most affected HRQOL domains in parents, while activity limitation was the most impaired domain in children. Some parents might limit their child's activity, due to emotional distress caused by anticipation of symptoms, and such behavior could explain the lack of correlation between emotion domain QLCCDQ and symptom or activity limitation domains in PAQLQ. It is of interest that parental HRQOL pattern is in line with the published qualitative evidence that parents tend to perceive symptoms of asthma in a child as intermittent acute episodes rather than a chronic condition (28). Such interpretation could explain the lack of diagnosis of episodic or mild asthma in our study. It cannot be excluded that such a presentation is not entirely neglected by parents, but treated by them as an annoying condition and not overt disease. Our finding could have some implication as far as screening is concerned - occurrence of symptoms is necessary

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3 but does not have to be a sufficient cause to seek medical advice. Other important
4
5 factors include individual experience, perception and emotions.
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8 The relationships between clinical indices and HRQOL were analyzed in many
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10 studies as an important observation for clinicians (29, 30, 31, 32). Our study has
11
12 shown that there were no statistically significant differences in both patient and
13
14 parental HRQOL scores between symptomatic and asymptomatic groups. However
15
16 some of analyzed relationships were suggested as significant; before the significance
17
18 level was lowered by applying Bonferroni correction to $p < 0.01$. As the example -
19
20 compared to parents of asymptomatic children, parents of children complaining of
21
22 wheezing had a lower ($p=0.02$) mean score in emotional function and symptom
23
24 domain. As well the group of children possessing dyspnea showed a lower mean
25
26 parental emotional function score ($p=0.04$) than in asymptomatic children. In children
27
28 an emotional function score was lower in the group of children complaining of cough
29
30 in the past 12 months ($p=0.01$) as compared to asymptomatic children.
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35 Correlations were observed for exercise lung function and QLCCDQ domains, such
36
37 as emotional, family and social functions. Worthy to note, that the correlations
38
39 between children's lung function and parental HRQOL domains were stronger than
40
41 analogous correlations concerning HRQOL in children. The most impaired parent
42
43 HRQOL domain - emotions, significantly correlated with FEV₁ % FVC. Activity
44
45 limitation, the most impaired patient domain, correlated with PEF and MEF 25-75.
46
47 Even if the correlations between clinical indices and HRQOL scores were observed
48
49 only for few variables it should not determine a limitation of HRQOL protocol in early
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51 diagnosis. As HRQOL is not a diagnostic scale nor a disease or symptom severity
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53 scale index – the impact of disease is not systematically correlated with the disease
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55 severity as it is categorized (32) by health –care providers. Patient' or caregiver –
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3 based assessment can complement traditional clinical or biological evaluation, which
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5 could suggest that HRQOL could function as part of an early assessment or as part
6
7 of disease monitoring.
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10 Our findings were obtained in newly diagnosed and mild cases of asthma. Studies
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12 addressing established childhood asthma showed that the correlations between the
13
14 clinical status and HRQOL scores are weak to moderate, even for disease-specific
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16 measures (29, 30, 31). A perception of dyspnea, although a crucial asthma
17
18 symptom, might show interpersonal and intrapersonal variations (33). Although
19
20 children with severe asthma tend to have a poorer quality of life than children with
21
22 milder disease (34), parental and children's perception can be influenced by a
23
24 number of factors. Consistent with findings in the G. Guyatt's study, in children aged
25
26 7-10, clinicians cannot rely on parental reports to provide insight into the child's
27
28 HRQOL. This study also showed that the patient's assessment of change in
29
30 symptoms were more closely related to HRQOL scores than parental assessment
31
32 (20). A different effect provided by our study could be discussed in terms of early
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34 diagnosis and mild clinical presentation of the newly diagnosed cases.
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40 Parental experience of their child's disease is very important for the diagnosis of
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42 asthma, and it would confirm the importance of screening programs addressed to
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44 parents, including emotional context of their functioning in relation to the child's
45
46 symptoms. Parental HRQOL could be recommended as a valuable method of a more
47
48 holistic assessment of disease impact on everyday functioning of child and their
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50 family. Both patient and parental perception are important in care strategies
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52 planning and implementation. Children are influenced by their parents and reduction
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54 of parental distress could be beneficial for child's family life and integration within
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3 society (35). In contrast an increasing parental stress could diminish compliance and
4
5 adjustments to illness (35, 36).
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8 The limitation of the study is its relatively small sample, although over 2000
9
10 randomly selected children were involved in the study. Despite the response rate
11
12 being 80.8% (1822 children) during the first stage of study, fewer children
13
14 responded to invitation for clinical evaluation (the response rates ranged from 25.6 to
15
16 70.8% depending the clinical group). Decreasing response rates should be
17
18 considered as a limitations if longitudinal assessment would be considered. Final
19
20 data collection (HRQOL) was completed on 29 newly diagnosed asthmatic children
21
22 and 21 parents. Thus not all parents responded to HRQOL assessment and this
23
24 should be also considered as the limitation of this study.
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29 More complete data could be received if a multicenter study was conducted
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31 or if rural areas were included. Further studies are necessary to determine whether
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33 similar results could be found in other areas.
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36 Other aspects should be considered, for example parental education or
37
38 financial situation. Such conditions could be considered as possible mediators in a
39
40 future research. Further studies could explain the role of social factors in the
41
42 underdiagnosis of asthma in children.
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45 Nevertheless the method used in our study provides pertinent data concerning
46
47 the parental perception of patient disease and the questionnaire is a useful method to
48
49 describe the impact of disease on parental quality of life. Pre and post-intervention
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51 HRQOL as an outcome measure could be implemented for evaluation education or
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53 coaching programs, and provide important information if strategies satisfy individual
54
55 needs and health expectations.
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3 A general message provided by our study is that even unrecognized asthma
4 (usually mild cases) has an important impact on every-day family functioning. What
5
6 seems to be of importance is that asthma-related emotional changes were visible
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8 both in parents and in affected children. This observation could translate into a
9
10 practically important result. The added value of the assessment of HRQOL extends
11
12 beyond the diagnostic phase. It offers a better means of asthma management, such
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14 as for example family-tailored education and coaching. Therefore it is necessary to
15
16 consider a multidisciplinary approach in the childhood asthma, even in mild cases, as
17
18 ill children and their parents are subjects of care.
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25 In conclusion, HRQOL newly recognized children with asthma and their
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27 parents doesn't correlate closely with clinical status. Patient and parental HRQOL
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29 should be considered as independent dimensions.
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31 Acknowledgements

32
33 The respiratory survey was sponsored by scientific grant from State Committee for
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35 Scientific Research (Polish Ministry of Scientific Research and Information
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37 Technology). The authors are grateful to Professor Elizabeth Juniper for her kind
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39 permission to use the PAQLQ.
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3 ***Quality of Life Protocol in the Early Asthma Diagnosis in Children***
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23 **Key words:** asthma, pediatrics, health-related quality of life, early diagnosis
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Abbreviated title: QOL in early asthma diagnosis

Summary

Introduction. Asthma is considered an important problem in children and influences on their everyday functioning. This study was concerned with the impact of asthma on the health related quality of life (HRQOL) of newly recognized pediatric asthma patients and their parents.

Methods. Patients were identified by a general respiratory survey. HRQOL was assessed by self-report measures: disease-specific questionnaire for children, the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and generic for parents - the Quality of Life in Child's Chronic Disease Questionnaire (QLCCDQ).

Results. 29 newly diagnosed asthmatic children aged 7-11 years (mean age = 8.6 SD=1.4) were identified from a population-based respiratory health survey. The most impaired HRQOL domains differed in parents and children. In children, activity limitation was the most impaired; however in parents, emotional functioning and symptom perception domains were most impaired. There were no statistically significant differences in patient and parental HRQOL observed in either the group where symptoms were present or in the group where symptoms were not present.

Baseline spirometry showed correlation for FEV₁ %FVC and PAQLQ symptom domain (r=0.42). Exercise test showed correlations between FEV₁% FVC and QLCCDQ emotional domain (r=0.7); MEF_{25-75%} and family roles (r=0.81), as well as social functioning (r=0.81). Activity limitation on the PAQLQ correlated with the MEF_{25-75%} (r=0.44) and PEF (r=0.55).

Conclusions. HRQOL newly recognized children with asthma and their parents does not correlate closely with clinical status. Patient and parental HRQOL should be considered as independent dimensions.

Introduction

The results of International Study of Asthma and Allergies in Childhood (ISAAC) have shown that childhood asthma represents an important public health problem worldwide (1). Previously increasing prevalence of childhood asthma, well documented in many countries (2, 3, 4) can be observed in Eastern Europe over the years 1994–2007 (1, 5, 6, 7). The magnitude of the problem could be underestimated because of underdiagnosis (8). The resulting public health burden justifies the development and implementation of population-based measures. Asthma not only has a profound impact on public health, but also on the everyday lives of individual patients.

A patients' burden of chronic illness cannot be assessed by disease severity; it requires measurement reflecting personal perception. There is an increasing interest in activity limitation, emotional functioning, impact on every-day life due to disease and the implementation of health-related quality of life (HRQOL) questionnaires. Deterioration of HRQOL has been described in children and adults with allergic diseases, such as eczema (9) and rhinitis (10). HRQOL assessment highlights important and troublesome problems experienced by patients with asthma (11,12,13). Children with asthma suffer from activity limitation, emotional problems such frustration, fear and irritation (14). Although HRQOL does not correlate closely with asthma control, it is known that children with very severe asthma tend to have a poorer quality of life than those suffering from mild or moderate condition (15). Parents of children with asthma could be limited in normal daily activities and experience emotional distress (16).

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3 Clinical experience shows that a caregiver's HRQOL and their perception of
4 a child's symptoms are important in diagnosis and control of established asthma (17).
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8 Less is known about the potential impact of disease on HRQOL in newly recognized
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10 children with asthma which were found as the result of screening programs. It
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12 remains unknown to what extent such a procedure could be helpful in both early
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14 assessment of asthma and its impact on patients' and parental quality of life.
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17 We implemented the HRQOL protocol in examination of newly identified
18
19 pediatric asthma patients and their families, participants of a large population-based
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21 respiratory health survey. The goal of the study was to determine the impact of
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23 asthma on the health related quality of life of newly recognized pediatric asthma
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25 patients and their parents.
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Materials and Methods

A large population-based respiratory health survey resulted in identification of new pediatric asthma patients. All newly identified children with asthma aged 7-11 years and their parents were involved in HRQOL study. A disease-specific quality-of-life questionnaire was used for the children and a generic questionnaire for parents. Clinical status data was obtained prior to an HRQOL assessment.

Participants

Children were recruited using cluster sampling during a respiratory health survey study in primary schools in Katowice (Southern Poland). 2254 children grades I-IV, in 7 out of 51 schools in the town were invited (17.0% of the town population in the defined age group) for respiratory questionnaire assessment. This was a validated questionnaire, used in The Central European Study of Air Pollution and Respiratory Health (CESAR) [Table 1] and other surveys (22, 23, 24). The response rate was 80.8% (1822 children). Study design is shown in Fig. 1

Figure 1. Study design

Based on the questionnaire results children were categorized into three mutually exclusive groups: "Asthma" (5.4% - diagnosis of asthma established before the survey); "Respiratory Symptoms" (27.9% - no previous diagnosis of asthma and one or more symptoms of persistent cough excluding infections, chest wheezing, dyspnea during the last 12 months), "No Respiratory Symptoms" (66.7% - no previous diagnosis of asthma and no respiratory symptoms during the last 12 months).

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3 [Table 1] - Respiratory Questionnaire (examples of questions)
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5
6 Clinical evaluation was proposed to all children in "Asthma"- group and 60%
7
8 samples from groups "Respiratory Symptoms" and "No Respiratory Symptoms", with
9
10 the response rates: 41.4%, 70.8% and 25.6%, respectively. A certified pulmonologist
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12 (Department of Pneumonology, Medical University of Silesia) examined 415 children.
13
14 The physician was blind to the results of the questionnaire. Diagnostic procedures
15
16 were based on GINA guidelines for childhood asthma (25). Forced expiratory
17
18 volumes were measured according to ERS/ATS recommendations (26). Spirometry
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20 was considered normal if FEV₁, FVC and PEF values exceeded 80% predicted and if
21
22 FEV₁ %FVC ratio was greater than 75%. If actual values presented predicted values,
23
24 a further challenge test of bronchial hyperresponsiveness, described by Gerald et al
25
26 (27), was used. A sub-maximal exercise test (stepping up and down on a single step
27
28 with metronome rhythm) was followed by spirometry obtained at minutes 3, 5 and 10
29
30 after exercise. An FEV₁ decrease greater than 15% was considered positive for
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32 asthma. Medical records were provided; additional skin allergy tests and a chest
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34 radiograph were carried out, where needed.
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41 Clinical assessment of 415 children confirmed 33 previously known and revealed 29
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43 new cases of asthma. All newly identified children with asthma and their parents
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45 were invited to HRQOL assessment.
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53 HRQOL measurements

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55 Quality of life questionnaires were completed by children with asthma at school in the
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57 patient's normal psychosocial environment. Parents of newly diagnosed children
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3 with asthma completed HRQOL questionnaire as well at school, before the diagnosis
4
5 was communicated.
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7 8 *The Paediatric Asthma Quality of Life Questionnaire*

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10 The Paediatric Asthma Quality of Life Questionnaire (PAQLQ), dedicated to children
11
12 aged 7-17 years old, was used as a well-validated and reliable measure of HRQOL in
13
14 childhood asthma. The questionnaire consists of 23 questions, covering symptoms,
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16 emotional function and limitations of activity. Children were asked to recall their
17
18 experiences over the previous week and responded on a 7- point scale (7 – no
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20 impairment, 1 – severe impairment). Patients completed the questionnaire with
21
22 physicians experienced in HRQOL research. Interviewer-administration was used to
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24 avoid parental interference with patient responses.
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28 29 *Quality of Life in a Child's Chronic Disease Questionnaire*

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31 An accompanying questionnaire for parents was devised by the authors, based on
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33 standard procedure – starting from initial questions (identification of needs, definition
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35 of operational objectives), tool development, pretesting and final version (format,
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37 wording) preparation, pilot testing and validation of the questionnaire (19, 20).
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40
41 Quality of Life in a Child's Chronic Disease Questionnaire (QLCCDQ) is concerned
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43 with daily problems and limitations that concern parents of children with chronic
44
45 disease. QLCCDQ is a self – report measure of parent's HRQOL, only symptoms
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47 subscale is parent-proxy measure. Most questions concern parents' functioning, only
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49 the symptom subscale reflects parents' perception of symptoms presence.
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53 QLCCDQ consisted of 15 questions and covered patient-perceived symptoms (e.g
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55 Did the child show any worrying symptoms?) , emotions (e.g. Have you experienced
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57 anxiety because of your child's health problems?) and activity limitation in roles
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59 function: social (e.g. Please indicate how much you have been limited by your child's
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3 disease in listed activities in past two weeks: going to church, cinema, visiting
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5 friends), family roles (e.g. Do you struggle to find time to spend with other family
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7 members (spouse, another child) because of your child' disease?) and occupational
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9 (e.g. Please indicate how much you have been limited by your child's disease in work
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11 related activities in past two weeks).
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15 The questionnaire required circling a choice from seven responses devised for each
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17 question, from 1 (most bothered or limited) to 7 (not bothered or limited). All
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19 questions concerned parental HRQOL of previous two-week period.
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22 23 24 *Psychometric data*

25 26 27 PAQLQ

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29 The instrument is reproducible (ICC =0.95) and has shown ability to detect HRQOL
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31 changes as a result of treatment (p<0.001). Estimation of reliability in stable asthma
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33 has shown that it was consistent throughout all domains (ICC: 0.84-0.93).
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36 37 QLCCDQ

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39 Reproducibility based on the weighted kappa coefficients showed an expected level
40
41 of agreement. Values of weighed kappa coefficients suggested almost perfect
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43 agreement (0.81-1.0) in case of 8 questions, substantial (0.61-0.8) for 5 questions
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45 and moderate (0.41-0.6) for 2 questions. The reliability of the defined subscales was
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47 evaluated by means of Cronbach's α . The values of α ranged between 0.74 and
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49 0.94: symptoms: 0.93, emotions: 0.91, family roles: 0.77, social roles: 0.79,
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51 occupational roles: 0.92 and activity limitations in roles function: 0.91.
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57 58 *Child's school grades and absenteeism*

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3 Supplementary data such as school grades and absenteeism (missed school days
4
5 due to asthma symptoms) were provided to determine if there **were** relationships
6
7 between reported HRQOL and child's functioning at school. It could be expected that
8
9 untreated asthma has an impact on school functioning resulting **in** children lower
10
11 school grades and missed school days. Polish school grades assessment is based
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13 on 6- point scale: from 1 (Fail) to 6 (Excellent).
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20 The study protocol was approved by the ethics committee (Medical University
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22 of Silesia). Each child admitted to the study had the written consent of a parent.
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27 **Statistical analyses**

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32 The statistical analysis was performed using standard procedures available in
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34 the Statistica 7.1 package and SAS, version 9.2 (SAS Institute Inc., Gary, NC).
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36 Normality of distributions of continuous variables was analyzed using the Shapiro–
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38 Wilk test. Statistical significance of differences between continuous variables was
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40 analyzed by t-Student test and ANOVA while **for data with** non-normal distribution, U
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42 Mann-Whitney and Kruskal-Wallis tests were used. Differences between categorical
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44 variables were examined by the chi-square test. Strength of associations, due to non-
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46 normal distributions, were measured by Spearman's rank correlation coefficient.
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49 The statistical inferences were based **on confidence levels** $p < 0.05$. If multiple
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51 comparisons **were** used statistical significance was lowered according to the
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53 Bonferroni adjustment.
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3 Variables included patient and parental HRQOL assessment, symptoms over the
4
5 previous 12 months, baseline and exercise spirometry, school grades and
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7 absenteeism.
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10 Correlations between child's and parental HRQOL scores were analyzed. Relations
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12 between clinical status (symptoms, lung function tests) and HRQOL were examined,
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14 as well as links between educational markers (school grades and absenteeism) and
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16 patient HRQOL scores. Gender and age effects on HRQOL were also analyzed.
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For Peer Review

Results

Participating children

In children with newly diagnosed asthma (mean age = 8.6 years; SD=1.4 years), classified according to GINA protocol, the disease was either episodic (20 children: 6 boys and 14 girls) or chronic mild (9 children: 4 boys and 5 girls). New diagnoses of asthma were made in 10.9% of children from the “Respiratory Symptoms” group and in 3.6% of children from the “No Respiratory Symptoms” group. All 29 newly diagnosed children with asthma and 21 parents responded to the subsequent HRQOL questionnaire.

[Table 2] - Demographic and asthma severity

Patient and parental HRQOL

HRQOL was assessed for each domain, the subscale mean ranging from 1.0 to 7.0. Lower HRQOL scores reflected greater impact of disease on every-day functioning. Children’s most affected HRQOL domain was limitation of activity. Parents’ impairment was most severe in emotional functioning and perceived symptoms, while less impaired domains included social functioning. Domains and overall HRQOL scores for children and parents appear in the table 3.

[Table 3]. HRQOL - domains and overall scores

Statistically important positive correlations were observed between all PAQLQ subscales, as well as most QLCCDQ subscales [Table 4]. QLCCDQ symptom perception subscale correlated only with parental emotional functioning, while

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3 correlations were found between most subscales describing roles functioning.
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5 Bonferroni correction suggested significance level was $p < 0.0001$.
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8
9 [Table 4]. PAQLQ and QLCCDLQ subscales Spearman's correlations
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12 13 14 15 16 HRQOL measures and clinical assessment

17 18 *Symptoms*

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20 The differences of mean QLCCDQ and PAQLQ subscales scores between groups of
21
22 **symptomatic and nonsymptomatic** children **over** in the past 12 months were
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24 analyzed. Both for QLCCDQ and PAQLQ the differences in scores **did not** reach
25
26 statistical significance. Bonferroni correction suggested significance level was $p <$
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31 0.01.
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34 35 *Lung function tests*

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37 Statistically important correlations were found between HRQOL and
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39 spirometry. Challenge tests were done in 23 of the 29 children – 3 children did not
40
41 obtain reproducible spirometry after exercise, 2 children were wheezing before
42
43 exercise **commenced**, 1 child refused **to cooperate**. Baseline FEV₁%FVC and
44
45 symptom domain in children showed a correlation ($r=0.42$), while exercise value
46
47 FEV₁%FVC correlated with emotional domain ($r=0.7$). MEF_{25-75%} correlated with
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49 QLCCDQ family roles ($r=0.81$) and social functioning ($r=0.81$). PAQLQ activity
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51 limitation was correlated with MEF 25-75% ($r=0.44$) and PEF ($r=0.55$), both obtained
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53 during the exercise test. All exercise test correlations were based on spirometry
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55 results collected 10 minutes after the challenge test [Table 5].
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[Table 5]. HRQOL scores and lung function - Spearman's correlations

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6 School grades and absenteeism
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8 Higher scores on the symptoms subscale of PAQLQ correlated with better
9 school grades ($r= 0.64$; $p=0.02$) and fewer missed school days ($r= -0.53$; $p=0.02$).
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12 No correlations were observed in parents' HRQOL and missed school days or school
13 marks.
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20 Patient gender and age
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22 Females showed a significantly lower symptom score in comparison to males
23 ($p=0.01$), however this effect was not translated into total PAQLQ scores nor into
24 parents' HRQOL.
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29 The relationship between HRQOL scores and age were not statistically significant.
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Discussion

Our study focused on the implementation of the HRQOL protocol in early diagnosis of childhood asthma. The analysis involved data obtained in children with newly diagnosed asthma and in their parents. Since asthma cases were identified through population-based screening, it is not surprising that all previously undiagnosed cases represented either episodic or mild asthma – children with more advanced disease had been diagnosed on regular basis, via pediatric health care. An important finding of our study is that the profile of HRQOL impairment is different in children with asthma and in their parents. Not only did PAQLQ and QLCCDQ scores not correlate but – in addition – the highest impaired domains differed between children and parents. Symptom perception and emotional functioning appeared to be the most affected HRQOL domains in parents, while activity limitation was the most impaired domain in children. Some parents might limit their child's activity, due to emotional distress caused by anticipation of symptoms, and such behavior could explain the lack of correlation between emotion domain QLCCDQ and symptom or activity limitation domains in PAQLQ. It is of interest that parental HRQOL pattern is in line with the published qualitative evidence that parents tend to perceive symptoms of asthma in a child as intermittent acute episodes rather than a chronic condition (28). Such interpretation could explain the lack of diagnosis of episodic or mild asthma in our study. It cannot be excluded that such a presentation is not entirely neglected by parents, but treated by them as an annoying condition and not overt disease. Our finding could have some implication as far as screening is concerned - occurrence of symptoms is necessary

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3 but does not have to be a sufficient cause to seek medical advice. Other important
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5 factors include individual experience, perception and emotions.
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8 The relationships between clinical indices and HRQOL were analyzed in many
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10 studies as an important observation for clinicians (29, 30, 31, 32). Our study has
11
12 shown that there were no statistically significant differences in both patient and
13
14 parental HRQOL scores between symptomatic and asymptomatic groups. However
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16 some of analyzed relationships were suggested as significant; before the significance
17
18 level was lowered by applying Bonferroni correction to $p < 0.01$. As the example -
19
20 compared to parents of asymptomatic children, parents of children complaining of
21
22 wheezing had a lower ($p=0.02$) mean score in emotional function and symptom
23
24 domain. As well the group of children possessing dyspnea showed a lower mean
25
26 parental emotional function score ($p=0.04$) than in asymptomatic children. In children
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28 an emotional function score was lower in the group of children complaining of cough
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30 in the past 12 months ($p=0.01$) as compared to asymptomatic children.
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36 Correlations were observed for exercise lung function and QLCCDQ domains, such
37
38 as emotional, family and social functions. Worthy to note, that the correlations
39
40 between children's lung function and parental HRQOL domains were stronger than
41
42 analogous correlations concerning HRQOL in children. The most impaired parent
43
44 HRQOL domain - emotions, significantly correlated with FEV 1 % FVC. Activity
45
46 limitation, the most impaired patient domain, correlated with PEF and MEF 25-75.
47
48 Even if the correlations between clinical indices and HRQOL scores were observed
49
50 only for few variables it should not determine a limitation of HRQOL protocol in early
51
52 diagnosis. As HRQOL is not a diagnostic scale nor a disease or symptom severity
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54 scale index – the impact of disease is not systematically correlated with the disease
55
56 severity as it is categorized (32) by health –care providers. Patient' or caregiver –
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3 based assessment can complement traditional clinical or biological evaluation, which
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5 could suggest that HRQOL could function as part of an early assessment or as part
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7 of disease monitoring.
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10 Our findings were obtained in newly diagnosed and mild cases of asthma. Studies
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12 addressing established childhood asthma showed that the correlations between the
13
14 clinical status and HRQOL scores are weak to moderate, even for disease-specific
15
16 measures (29, 30, 31). A perception of dyspnea, although a crucial asthma
17
18 symptom, might show interpersonal and intrapersonal variations (33). Although
19
20 children with severe asthma tend to have a poorer quality of life than children with
21
22 milder disease (34), parental and children's perception can be influenced by a
23
24 number of factors. Consistent with findings in the G. Guyatt's study, in children aged
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26 7-10, clinicians cannot rely on parental reports to provide insight into the child's
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28 HRQOL. This study also showed that the patient's assessment of change in
29
30 symptoms were more closely related to HRQOL scores than parental assessment
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32 (20). A different effect provided by our study could be discussed in terms of early
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34 diagnosis and mild clinical presentation of the newly diagnosed cases.
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40 Parental experience of their child's disease is very important for the diagnosis of
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42 asthma, and it would confirm the importance of screening programs addressed to
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44 parents, including emotional context of their functioning in relation to the child's
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46 symptoms. Parental HRQOL could be recommended as a valuable method of a more
47
48 holistic assessment of disease impact on everyday functioning of child and their
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50 family. Both patient and parental perception are important in care strategies
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52 planning and implementation. Children are influenced by their parents and reduction
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54 of parental distress could be beneficial for child's family life and integration within
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3 society (35). In contrast an increasing parental stress could diminish compliance and
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5 adjustments to illness (35, 36).
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8 The limitation of the study is its relatively small sample, although over 2000
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10 randomly selected children were involved in the study. Despite the response rate
11
12 being 80.8% (1822 children) during the first stage of study, fewer children
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14 responded to invitation for clinical evaluation (the response rates ranged from 25.6 to
15
16 70.8% depending the clinical group). Decreasing response rates should be
17
18 considered as a limitations if longitudinal assessment would be considered. Final
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20 data collection (HRQOL) was completed on 29 newly diagnosed asthmatic children
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22 and 21 parents. Thus not all parents responded to HRQOL assessment and this
23
24 should be also considered as the limitation of this study.
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29 More complete data could be received if a multicenter study was conducted
30
31 or if rural areas were included. Further studies are necessary to determine whether
32
33 similar results could be found in other areas.
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36 Other aspects should be considered, for example parental education or
37
38 financial situation. Such conditions could be considered as possible mediators in a
39
40 future research. Further studies could explain the role of social factors in the
41
42 underdiagnosis of asthma in children.
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45 Nevertheless the method used in our study provides pertinent data concerning
46
47 the parental perception of patient disease and the questionnaire is a useful method to
48
49 describe the impact of disease on parental quality of life. Pre and post-intervention
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51 HRQOL as an outcome measure could be implemented for evaluation education or
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53 coaching programs, and provide important information if strategies satisfy individual
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55 needs and health expectations.
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3 A general message provided by our study is that even unrecognized asthma
4 (usually mild cases) has an important impact on every-day family functioning. What
5 seems to be of importance is that asthma-related emotional changes were visible
6 both in parents and in affected children. This observation could translate into a
7 practically important result. The added value of the assessment of HRQOL extends
8 beyond the diagnostic phase. It offers a better means of asthma management, such
9 as for example family-tailored education and coaching. Therefore it is necessary to
10 consider a multidisciplinary approach in the childhood asthma, even in mild cases, as
11 ill children and their parents are subjects of care.
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24 In conclusion, HRQOL newly recognized children with asthma and their
25 parents doesn't correlate closely with clinical status. Patient and parental HRQOL
26 should be considered as independent dimensions.
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31 Acknowledgements

32
33 The respiratory survey was sponsored by scientific grant from State Committee for
34
35 Scientific Research (Polish Ministry of Scientific Research and Information
36
37 Technology). The authors are grateful to Professor Elizabeth Juniper for her kind
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39 permission to use the PAQLQ.
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Figure 1. Study design

Respiratory Health Survey	2254 children invited ↓ 1822 responders divided into three groups		
	Asthma n=99 ↓	Respiratory Symptoms n=508 ↓	No Respiratory Symptoms n=1215 ↓
Clinical Assessment	n=99 ↓ n=41	Invited for clinical examination n=315 ↓ Agreed to undergo clinical examination n=192 ↓	n=749 ↓ n=223 ↓
Asthma	41 Confirmed	21 New cases	8 New cases
HRQOL	Children Previously Diagnosed PAQLQ (n=33)	Children newly diagnosed and their parents PAQLQ (n=29) and QLCCDQ (n=21) STUDY GROUP	

Table 1. Respiratory Questionnaire

Symptom	Question	Clinical variables
Wheezing	Has the child ever had chest wheezing	
	Has the child had chest wheezing past 12 months	✓
Dyspnea	Has the child ever had attack of dyspnea	
	Has the child had attack of dyspnea during last 12 months	✓
Dry cough	In past 12 months has the child had a dry cough at night, apart from a cough associated with a cold or chest infection	✓
Morning cough	Has the child had a morning cough during autumn and winter	✓
Chronic cough	Has the child coughed on most days for a minimum of three months yearly for two years	✓
Exercise induced symptoms	Has the child had exercise-induced wheezing, dyspnea or cough in the last 12 months	✓
Previous diagnosis	Has the child ever had recognized obstructive bronchitis, bronchial obstruction or asthma by physician	

Table 2. Demographic and asthma severity

	Males		Females	
	Number	Percent	Number	percent
GINA classification				
I	6	60	14	73,68
II	4	40	5	26,32
Total	10	34,5	19	65,5
Age				
Average (SD)	8,6 (1,4)		8,9 (1,0)	

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Table 3. HRQOL - domains and overall scores

	Mean	SD	Min	Max
QLCCDQ domain				
Role functioning				
Family	5.9	0.8	4.0	7.0
Social	6.1	0.7	4.3	7.0
Occupational	5.7	1.0	3.7	7.0
Roles activity limitations	5.8	0.8	4.2	7.0
Symptoms	4.0	1.1	2.0	6.3
Emotions	4.1	0.7	3.7	6.2
Overall points	81.7	10	66	98
Overall mean	5.4	0.7	4.4	6.5
PAQLQ domain				
Symptoms	5.4	1.2	2.1	7.0
Activity limitation	4.7	1.1	1.4	7.0
Emotions	5.9	1.3	1.4	7.0
Overall points	126.8	24,98	41	161
Overall mean	5.5	1.1	1.8	7.0

Table 4. QLCCDQ and PAQLQ subscales Spearman's' correlations

	Family roles	Social roles	Occupational roles	Activity limitation	Symptoms perception	Emotions
Domain¹ QLCCDQ						
Family roles	-					
Social roles	0.7 (0.0001)	-				
Occupational Roles	0.6 (0.007)	0.6 (0.007)	-			
Roles activity limitation	0.8 (0.0001)	0.8 (0.0001)	0.9 (0.0001)	-		
Symptoms perception	0.07 (0.7)	-0.005 (0.9)	0.4 (0.08)	0.2 (0.31)	-	
Emotions	0.2 (0.4)	0.2 (0.3)	0.4 (0.05)	0.4 (0.09)	0.9 (0.0001)	-
Domain² PAQLQ						
Activity Limitation				-		
Symptoms				0.7 (0.0001)	-	
Emotions				0.6 (0.0001)	0.7 (0.0001)	-

p- value in brackets

1 - according to Bonferroni adjustment significance level p<0.001

2- according to Bonferroni adjustment significance level p<0.008

Table 5. HRQOL scores and lung function - Spearman's correlations

	Lung function test (10 minutes after exercises test)				
	FEV1	FEV1 %FVC	FVC	PEF	MEF 25-75%
QLCCDQ domain					
Role functioning					
Family roles	0.5	0.3	0.1	-0.3	0.8
Social roles	0.1	0.01	0.07	-0.1	0.8
Occupational roles	0.2	0.3	0.1	0.2	0.2
Roles activity limitation	0.2	0.3	0.1	0.2	0.6
Symptoms	0.06	0.6	-0.02	0.2	0.2
Emotions	0.02	0.7	-0.09	0.2	0.2
PAQLQ domain					
Symptoms	0.01	0.2	0.4	0.2	0.2
Activity limitation	0.2	0.2	0.4	0.5	0.4
Emotions	-0.05	0.2	0.2	0.09	0.2
p<0.01 statistically significant in bold					