

TITLE

The relationship of psychological factors and asthma control to health-related quality of life

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Abstract: 232 words

Text: 3500

ABSTRACT

BACKGROUND: Psychological variables (anxiety, depression and coping strategies) and asthma control (assessed from the patient's perspective or from the physician's perspective) affect health-related quality of life (HRQoL) in asthmatic patients. However, no study has simultaneously evaluated these variables to understand the independent contribution of each one of these factors on HRQoL.

OBJECTIVE: To determine the impact of anxiety, depression, coping strategies and asthma control on HRQoL, and to compare the impact of asthma control on HRQoL when it is established by the physician versus when it is considered by the patient.

METHODS: 373 asthmatics completed the Hospital Anxiety and Depression Scale, Coping Orientations to Problems Experienced Inventory, 36-Item Short-Form Health Survey (SF-36) and St George Respiratory Questionnaire (SGRQ). Asthma control was measured by the patient with Asthma Control Test and by the physician with the classification asthma control of Global Initiative for Asthma. Demographic and clinical characteristics were also collected.

RESULTS: Anxiety, depression and poor patient-rated asthma control status were associated with worse HRQoL in all dimensions (except Mental Health for asthma control). Physician-rated asthma control was related to worse HRQoL in physical generic and specific dimensions. Among coping strategies, only avoidant coping impacted HRQoL in a few dimensions.

CONCLUSIONS: Anxiety, depression and asthma control (specially patient-rated asthma control) were important independent predictors of asthma HRQoL, and all of them should therefore be considered in interventions to improve HRQoL in asthmatic patients.

HIGHLIGHTS BOX

What is already known about this topic? Anxiety, depression, avoidant coping and asthma control (estimated by the patient or by the physician) affect quality of life; however, these factors have not been concurrently evaluated to determine their independent contribution to asthma quality of life.

What does this study add to our knowledge? Anxiety, depression and patient-rated asthma control are important independent contributors to asthma quality of life and they are associated almost all dimensions. The impact of physician-rated control and avoidant coping on quality of life is lower.

How does this study impact current management guidelines? Anxiety, depression and control of asthma (preferably estimated by the patient) should be routinely screened in asthmatic patients, and interventions focused on these potentially modifiable factors should be implemented to improve quality of life in asthmatic patients.

Keywords:

Asthma; Asthma control; Health-related quality of life; Anxiety; Coping strategies; Depression.

Conflict of interest

Beatriz González Freire has received research support from the María Barbeito Programme of the Consellería de Innovación e Industria de la Xunta de Galicia. The rest of the authors declare that they have no relevant conflicts of interest

ABBREVIATIONS USED

ACT: Asthma Control Test

B: non-standardized regression coefficient

BMI: Body mass Index

CI: Confidence Interval

COPE: Coping Orientations to Problems Experienced Inventory

GINA: Global Initiative for Asthma

HADS: Hospital Anxiety and Depression Scale

HADS-A: Hospital Anxiety and Depression Scale – Anxiety Subscale

HADS-D: Hospital Anxiety and Depression Scale –Depression Subscale

HRQoL: Health-related quality of life

M: Mean

Max: Maximum

Mdn: Median

Min: Minimum

N: Total sample size

R^2 : Coefficient of determination

SD: Standard deviation

SF-36: 36-Item Short-Form Health Survey

SGRQ: St. George's Respiratory Questionnaire

% FEV₁: percentage of predicted value of forced expiratory volume in 1 second

Introduction

Asthma can affect health-related quality of life (HRQoL), but the degree to which this chronic disease influences HRQoL depends on multiple factors.

Most of the investigations have focused on the role played by sociodemographic, lifestyle or clinical variables on HRQoL [1-8], but the influence of psychological variables have received less attention. Among psychological variables, anxiety and depression are the most frequently evaluated (because comorbidity is common in patients with asthma [9-13]), whereas the coping strategies used by the patient to deal with the disease have been evaluated in a smaller number of studies [14].

Anxiety, depression and coping strategies are associated with HRQoL independent of other potentially confounding variables such as sociodemographic, lifestyle, and clinical variables [15-22], but only a few studies have evaluated the role of some of these psychological variables (anxiety or depression but not coping) on HRQoL also considering the effect of asthma control and their results are inconclusive [23-26]. Considering at the same time the effect of these three psychological variables and asthma control is important because poor asthma control has been associated with higher anxiety and depression [21,27-29] and a higher use of avoidant coping strategies [30], and poor asthma control has also been closely associated with worse HRQoL [31-34]. Hence, is still necessary to better understand the interplay and the unique contribution of each one of these factors on HRQoL. However, to the best of our knowledge, no study has simultaneously evaluated the effect of anxiety, depression and coping strategies and of asthma control on HRQoL.

In addition, there is a no gold standard measure for asthma control, so that usually two types of approaches are employed: from the patient's perspective, using validated self-

report measures, or from the physician's perspective, according to clinical and pulmonary function parameters. Both types of control measures provide only fair to moderate agreement [35], and so far, whether there is a differential impact of asthma control on HRQoL as a function of the type of assessment used has not been evaluated.

The aim of this study was to determine the impact of anxiety, depression, coping strategies, and asthma control on generic and specific domains of HRQoL in asthmatic patients and to provide an insight of the impact of asthma control on HRQoL when asthma control is established by a physician versus when control is considered by the patient.

Methods

Patients

Using a cross-sectional study, we recruited participants consecutively from outpatients of the allergy or pneumology practices of the University Hospital Complex of Ourense (Spain) a tertiary center belonging to the Spanish public healthcare system that attends to patients referred from primary care. Inclusion criteria were: 1) a physician's diagnosis of asthma; 2) at least 6-months since the diagnosis; 3) age between 18 and 75 years; 4) reading-writing ability in Spanish; and 5) no diagnosis of other physical or psychiatric chronic comorbid illnesses, except for rhinitis.

A psychologist collected the sociodemographic (sex, age, educational level, employment situation, self-reported social class and marital status) and lifestyle data (smoking and body mass index) in an interview. The specialized physician responsible for the patient's treatment filled in a clinical data form with the following information: age at asthma diagnosis, duration of disease, percentage of predicted value of forced expiratory volume in 1 second (% FEV₁), asthma control level according to the Global Initiative for Asthma criteria (GINA, 2006) [36] and severity of asthma according to GINA (2009) criteria [37].

Patients also completed the following questionnaires: Hospital Anxiety and Depression Scale (HADS) [38]; Coping Orientations to Problems Experienced Inventory (COPE) [39]; Asthma Control Test (ACT) [40]; 36-Item Short-Form Health Survey (SF-36) [41]; St. George's Respiratory Questionnaire (SGRQ) [42]. The Spanish adaptations of the questionnaires were used in all cases [43-47].

The study was approved by the Galician Ethical Research Committee with the code 2009/408.

Statistical Analysis

For the descriptive analysis, the continuous variables are presented as mean, standard deviation, and range, and the categorical variables as frequency and percentage (excluding missing values) with a confidence level of 95%.

To quantify the impact of bronchial asthma on HRQoL we considered the scores in the eight dimensions of the SF-36 expressed on a scale from 0 (maximum impairment) to 100 (no impairment) and the three dimensions and overall score of SGRQ in a scale from 0 (minimum impairment) to 100 (maximum impairment). In addition, the scores in the eight dimensions of the SF-36 questionnaire were standardized according to Spanish population reference standards obtained by Alonso et al. [48]. Standardized values are expressed in standard deviations from the score of the Spanish general population of the same age and sex (which would receive the value of 0).

The degree of asthma control according to ACT criteria was divided into two categories: controlled asthma ($ACT \geq 20$) vs uncontrolled asthma ($ACT < 20$). The classification of control performed by the physician according to GINA criteria [36] also had two categories: controlled asthma vs uncontrolled asthma (patients with partially controlled asthma or uncontrolled asthma). To study the concordance between two classification of asthma control (ACT and GINA criteria) Kappa index was calculated.

When the two classifications of control were considered simultaneously, patients with $ACT \geq 20$ plus controlled asthma according to GINA criteria [36] were categorized as controlled asthma. All other cases were considered as uncontrolled asthma.

For the univariate analysis between HRQoL scores (standardized SF-36 and direct SGRQ scores) and sociodemographic, clinical, and psychological variables, we applied

Student's *t*-test or ANOVA and the U-Mann-Whitney or Kruskal-Wallis test (as appropriate after verifying the normality with the Kolmogorov-Smirnov test and the number of categories of the variables analyzed) and Spearman's rho correlation coefficient.

Using results from the univariate analysis, we developed general linear models for each of the standardized dimensions of the SF-36 scores and for the SGRQ scores. When the requirement of normality in HRQoL scores was not met, we used the Box-Cox family of transformations. In all the analyses, sex, age, smoking, and asthma control level (considering ACT criteria plus GINA criteria [36]) were included as independent variables as well as all the sociodemographic, clinical, and psychological variables that obtained a level of significance $<.20$ in the univariate analyses. For the inclusion of anxiety and depression in these models, and due to the small number of patients presenting with only depression, the participants were classified into three groups: (a) no anxiety or depression ($\text{HADS-A} < 8$ and $\text{HADS-D} < 8$); (b) only anxiety ($\text{HADS-A} \geq 8$ and $\text{HADS-D} < 8$); and (c) suffering from depression with or without anxiety (depression $\text{HADS-D} \geq 8$ and $\text{HADS-A} < 8$ or ≥ 8). These models also considered the effect of the interactions between variables.

With the aim of identifying which of the two classifications of asthma control (estimated by the patient vs estimated by the doctor) was the best predictor of HRQoL, the general linear models for each of the evaluated HRQoL dimensions were replicated, considering the degree of control only via ACT criteria or only via GINA criteria [36].

A sample size of $n=373$ was included, which allows to estimate patients' characteristics with a precision of $\pm 5.1\%$ and 95% confidence. Since asthma was evaluated with both

methods (ACT plus GINA criteria) in only 285 patients, percentage of patients with controlled asthma could be estimated with a precision of $\pm 5.8\%$ and 95% confidence.

In all statistical analyses, an alpha level of .05 was established. The SPSS 19.00 package for Windows and the 2.12.2 version R package were used.

Results

A total of 373 asthmatic patients (55.3% were recruited in allergy practices, and 44.7% in pneumology practices) participated in the study. Characteristic of the sample are summarized in Table 1. The mean age of this sample was 36.88 ± 14.90 years (range 18 – 75), the mean age of the patients when they were diagnosed with asthma was 25.62 ± 14.82 years (range 1– 67), and the mean duration of the disease was 11.98 ± 10.90 years (range 0 - 67). The treatment the patients were prescribed is described in Table 1.

Regarding asthma control, the administration of the ACT questionnaire revealed that 57.7% of the patients had well-controlled asthma and regarding the classification of the degree of control established by the physician according to GINA criteria [36] 65.6% were categorized as well-controlled asthma. The Kappa index between the two methods used to measure asthma control was 0.45 (95% CI 0.34-0.55). Among the 285 patients in whom control of asthma was evaluated with both methods (ACT plus GINA criteria), asthma was categorized as controlled in 49.1% of the patients. In these controlled patients, the asthma severity classification according to GINA criteria [37] was: 51.4% intermittent asthma, 7.8% mild persistent asthma, 25% moderate persistent asthma, and 15.7% severe persistent asthma.

With regard to the psychological variables, 35.4% of the patients suffered from anxiety ($\text{HADS-A} \geq 8$), and 14.3% of the patients presented depression ($\text{HADS-D} \geq 8$). In the total sample, 11% of the patients had combined anxiety and depression ($\text{HADS-A} \geq 8$ and $\text{HADS-D} \geq 8$). The most frequently used coping strategy was Behavioral Coping

with the problem (2.87 ± 0.44), while the least frequently used were Consumption of alcohol and/or drugs (1.05 ± 0.21) (see Table 2).

Considering direct scores in the generic SF-36 questionnaire, the most affected dimension were General Health in SF-36 (53.58 ± 21.42) and Symptoms in SGRQ (40.22 ± 19.93) whereas the least affected were Social Functioning in SF-36 (81.57 ± 24.76) and Impact in SGRQ (22.87 ± 19.39) (see Table 3).

Compared with the general population, using standardized scores of SF-36, the sample of asthmatic patients evaluated had poorer HRQoL in all the dimensions of the SF-36, and General Health (-1.03 ± 1.15) was the most affected, whereas the least affected was Mental Health (-0.25 ± 1.08) (see Figure 1).

For each dimension of the SF-36 and the SGRQ, the sociodemographic, clinical and psychological variables identified by univariate analysis were entered as candidate predictors in the multivariable analysis (data not shown).

The results of the multivariable analyses of the SF-36 and SGRQ questionnaires are shown in Tables 4 and 5, respectively. In the multivariable regression analysis, using data from $n=285$ with both ACT and GINA criteria available, the only demographic and lifestyle variables retained as significant predictors of poorer HRQoL were female sex, younger age, non-active working situation, former smoker, and obesity ($p < .05$). The interaction effect between age and sex was significant in Physical Functioning ($p = .025$) indicating that an increase in age was associated with an increase of the Physical Functioning score, and this increase was greater among females. The effect of obesity on the dimension Activity and Overall score SGRQ was higher when the patient was actively employed ($p < .05$). Among the clinical variables, only $FEV_1 < 80\%$ of the predicted value was related to Physical Functioning and General Health of the SF-36

($p < .05$) and to Activity of the SGRQ ($p = .038$). By contrast, in all the generic and specific scales, anxiety and/or depression were associated with poorer HRQoL. The presence of depression or depression plus anxiety was consistently associated with worse HRQoL, both in the dimensions of the SF-36 questionnaire ($p < .001$) and in those of the SGRQ questionnaire, as well as in its Overall score ($p < .01$). The presence of only anxious symptoms was also associated with significantly worse HRQoL in all the dimensions of the SF-36 ($p < .01$, with the exception of the Role Physical dimension) and in all dimensions and the Overall score SGRQ ($p < .05$). There were significant interactions between sex and anxiety symptoms in the Mental Health dimension of the SF-36 ($p = .027$) and in the Impact dimension ($p = .028$) and the Overall score SGRQ ($p = .011$). There were also significant interactions between sex and depressive or anxious plus depressive symptomatology in the dimensions Activity ($p = .027$) and Impact ($p = .043$) of the SGRQ. In all cases, the effect of psychological comorbidity on HRQoL was slightly higher in males. Poor asthma control was also closely related to HRQoL in the physical dimensions of the SF-36: Physical Functioning, Role Physical, Bodily Pain, General Health, and Vitality ($p \leq .001$), as well as with all domains and the Overall score SGRQ ($p < .001$). The impact of coping strategies on HRQoL was more limited. A greater use of Cognitive Avoidant was associated with greater deterioration in the dimensions of Social Functioning and Role Emotional of the SF-36 ($p < .01$), and a greater use of Behavioral Avoidant was associated with greater impact on the Symptoms dimension of the SGRQ ($p = .022$).

The selected characteristics explained an acceptable proportion of variability (R^2), ranging from 15% in Bodily Pain to 44% in Mental Health in the dimensions of the SF-36, and ranging from 28% in Symptoms to 56% in the Overall score SGRQ (see Tables 4 and 5). In 9 of the 12 analyzed models, the percentages of explained variance

exceeded 25%, generally taken as the minimum above which the model can be considered acceptable [49].

Results of multivariable analysis of HRQoL, considering separately each of the two classifications of the degree of asthma control, using n=303 patients with ACT criteria (Model 1) and n=288 with GINA criteria (Model 2), respectively, showed that, the percentage of explained variance of the generic and specific dimensions of HRQoL was slightly higher when asthma control was considered according to ACT criteria (in the SF-36, values ranging between 17% of Bodily Pain and 48% of Mental Health, and in the SGRQ, between 29% of Symptoms and 53% of the Overall score SGRQ) than when asthma control was considered according to GINA criteria [36] (in the SF-36, values ranging between 11% of Bodily Pain and 48% of Mental Health, and in the SGRQ, between 21% of Symptoms and 47% of the Overall score SGRQ). According to the ACT classification, a significant effect of asthma control was found in eleven of the twelve models (Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, and Role Emotional of the SF-36, and Overall score SGRQ and by SGRQ dimensions) and only in eight (Physical Functioning, Role Physical, General Health, and Vitality of the SF-36 and all dimensions and Overall score SGRQ) when the classification of control was established based on GINA criteria [36] (see Tables 6 and 7).

Discussion

Our results show that asthma affects both generic dimensions and specific dimensions of HRQoL, and the main variables that determine this impact on HRQoL are anxiety, depression and patient-rated asthma control.

The impact of asthma on HRQoL was assessed using two complementary approaches: a generic questionnaire (SF-36) and a specific questionnaire (SGRQ). Both questionnaires coincided in indicating the physical dimensions as the most damaged, whereas the mental dimensions remain the least affected in line with previous studies [50,51].

The analysis of the variables that determine HRQoL revealed the significance of several sociodemographic variables (sex, age, employment situation, and obesity) and the pulmonary function. However, these variables have a rather limited effect, and each one only affected one or a few domains. In contrast, anxiety and depression and asthma control were strong predictors of generic and specific domains.

Anxiety and depression are the psychological disorders most frequently found in asthmatic patients [9-13,52,53]. In our study, 35% of the patients had symptoms of anxiety and 14% of the patients had depressive symptoms, and these figures are within the prevalence range reported in other studies [10,26,54].

As could be expected, these psychosocial variables explained the variance in mental health domains (Mental Health and Social Functioning of the SF-36 and Impact of the SGRQ), but it is important to note that anxiety and depression also contributed to explain the perception of physical status (Physical Functioning, Bodily Pain, and Vitality of the SF-36 and Symptoms of the SGRQ) and of functional capacity (Role Physical and Role Emotional of the SF-36 and Activity of the SGRQ).

Confirming prior literature, poor asthma control also substantially impaired HRQoL [31-34]. In the present study, the determination of the degree of asthma control was established by two methods: patient-rated asthma control status using the ACT and physician-rated asthma control using GINA criteria [36]. The concordance between ACT and GINA criteria [36] was moderate, similar to the study of Thomas et al. [35]

and the same as other studies [29,35] in finding that the rates of control reported by asthmatic patients are lower than the rates determined by physicians.

Regardless of the procedure used to estimate asthma control (ACT plus GINA, only ACT, or only GINA), we found that subjects with poor asthma control have substantially impaired generic physical domains and disease-specific domains of the HRQoL.

When we examined the association between control level estimated by the patient and by the doctor and HRQoL separately, patient-rated asthma control is related not only to generic physical dimensions but also to generic mental dimensions. A possible explanation would be that, both in the ACT and the HRQoL instruments used, we are collecting information from the same perspective (provided by the patient) and there may be a biased symptom reporting that affects perception of HRQoL. However, to our knowledge, this research is the first study that compared the impact on HRQoL of the different methods used to classify the degree of asthma control, and future research is necessary.

Regarding coping strategies, our results show that avoidance coping was related to worse HRQoL, in line with previous studies in asthmatic patients [15, 18]. Studies of patients with other chronic illnesses have found that avoidance coping is associated with poor medication adherence and may result in poorer long-term outcomes for many patients [55, 56]. However, the effect of avoidance coping is much more limited than that found for the other psychological variables evaluated (anxiety and depression), and it was only related to the dimensions Social Functioning and Role Emotional of the SF-36 and Symptoms of the SGRQ.

The impact of anxiety, depression, and coping strategies on HRQoL could be attributed to the relationship between these psychological variables with worse asthma control. This relationship was shown in several studies [27-29,30] and it could be established through several pathways including behavioral pathways (disorganized self-care and poor health behaviors) or through the direct physiological effects of emotional status on the autonomic nervous and immune systems, which increase asthma symptomatology [57]. Poor asthma control could finally lead to deterioration of HRQoL. Our result showed the effect of the evaluated psychological variables on HRQoL is present even after controlling for asthma control.

In conclusion, our findings support to the proposal that, although they are interrelated concepts, anxiety, depression, coping strategies and asthma control each contribute independently to HRQoL.

Our study has several strengths. To our knowledge, this is the first study to indicate a strong and independent association between anxiety, depression, coping strategies and asthma control and HRQoL. In addition, we used two complementary approaches to evaluate HRQoL: the SF-36, a generic questionnaire that allows comparing the health status across different diseases and with general populations, and the SGRQ, a specific questionnaire sensitives to patients' specific problematic respiratory areas. Finally, we also considered two ways to assess asthma control (estimated by the physician and by the patient) to determine whether there are differences between the two in terms of their relationship with HRQoL.

It is also necessary to take into account some limitations of the study. Firstly, the sample was only drawn from the tertiary asthma clinic and most of the patients present intermittent asthma, which can affect the generalizability of our results. Moreover, we established as exclusion criteria the presence of physical comorbidity, therefore,

findings may not generalize to overall population of asthmatics. However, this creates a homogeneous sample in which the patients evaluated only suffered from bronchial asthma, thus avoiding the possible effect of other comorbid diseases on HRQoL. Finally, this study may be limited by the cross-sectional nature of the design that does not allow the prediction of the direction of causality. Prospective studies are needed to better delineate the relationships found between psychological variables, asthma control, and HRQoL.

Given that the findings of this study showed that anxiety, depression, coping strategies, and asthma control are variables that affect HRQoL independently, all of them should be taken into account when considering HRQoL scores as an outcome measure in asthma. It would be advisable to train healthcare professionals so that, when evaluating asthmatic patients, they include screening for psychological variables and asthma control estimated by the patient. Brief and easy to complete tools such as HADS and ACT allow introducing the measurement of anxiety, depression and patient-rated control in the routine clinical practice, in order to detect these characteristics in patients. Effectively treating asthma symptoms improves asthma control and may reduce anxiety and depression. A recent study has found that a significantly number of patients with asthma improved anxiety and depression after 6 months of standardized treatment and regular specialist care [58]. In cases where it is necessary, interventions specifically focused on psychological factors should also be implemented in an attempt to improve HRQoL in asthmatic patients.

This study was funded by María Barbeito Programme of the Consellería de Innovación e Industria de la Xunta de Galicia.

Acknowledgments The authors thank Dr. José Manuel García Pazos, Dr. Pedro Marcos Velázquez, Dr. Carlos García de la Cuesta, Dra. María Genoveva Álvarez Eire and Dra. Susana Varela for their support in register the clinic data of the patients. We also thank Dr. Salvador Pita Fernández† his valuable contribution in the development of this study.

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Figure Legends

Figure 1. Standardized scores in the eight dimensions of SF-36.

Table 1. Sociodemographic, life style and clinical characteristics of the sample

Characteristics	N	%	95% CI
Sex			
Female	263	70.5	[65.74, 74.72]
Male	110	29.5	[25.27, 34.25]
Education level			
Without education /primary	134	35.9	[30.92, 40.92]
Secondary	165	44.2	[39.06, 49.41]
College	74	19.8	[15.65, 24.02]
Marital status			
Single/divorced/widowed	166	44.5	[39.32, 49.68]
Married/living with a stable partner	207	55.5	[50.31, 60.67]
Employment situation			
Active	203	54.4	[49.23, 59.61]
Non-active	170	45.6	[40.38, 50.76]
Self-reported Social class			
Lower/lower-middle	78	21	[16.74, 25.30]
Middle-middle	260	70.1	[65.28, 74.87]
Upper/middle-upper	33	8.9	[5.86, 11.92]
Smoking habit			
Smoker	70	18.8	[14.67, 22.86]
Former	60	16.1	[12.22, 19.94]
Non-smoker	243	65.1	[60.17, 70.11]
BMI			
< 18.5	6	1.6	[0.20, 3.10]
18.5 – 24.99	181	49.9	[44.58, 55.14]
25 – 29.99	104	28.7	[23.86, 33.43]
≥ 30	72	19.8	[15.59, 24.07]
% FEV ₁ of predicted value			
≥ 80%	265	71.4	[66.69, 76.16]
60-80%	85	22.9	[18.50, 27.32]
< 60%	21	5.6	[3.17, 8.14]
Prescribed medications			
None daily controller medication	120	32.3	[27.45, 37.24]
Low-dose ICS or LTRA	32	8.6	[5.63, 11.62]
Low-to-medium dose ICS + LABA or medium dose ICS+ theophylline/LTRA or high-dose ICS	174	46.9	[41.69, 52.11]
High-dose ICS + LABA associated or not with theophylline, LTRA, oral glucocorticosteroid or Anti-IgE	45	12.1	[8.67, 15.59]
Level of asthma control according to ACT			
Controlled asthma	175	57.7	[52.02, 63.48]
Uncontrolled asthma	128	42.2	[36.65, 47.84]
Level of asthma control according to GINA (2006)			
Controlled asthma	189	65.6	[59.96, 71.28]
Partly controlled	56	19.4	[14.70, 24.18]
Uncontrolled asthma	43	14.9	[10.64, 19.22]
Severity of asthma according to GINA (2009) in controlled patients			
Intermittent asthma	72	51.4	[42.79, 60.06]
Mild persistent asthma	11	7.8	[3.04, 12.67]
Moderate persistent asthma	35	25	[17.47, 32.53]
Severe persistent asthma	22	15.7	[9.32, 22.10]

Note: % FEV₁ = Percentage of predicted value of forced expiratory volume in 1 s; ACT = Asthma Control Test; GINA = Global Initiative for Asthma; BMI = Body mass index; ICS= inhaled corticosteroids; LABA=long-acting beta agonists; LTRA= leukotriene-receptor antagonists

Table 2. *Psychological characteristics of the sample*

Psychological variables	<i>n</i>	<i>M</i> ± <i>SD</i>	<i>Mdn</i>	<i>Min</i>	<i>Max</i>
HADS-A	369	6.50 ± 4.35	6	0	21
HADS-D	369	3.85 ± 3.77	3	0	19
COPE					
Behavioral coping of the problem	361	2.87 ± 0.44	2.82	1.55	4
Cognitive coping of the problem	355	2.20 ± 0.39	2.20	1	3.33
Behavioral avoidance	358	2.60 ± 0.38	2.57	1	3.86
Cognitive avoidance	359	1.64 ± 0.46	1.55	1	3.64
Emotion-focused coping	363	2.48 ± 0.57	2.42	1	4
Alcohol-drug consumption	366	1.05 ± 0.21	1	1	2.50

Note. HADS-A = Anxiety subscale of Hospital Anxiety and Depression Scale; HADS-D = Depression subscale of Hospital Anxiety and Depression Scale; COPE = Coping Orientations to Problems Experienced Inventory.

Table 3

Direct HRQOL scores in SF-36 and SGRQ

HRQOL questionnaires	<i>n</i>	<i>M</i> ± <i>SD</i>	<i>Mdn</i>	<i>Mín</i>	<i>Max</i>
SF-36					
Physical functioning	371	80.12 ± 20.88	95	10	100
Role physical	371	75.00 ± 37.93	100	0	100
Bodily pain	369	68.73 ± 25.82	100	0	100
General health	371	53.58 ± 21.42	72	0	100
Vitality	371	60.40 ± 21.23	70	0	100
Social function	371	81.57 ± 24.76	100	0	100
Role emotional	371	72.59 ± 40.42	100	0	100
Mental health	371	68.37 ± 21.85	76	0	100
SGRQ					
Overall	367	29.67 ± 19.45	25.44	0	87.65
Symptoms	372	40.22 ± 19.93	38.89	0	90.82
Activity	370	35.86 ± 26.53	35.47	0	100
Impact	369	22.87 ± 19.39	17.85	0	90.94

Note. HRQOL = Health-related quality of life; SF-36 = 36-Item Short-Form Health Survey; SGRQ = St. George's Respiratory Questionnaire.

Table 4. Multivariable analysis of SF-36 questionnaire domains adjusting for asthma control level according to ACT criteria plus GINA (2006) criteria

SF-36	Predictors	B (95% CI)	P	R ² corrected
Physical Functioning				.37
	Female sex	-91.38 (-150.94 to -31.82)	.003	
	Age	1.64 (0.37 to 2.92)	.012	
	BMI $\geq$ 30	-39.02 (-67.24 to -10.81)	.007	
	FEV ₁ of predicted value < 80%	-28.55 (-53.20 to -3.90)	.023	
	Uncontrolled asthma	-72.65 (-95.13 to -50.17)	<.001	
	Anxiety	-37.04 (-61.34 to -12.75)	.003	
	Depression or Anxiety plus Depression	-81.94 (-112.93 to -50.96)	<.001	
	Age x Sex (female)	1.73 (0.22 to 3.24)	.025	
Role Physical				.17
	Female sex	3.94 (0.74 to 7.14)	.016	
	Uncontrolled asthma	-7.88 (-10.85 to -4.90)	<.001	
	Depression or Anxiety plus Depression	-8.84 (-13.07 to -4.61)	<.001	
Bodily Pain				.15
	Uncontrolled asthma	-0.57 (-0.89 to -0.24)	.001	
	Anxiety	-0.68 (-1.06 to -0.30)	<.001	
	Depression or Anxiety plus Depression	-1.03 (-1.49 to -0.58)	<.001	
General Health				.33
	Age	0.03 (0.02 to 0.04)	<.001	
	FEV ₁ of predicted value < 80%	-0.28 (-0.55 to -0.01)	.043	
	Uncontrolled asthma	-0.51 (-0.75 to -0.27)	<.001	
	Anxiety	-0.64 (-0.91 to -0.38)	<.001	
	Depression or Anxiety plus Depression	-1.21 (-1.54 to -0.88)	<.001	
Vitality				.37
	Age	0.04 (0.03 to 0.06)	<.001	
	Former smoker	-0.85 (-1.60 to -0.10)	.027	
	Uncontrolled asthma	-1.08 (-1.54 to -0.63)	<.001	
	Anxiety	-1.38 (-1.90 to -0.87)	<.001	
	Depression or Anxiety plus Depression	-3.01 (-3.67 to -2.36)	<.001	
Social Functioning				.26
	Age	0.29 (0.16 to 0.41)	<.001	
	Anxiety	-12.51 (-16.91 to -8.12)	<.001	
	Depression or Anxiety plus Depression	-25.86 (-31.57 to -20.15)	<.001	
	Cognitive avoidance	-6.87 (-11.13 to -2.61)	.002	
Role Emotional				.21
	Anxiety	-23.57 (-33.54 to -13.60)	<.001	
	Depression or Anxiety plus Depression	-40.15 (-53.06 to -27.25)	<.001	
	Cognitive avoidance	-15.48 (-24.87 to -6.09)	.001	
Mental Health				.44
	Anxiety	-3.60 (-4.50 to -2.70)	<.001	
	Depression or Anxiety plus Depression	-5.35 (-6.94 to -3.77)	<.001	
	Sex (female) x Anxiety	1.20 (0.14 to 2.25)	.027	

Table 5. Multivariable analysis of SGRQ questionnaire domains and overall score adjusting for asthma control level according to ACT criteria and GINA (2006) criteria

SGRQ	Predictors	B (95% CI)	P	R ² corrected
Overall				.56
	Female sex	1.42 (0.83 to 2.00)	<.001	
	Age	0.03 (0.02 to 0.05)	<.001	
	Employment situation (non active)	0.75 (0.28 to 1.21)	.002	
	BMI $\geq$ 30	1.57 (0.66 to 2.49)	.001	
	Uncontrolled asthma	2.53 (2.09 to 2.98)	<.001	
	Anxiety	1.97 (1.00 to 2.94)	<.001	
	Depression or Anxiety plus Depression	2.79 (1.37 to 4.21)	<.001	
	Sex (female) x Anxiety	-1.47 (-2.59 to -0.35)	.011	
	Employment situation (non active) x BMI $\geq$ 30	-1.43 (-2.57 to -0.30)	.014	
Symptoms				.28
	Age	0.16 (0.02 to 0.30)	.028	
	Uncontrolled asthma	16.81 (12.57 to 21.05)	<.001	
	Anxiety	4.91 (0.05 to 9.78)	.048	
	Depression or Anxiety plus Depression	8.31 (2.22 to 14.39)	.008	
	Behavioral avoidance	6.56 (0.94 to 12.18)	.022	
Activity				.47
	Female sex	4.08 (2.68 to 5.48)	<.001	
	Age	0.04 (0.00 to 0.08)	.034	
	Employment situation (non active)	2.11 (0.99 to 3.23)	<.001	
	BMI $\geq$ 30	3.66 (1.47 to 5.85)	.001	
	FEV ₁ of predicted value < 80%	1.30 (0.07 to 2.52)	.038	
	Uncontrolled asthma	4.35 (3.25 to 5.46)	<.001	
	Anxiety	3.35 (1.01 to 5.69)	.005	
	Depression or Anxiety plus Depression	6.02 (2.61 to 9.43)	.001	
	Sex (female) x Depression or Anxiety plus Depression	-4.18 (-7.88 to -0.47)	.027	
	Employment situation (non active) x BMI $\geq$ 30	-3.15 (-5.88 to -0.43)	.023	
Impact				.49
	Female sex	0.91 (0.39 to 1.44)	.001	
	Age	0.03 (0.02 to 0.04)	<.001	
	Employment situation (non active)	0.40 (0.02 to 0.78)	.042	
	Uncontrolled asthma	1.97 (1.57 to 2.36)	<.001	
	Anxiety	1.53 (0.67 to 2.39)	.001	
	Depression or Anxiety plus Depression	2.85 (1.56 to 4.14)	<.001	
	Sex (female) x Anxiety	-1.12 (-2.12 to -0.12)	.028	
	Sex (female) x Depression or Anxiety plus Depression	-1.44 (-2.84 to -0.04)	.043	

Table 6. Multivariable analysis of SF-36 questionnaire domains adjusting for asthma control level according to only ACT criteria (Model 1) and according to only GINA (2006) criteria (Model 2)

SF-36		M1 asthma control according to only ACT criteria			M2 asthma control according to only GINA criteria		
	Predictors	B (95% CI)	p	R ² corrected	B (95% CI)	p	R ² corrected
Physical Functioning				.37			.33
	Female sex	-91.87 (-150.93 to -32.82)	.002		-87.62 (-147.72 to -27.51)	.004	
	Age	1.69 (0.45 to 2.93)	.008		1.69 (0.41 to 2.97)	.010	
	BMI $\geq$ 30	-39.95 (-67.70 to -12.20)	.005		-32.91 (-61.62 to -4.20)	.025	
	FEV ₁ of predicted value < 80%	-35.94 (-59.74 to -12.13)	.003		-38.15 (-63.40 to -12.89)	.003	
	Uncontrolled asthma	-74.01 (-96.10 to -51.91)	<.001		-44.58 (-68.52 to -20.64)	<.001	
	Anxiety	-32.12 (-56.64 to -7.61)	.010		-51.11 (-75.93 to -26.29)	<.001	
	Depression or Anxiety plus Depression	-76.00 (-107.39 to 44.61)	<.001		-93.16 (-125.02 to -61.31)	<.001	
Role Physical	Age x Sex (female)	1.77 (0.28 to 3.26)	.020		1.72 (0.18 to 3.25)	.028	
				.19			.15
	Female sex	3.89 (0.78 to 6.99)	.014		4.65 (1.40 to 7.90)	.005	
	Uncontrolled asthma	-9.18 (-12.15 to -6.20)	<.001		-6.17 (-9.38 to -2.97)	<.001	
Bodily Pain	Anxiety	---	---		-4.09 (-7.60 to -0.57)	.023	
	Depression or Anxiety plus Depression	-7.67 (-11.88 to -3.46)	<.001		-9.62 (-13.97 to -5.27)	<.001	
				.17			.11
	Uncontrolled asthma	-0.76 (-1.09 to -0.43)	<.001		---	---	
General Health	Anxiety	-0.59 (-0.97 to -0.22)	.002		-0.75 (-1.14 to -0.36)	<.001	
	Depression or Anxiety plus Depression	-0.92 (-1.38 to -0.46)	<.001		-1.20 (-1.68 to -0.73)	<.001	
				.34			.32
	Age	0.03 (0.02 to 0.04)	<.001		0.03 (0.02 to 0.04)	<.001	
Vitality	FEV ₁ of predicted value < 80%	-0.33 (-0.59 to -0.07)	.013		-0.33 (-0.60 to -0.06)	.019	
	Uncontrolled asthma	-0.55 (-0.79 to -0.31)	<.001		-0.42 (-0.68 to -0.16)	.002	
	Anxiety	-0.60 (-0.86 to -0.33)	<.001		-0.73 (-1.00 to -0.46)	<.001	
	Depression or Anxiety plus Depression	-1.15 (-1.48 to -0.81)	<.001		-1.21 (-1.55 to -0.87)	<.001	
Social Functioning				.38			.36
	Age	0.04 (0.03 to 0.06)	<.001		0.04 (0.03 to 0.06)	<.001	
	Former smoker	-0.87 (-1.60 to -0.13)	.021		---	---	
	Uncontrolled asthma	-1.28 (-1.73 to -0.82)	<.001		-0.68 (-1.16 to -0.20)	.006	
Role Emotional	Anxiety	-1.23 (-1.75 to -0.72)	<.001		-1.71 (-2.24 to -1.19)	<.001	
	Depression or Anxiety plus Depression	-2.87 (-3.53 to -2.22)	<.001		-3.31 (-3.97 to -2.65)	<.001	
				.30			.29
	Age	0.32 (0.18 to 0.46)	<.001		0.30 (0.16 to 0.45)	<.001	
Mental Health	Uncontrolled asthma	-5.10 (-9.33 to -0.87)	.018		---	---	
	Anxiety	-12.27 (-17.20 to -7.35)	<.001		-13.16 (-18.13 to -8.20)	<.001	
	Depression or Anxiety plus Depression	-25.54 (-31.83 to -19.24)	<.001		-26.99 (-33.32 to -20.66)	<.001	
	Cognitive avoidance	-5.58 (-10.35 to -0.81)	.022		---	---	
Role Emotional				.23			.22
	Duration of asthma	---	---		0.48 (0.02 to 0.94)	.043	
	Uncontrolled asthma	-9.81 (-19.57 to -0.05)	.049		---	---	
	Anxiety	-25.60 (-37.03 to -14.17)	<.001		-27.16 (-38.65 to -15.66)	<.001	
Mental Health	Depression or Anxiety plus Depression	-33.75 (-48.33 to -19.18)	<.001		-37.46 (-52.07 to -22.86)	<.001	
	Cognitive avoidance	-16.14 (-26.76 to -5.51)	.003		-15.43 (-26.42 to -4.44)	.006	
				.48			.48
	Anxiety	-3.74 (-4.73 to -2.75)	<.001		-2.92 (-3.45 to -2.38)	<.001	
Mental Health	Depression or Anxiety plus Depression	-5.18 (-6.77 to -3.60)	<.001		-4.45 (-5.13 to -3.78)	<.001	
	Sex (female) x Anxiety	1.35 (0.21 to 2.50)	.021		---	---	

Table 7. Multivariable analysis of SGRQ questionnaire domains adjusting for asthma control level according to only ACT criteria (Model 1) and according to only GINA (2006) criteria (Model 2)

SGRQ	Predictors	M1 asthma control according to only ACT criteria			M2 asthma control according to only GINA criteria		
		B (95% CI)	p	R ² corrected	B (95% CI)	p	R ² corrected
Overall				.53			.47
	Female sex	1.40 (0.81 to 1.99)	<.001		1.49 (0.85 to 2.13)	<.001	
	Age	0.03 (0.02 to 0.05)	<.001		0.04 (0.02 to 0.05)	<.001	
	Non active employment situation	0.64 (0.17 to 1.12)	.009		0.72 (0.20 to 1.25)	.007	
	BMI ≥ 30	1.65 (0.73 to 2.57)	<.001		1.35 (0.37 to 2.33)	.007	
	Uncontrolled asthma	2.42 (1.96 to 2.88)	<.001		1.88 (1.36 to 2.39)	<.001	
	Anxiety	1.84 (0.84 to 2.84)	<.001		2.66 (1.59 to 3.73)	<.001	
	Depression or Anxiety plus Depression	2.84 (1.39 to 4.30)	<.001		3.71 (2.16 to 5.25)	<.001	
	Sex (female) x Anxiety	-1.46 (-2.61 to -0.31)	.013		-1.90 (-3.15 to -0.64)	.003	
	Sex (female) x Depression or Anxiety plus Depression	---	---		-2.08 (-3.78 to -0.38)	.016	
	Employment situation (non active) x BMI ≥ 30	-1.38 (-2.52 to -0.23)	.019		-1.29 (-2.53 to -0.05)	.042	
Symptoms				.29			.21
	Age	0.19 (0.05 to 0.33)	.007		0.17 (0.02 to 0.32)	.027	
	Uncontrolled asthma	17.22 (12.98 to 21.46)	<.001		13.46 (8.68 to 18.24)	<.001	
	Anxiety	---	---		6.05 (0.85 to 11.24)	.023	
	Depression or Anxiety plus Depression	7.83 (1.73 to 13.96)	.012		8.74 (2.18 to 15.30)	.009	
	Behavioral avoidance	5.85 (0.43 to 11.26)	.034		7.03 (1.10 to 12.95)	.020	
Activity				.44			.42
	Female sex	3.97 (2.57 to 5.38)	<.001		4.20 (2.75 to 5.66)	<.001	
	Age	0.04 (0.00 to 0.08)	.046		0.05 (0.01 to 0.09)	.020	
	Non active employment situation	1.98 (0.84 to 3.11)	.001		2.00 (0.82 to 3.17)	.001	
	BMI ≥ 30	3.85 (1.66 to 6.04)	.001		3.23 (1.03 to 5.44)	.004	
	FEV ₁ of predicted value < 80%	1.95 (0.74 to 3.16)	.002		1.77 (0.48 to 3.07)	.007	
	Uncontrolled asthma	3.84 (2.73 to 4.96)	<.001		3.00 (1.79 to 4.22)	<.001	
	Anxiety	3.03 (0.63 to 5.43)	.013		4.46 (2.02 to 6.90)	<.001	
	Depression or Anxiety plus Depression	6.18 (2.72 to 9.65)	.001		7.72 (4.23 to 11.22)	<.001	
	Sex (female) x Depression or Anxiety plus Depression	-4.61 (-8.38 to -0.83)	.017		-5.56 (-9.40 to -1.71)	.005	
	Employment situation (non active) x BMI ≥ 30	-3.03 (-5.76 to -0.31)	.029		-2.95 (-5.75 to -0.14)	.040	
Impact				.47			.41
	Female sex	0.97 (0.45 to 1.49)	<.001		0.96 (0.40 to 1.52)	.001	
	Age	0.03 (0.02 to 0.05)	<.001		0.03 (0.02 to 0.05)	<.001	
	Non active employment situation	---	---		0.40 (0.02 to 0.78)	.042	
	Uncontrolled asthma	1.96 (1.56 to 2.37)	<.001		1.47 (1.02 to 1.92)	<.001	
	Anxiety	1.44 (0.57 to 2.32)	.001		2.09 (1.17 to 3.02)	<.001	
	Depression or Anxiety plus Depression	2.92 (1.61 to 4.22)	<.001		3.51 (2.13 to 4.88)	<.001	
	Sex (female) x Anxiety	-1.14 (-2.14 to -0.13)	.027		-1.58 (-2.67 to -0.49)	.005	
	Sex (female) x Depression or Anxiety plus Depression	-1.65 (-3.07 to -0.24)	.022		-2.06 (-3.56 to -0.55)	.008	

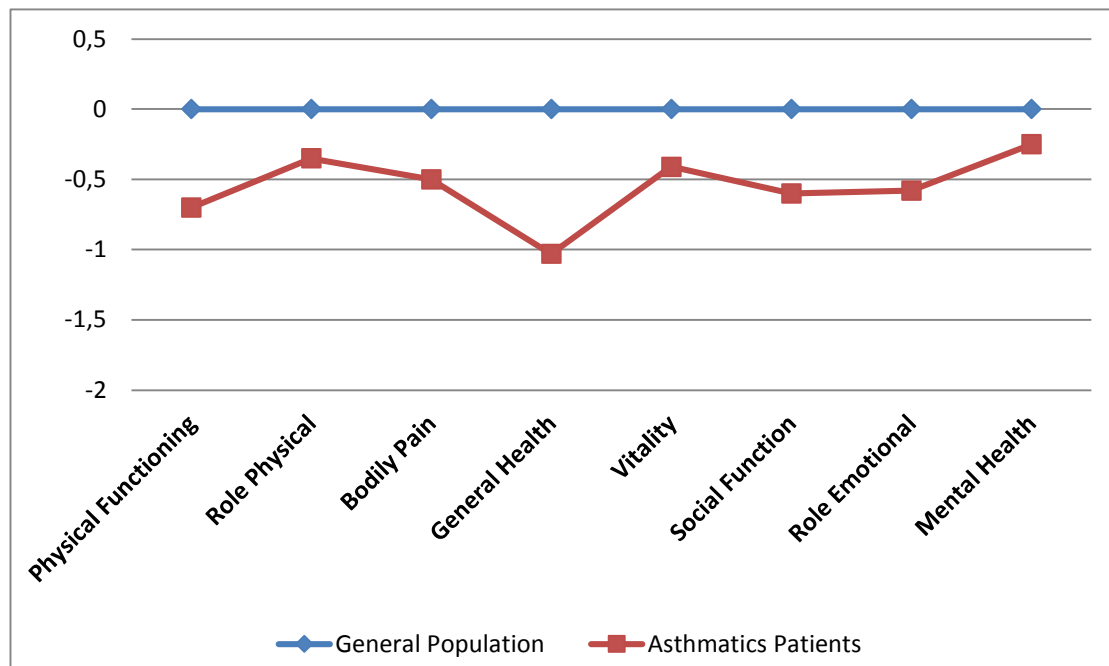


Figure 1. Standardized scores in the eight dimensions of SF-36.