1 **TITTLE**

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

3 life

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5 **Authors**

6 González-Freire, Beatriz[a] PhD; Vázquez, Isabel[b] PhD; Sonia Pértega-Díaz[c] PhD

7 [a] Beatriz Gónzalez-Freire

8 Private Psychological Practice Beatriz González Freire. Ourense. Spain

9 [b] Isabel Vázquez

10 Department of Clinical Psychology and Psychobiology. University of Santiago de

11 Compostela. Santiago de Compostela. Spain

12 [c] Sonia Pértega-Díaz

13 Clinical Epidemiology and Statistics Unit, Complejo Hospitalario Universitario. A

14 Coruña. Spain .

15
16
17 **Corresponding author:**

18 Mª Isabel Vázquez Rodríguez

19 *Departamento de Psicología Clínica y Psicobiología. Facultad de Psicología. Universidad de Santiago*

20 *de Compostela, Santiago de Compostela*

21 *15782 Santiago de Compostela. Spain.*

22 *Telephone: 34981563100 ext.13731*

23 *e- mail: mariaisabel.vazquez@usc.es*

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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.

51 **HIGHLIGHTS BOX**

52 ***What is already known about this topic?*** Anxiety, depression, avoidant coping and

53 asthma control (estimated by the patient or by the physician) affect quality of life;

54 however, these factors have not been concurrently evaluated to determine their

55 independent contribution to asthma quality of life.

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57 ***What does this study add to our knowledge?*** Anxiety, depression and patient-rated

58 asthma control are important independent contributors to asthma quality of life and they

59 are associated almost all dimensions. The impact of physician-rated control and

60 avoidant coping on quality of life is lower.

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62 ***How does this study impact current management guidelines?*** Anxiety, depression and

63 control of asthma (preferably estimated by the patient) should be routinely screened in

64 asthmatic patients, and interventions focused on these potentially modifiable factors

65 should be implemented to improve quality of life in asthmatic patients.

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76 **ABBREVIATIONS USED**

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78 ACT: Asthma Control Test

79 B: non-standardized regression coefficient

80 BMI: Body mass Index

81 CI: Confidence Interval

82 COPE: Coping Orientations to Problems Experienced Inventory

83 GINA: Global Initiative for Asthma

84 HADS: Hospital Anxiety and Depression Scale

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

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

87 HRQoL: Health-related quality of life

88 M: Mean

89 Max: Maximum

90 Mdn: Median

91 Min: Minimum

92 N: Total sample size

93 R^2: Coefficient of determination

94 SD: Standard deviation

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

96 SGRQ: St. George's Respiratory Questionnaire

97 % FEV_1: percentage of predicted value of forced expiratory volume in 1 second

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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-

128 report measures, or from the physician's perspective, according to clinical and

129 pulmonary function parameters. Both types of control measures provide only fair to

130 moderate agreement [35], and so far, whether there is a differential impact of asthma

131 control on HRQoL as a function of the type of assessment used has not been evaluated.

132 The aim of this study was to determine the impact of anxiety, depression, coping

133 strategies, and asthma control on generic and specific domains of HRQoL in asthmatic

134 patients and to provide an insight of the impact of asthma control on HRQoL when

135 asthma control is established by a physician versus when control is considered by the

136 patient.

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149   **Methods**

150   **Patients**

151   Using a cross-sectional study, we recruited participants consecutively from outpatients

152   of the allergy or pneumology practices of the University Hospital Complex of Ourense

153   (Spain) a tertiary center belonging to the Spanish public healthcare system that attends

154   to patients referred from primary care. Inclusion criteria were: 1) a physician's

155   diagnosis of asthma; 2) at least 6-months since the diagnosis; 3) age between 18 and

156   75 years; 4) reading-writing ability in Spanish; and 5) no diagnosis of other physical or

157   psychiatric chronic comorbid illnesses, except for rhinitis.

158   A psychologist collected the sociodemographic (sex, age, educational level,

159   employment situation, self-reported social class and marital status) and lifestyle data

160   (smoking and body mass index) in an interview. The specialized physician responsible

161   for the patient's treatment filled in a clinical data form with the following information:

162   age at asthma diagnosis, duration of disease, percentage of predicted value of forced

163   expiratory volume in 1 second (% FEV_1), asthma control level according to the Global

164   Initiative for Asthma criteria (GINA, 2006) [36] and severity of asthma according to

165   GINA (2009) criteria [37].

166   Patients also completed the following questionnaires: Hospital Anxiety and Depression

167   Scale (HADS) [38]; Coping Orientations to Problems Experienced Inventory (COPE)

168   [39]; Asthma Control Test (ACT) [40]; 36-Item Short-Form Health Survey (SF-36)

169   [41]; St. George's Respiratory Questionnaire (SGRQ) [42]. The Spanish adaptations of

170   the questionnaires were used in all cases [43-47].

171   The study was approved by the Galician Ethical Research Committee with the code

172   2009/408.

173 **Statistical Analysis**

174 For the descriptive analysis, the continuous variables are presented as mean, standard

175 deviation, and range, and the categorical variables as frequency and percentage

176 (excluding missing values) with a confidence level of 95%.

177 To quantify the impact of bronchial asthma on HRQoL we considered the scores in the

178 eight dimensions of the SF-36 expressed on a scale from 0 (maximum impairment) to

179 100 (no impairment) and the three dimensions and overall score of SGRQ in a scale

180 from 0 (minimum impairment) to 100 (maximum impairment)., In addition, the scores

181 in the eight dimensions of the SF-36 questionnaire were standardized according to

182 Spanish population reference standards obtained by Alonso et al. [48]. Standardized

183 values are expressed in standard deviations from the score of the Spanish general

184 population of the same age and sex (which would receive the value of 0).

185 The degree of asthma control according to ACT criteria was divided into two

186 categories: controlled asthma (ACT ≥ 20) *vs* uncontrolled asthma (ACT < 20). The

187 classification of control performed by the physician according to GINA criteria [36]

188 also had two categories: controlled asthma *vs* uncontrolled asthma (patients with

189 partially controlled asthma or uncontrolled asthma). To study the concordance between

190 two classification of asthma control (ACT and GINA criteria) Kappa index was

191 calculated.

192 When the two classifications of control were considered simultaneously, patients with

193 ACT ≥ 20 plus controlled asthma according to GINA criteria [36] were categorized as

194 controlled asthma. All other cases were considered as uncontrolled asthma.

195 For the univariate analysis between HRQoL scores (standardized SF-36 and direct

196 SGRQ scores) and sociodemographic, clinical, and psychological variables, we applied

197 Student's *t*-test or ANOVA and the U-Mann-Whitney or Kruskal-Wallis test (as

198 appropriate after verifying the normality with the Kolmogorov-Smirnov test and the

199 number of categories of the variables analyzed) and Spearman's rho correlation

200 coefficient.

201 Using results from the univariate analysis, we developed general linear models for each

202 of the standardized dimensions of the SF-36 scores and for the SGRQ scores. When the

203 requirement of normality in HRQoL scores was not met, we used the Box-Cox family

204 of transformations. In all the analyses, sex, age, smoking, and asthma control level

205 (considering ACT criteria plus GINA criteria [36]) were included as independent

206 variables as well as all the sociodemographic, clinical, and psychological variables that

207 obtained a level of significance <.20 in the univariate analyses. For the inclusion of

208 anxiety and depression in these models, and due to the small number of patients

209 presenting with only depression, the participants were classified into three groups: (a)

210 no anxiety or depression (HADS-A < 8 and HADS-D < 8); (b) only anxiety (HADS-A ≥

211 8 and HADS-D < 8); and (c) suffering from depression with or without anxiety

212 (depression HADS-D ≥ 8 and HADS-A < 8 or ≥ 8). These models also considered the

213 effect of the interactions between variables.

214 With the aim of identifying which of the two classifications of asthma control

215 (estimated by the patient vs estimated by the doctor) was the best predictor of HRQoL,

216 the general linear models for each of the evaluated HRQoL dimensions were replicated,

217 considering the degree of control only via ACT criteria or only via GINA criteria [36].

218 A sample size of n=373 was included, which allows to estimate patients' characteristics

219 with a precision of ± 5.1% and 95% confidence. Since asthma was evaluated with both

220 methods (ACT plus GINA criteria) in only 285 patients, percentage of patients with

221 controlled asthma could be estimated with a precision of ± 5.8% and 95% confidence.

222 In all statistical analyses, an alpha level of .05 was established. The SPSS 19.00

223 package for Windows and the 2.12.2 version R package were used.

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Results

242   A total of 373 asthmatic patients (55.3% were recruited in allergy practices, and 44.7%

243   in pneumology practices) participated in the study. Characteristic of the sample are

244   summarized in Table 1. The mean age of this sample was 36.88 ± 14.90 years (range 18

245   – 75), the mean age of the patients when they were diagnosed with asthma was $25.62 \pm$

246   14.82 years (range 1– 67), and the mean duration of the disease was 11.98 ± 10.90 years

247   (range 0 - 67). The treatment the patients were prescribed is described in Table 1.

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249   Regarding asthma control, the administration of the ACT questionnaire revealed that

250   57.7% of the patients had well-controlled asthma and regarding the classification of the

251   degree of control established by the physician according to GINA criteria [36] 65.6%

252   were categorized as well-controlled asthma. The Kappa index between the two methods

253   used to measure asthma control was 0.45 (95% CI 0.34-0.55). Among the 285 patients

254   in whom control of asthma was evaluated with both methods (ACT plus GINA criteria),

255   asthma was categorized as controlled in 49.1% of the patients. In these controlled

256   patients, the asthma severity classification according to GINA criteria [37] was: 51.4%

257   intermittent asthma, 7.8% mild persistent asthma, 25% moderate persistent asthma, and

258   15.7% severe persistent asthma.

259   With regard to the psychological variables, 35.4% of the patients suffered from anxiety

260   (HADS-A $\geq$ 8), and 14.3% of the patients presented depression (HADS-D $\geq$ 8). In the

261   total sample, 11% of the patients had combined anxiety and depression (HADS-A $\geq$ 8

262   and HADS-D $\geq$ 8). The most frequently used coping strategy was Behavioral Coping

263   with the problem (2.87 ± 0.44), while the least frequently used were Consumption of

264   alcohol and/or drugs (1.05 ± 0.21) (see Table 2).

265   Considering direct scores in the generic SF-36 questionnaire, the most affected

266   dimension were General Health in SF-36 (53.58 ± 21.42) and Symptoms in SGRQ

267   (40.22 ± 19.93) whereas the least affected were Social Functioning in SF-36 (81.57 ±

268   24.76) and Impact in SGRQ (22.87 ± 19.39 (see Table 3).

269   Compared with the general population, using standardized scores of SF-36, the sample

270   of asthmatic patients evaluated had poorer HRQoL in all the dimensions of the SF-36,

271   and General Health (-1.03 ± 1.15) was the most affected, whereas the least affected was

272   Mental Health (-0.25 ± 1.08) (see Figure 1).

273   For each dimension of the SF-36 and the SGRQ, the sociodemographic,.clinical and

274   psychological variables identified by univariate analysis were entered as candidate

275   predictors in the multivariable analysis (data not shown).

276   The results of the multivariable analyses of the SF-36 and SGRQ questionnaires are

277   shown in Tables 4 and 5, respectively. In the multivariable regression analysis, using

278   data from n=285 with both ACT and GINA criteria available, the only demographic

279   and lifestyle variables retained as significant predictors of poorer HRQoL were female

280   sex, younger age, non-active working situation, former smoker, and obesity ($p<. 05$).

281   The interaction effect between age and sex was significant in Physical Functioning ($p =$

282   .025) indicating that an increase in age was associated with an increase of the Physical

283   Functioning score, and this increase was greater among females. The effect of obesity

284   on the dimension Activity and Overall score SGRQ was higher when the patient was

285   actively employed ($p< .05$). Among the clinical variables, only $FEV_1< 80\%$ of the

286   predicted value was related to Physical Functioning and General Health of the SF-36

287 (p< .05) and to Activity of the SGRQ (p = .038). By contrast, in all the generic and

288 specific scales, anxiety and/or depression were associated with poorer HRQoL. The

289 presence of depression or depression plus anxiety was consistently associated with

290 worse HRQoL, both in the dimensions of the SF-36 questionnaire ($p < .001$) and in

291 those of the SGRQ questionnaire, as well as in its Overall score ($p < .01$). The presence

292 of only anxious symptoms was also associated with significantly worse HRQoL in all

293 the dimensions of the SF-36 ($p < .01$, with the exception of the Role Physical

294 dimension) and in all dimensions and the Overall score SGRQ (p< .05). There were

295 significant interactions between sex and anxiety symptoms in the Mental Health

296 dimension of the SF-36 (p = .027) and in the Impact dimension (p = .028) and the

297 Overall score SGRQ (p = .011). There were also significant interactions between sex

298 and depressive or anxious plus depressive symptomatology in the dimensions Activity

299 (p = .027) and Impact (p = .043) of the SGRQ. In all cases, the effect of psychological

300 comorbidity on HRQoL was slightly higher in males. Poor asthma control was also

301 closely related to HRQoL in the physical dimensions of the SF-36: Physical

302 Functioning, Role Physical, Bodily Pain, General Health, and Vitality ($p \leq .001$), as

303 well as with all domains and the Overall score SGRQ ($p < .001$). The impact of coping

304 strategies on HRQoL was more limited. A greater use of Cognitive Avoindant was

305 associated with greater deterioration in the dimensions of Social Functioning and Role

306 Emotional of the SF-36 (p< .01), and a greater use of Behavioral Avoindant was

307 associated with greater impact on the Symptoms dimension of the SGRQ (p = .022).

308 The selected characteristics explained an acceptable proportion of variability (R^2),

309 ranging from 15% in Bodily Pain to 44% in Mental Health in the dimensions of the SF-

310 36, and ranging from 28% in Symptoms to 56% in the Overall score SGRQ (see Tables

311 4 and 5). In 9 of the 12 analyzed models, the percentages of explained variance

312 exceeded 25%, generally taken as the minimum above which the model can be

313 considered acceptable [49].

314 Results of multivariable analysis of HRQoL, considering separately each of the two

315 classifications of the degree of asthma control, using n=303 patients with ACT criteria

316 (Model 1) and n=288 with GINA criteria (Model 2), respectively, showed that, the

317 percentage of explained variance of the generic and specific dimensions of HRQoL was

318 slightly higher when asthma control was considered according to ACT criteria (in the

319 SF-36, values ranging between 17% of Bodily Pain and 48% of Mental Health, and in

320 the SGRQ, between 29% of Symptoms and 53% of the Overall score SGRQ) than when

321 asthma control was considered according to GINA criteria [36] (in the SF-36, values

322 ranging between 11% of Bodily Pain and 48% of Mental Health, and in the SGRQ,

323 between 21% of Symptoms and 47% of the Overall score SGRQ). According to the

324 ACT classification, a significant effect of asthma control was found in eleven of the

325 twelve models (Physical Functioning, Role Physical, Bodily Pain, General Health,

326 Vitality, Social Functioning, and Role Emotional of the SF-36, and Overall score SGRQ

327 and by SGRQ dimensions) and only in eight (Physical Functioning, Role Physical,

328 General Health, and Vitality of the SF-36 and all dimensions and Overall score SGRQ)

329 when the classification of control was established based on GINA criteria [36] (see

330 Tables 6 and 7).

331 **Discussion**

332 Our results show that asthma affects both generic dimensions and specific dimensions

333 of HRQoL, and the main variables that determine this impact on HRQoL are anxiety,

334 depression and patient-rated asthma control.

335 The impact of asthma on HRQoL was assessed using two complementary approaches: a

336 generic questionnaire (SF-36) and a specific questionnaire (SGRQ). Both questionnaires

337 coincided in indicating the physical dimensions as the most damaged, whereas the

338 mental dimensions remain the least affected in line with previous studies [50,51].

339 The analysis of the variables that determine HRQoL revealed the significance of several

340 sociodemographic variables (sex, age, employment situation, and obesity) and the

341 pulmonary function. However, these variables have a rather limited effect, and each one

342 only affected one or a few domains. In contrast, anxiety and depression and asthma

343 control were strong predictors of generic and specific domains.

344 Anxiety and depression are the psychological disorders most frequently found in

345 asthmatic patients [9-13,52,53]. In our study, 35% of the patients had symptoms of

346 anxiety and 14% of the patients had depressive symptoms, and these figures are within

347 the prevalence range reported in other studies [10,26,54].

348 As could be expected, these psychosocial variables explained the variance in mental

349 health domains (Mental Health and Social Functioning of the SF-36 and Impact of the

350 SGRQ), but it is important to note that anxiety and depression also contributed to

351 explain the perception of physical status (Physical Functioning, Bodily Pain, and

352 Vitality of the SF-36 and Symptoms of the SGRQ) and of functional capacity (Role

353 Physical and Role Emotional of the SF-36 and Activity of the SGRQ).

354 Confirming prior literature, poor asthma control also substantially impaired HRQoL

355 [31-34]. In the present study, the determination of the degree of asthma control was

356 established by two methods: patient-rated asthma control status using the ACT and

357 physician-rated asthma control using GINA criteria [36]. The concordance between

358 ACT and GINA criteria [36] was moderate, similar to the study of Thomas et al. [35]

359 and the same as other studies [29,35] in finding that the rates of control reported by

360 asthmatic patients are lower than the rates determined by physicians.

361 Regardless of the procedure used to estimate asthma control (ACT plus GINA, only

362 ACT, or only GINA), we found that subjects with poor asthma control have

363 substantially impaired generic physical domains and disease-specific domains of the

364 HRQoL.

365 When we examined the association between control level estimated by the patient and

366 by the doctor and HRQoL separately, patient-rated asthma control is related not only to

367 generic physical dimensions but also to generic mental dimensions. A possible

368 explanation would be that, both in the ACT and the HRQoL instruments used, we are

369 collecting information from the same perspective (provided by the patient) and there

370 may be a biased symptom reporting that affects perception of HRQoL. However, to our

371 knowledge, this research is the first study that compared the impact on HRQoL of the

372 different methods used to classify the degree of asthma control, and future research is

373 necessary.

374 Regarding coping strategies, our results show that avoidance coping was related to

375 worse HRQoL, in line with previous studies in asthmatic patients [15, 18]. Studies of

376 patients with other chronic illnesses have found that avoidance coping is associated

377 with poor medication adherence and may result in poorer long-term outcomes for many

378 patients [55, 56]. However, the effect of avoidance coping is much more limited than

379 that found for the other psychological variables evaluated (anxiety and depression), and

380 its was only related to the dimensions Social Functioning and Role Emotional of the SF-

381 36 and Symptoms of the SGRQ.

382 The impact of anxiety, depression, and coping strategies on HRQoL could be attributed

383 to the relationship between these psychological variables with worse asthma control.

384 This relationship was shown in several studies [27-29,30] and it could be established

385 through several pathways including behavioral pathways (disorganized self-care and

386 poor health behaviors) or through the direct physiological effects of emotional status on

387 the autonomic nervous and immune systems, which increase asthma symptomatology

388 [57]. Poor asthma control could finally lead to deterioration of HRQoL. Our result

389 showed the effect of the evaluated psychological variables on HRQoL is present even

390 after controlling for asthma control.

391 In conclusion, our findings support to the proposal that, although they are interrelated

392 concepts, anxiety, depression, coping strategies and asthma control each contribute

393 independently to HRQoL.

394 Our study has several strengths. To our knowledge, this is the first study to indicate a

395 strong and independent association between anxiety, depression, coping strategies and

396 asthma control and HRQoL. In addition, we used two complementary approaches to

397 evaluate HRQoL: the SF-36, a generic questionnaire that allows comparing the health

398 status across different diseases and with general populations, and the SGRQ, a specific

399 questionnaire sensitives to patients' specific problematic respiratory areas. Finally, we

400 also considered two ways to assess asthma control (estimated by the physician and by

401 the patient) to determine whether there are differences between the two in terms of their

402 relationship with HRQoL.

403 It is also necessary to take into account some limitations of the study. Firstly, the sample

404 was only drawn from the tertiary asthma clinic and most of the patients present

405 intermittent asthma, which can affect the generalizability of our results. Moreover, we

406 established as exclusion criteria the presence of physical comorbidity, therefore,

407 findings may not generalize to overall population of asthmatics. However, this creates a

408 homogeneous sample in which the patients evaluated only suffered from bronchial

409 asthma, thus avoiding the possible effect of other comorbid diseases on HRQoL.

410 Finally, this study may be limited by the cross-sectional nature of the design that does

411 not allow the prediction of the direction of causality. Prospective studies are needed to

412 better delineate the relationships found between psychological variables, asthma

413 control, and HRQoL.

414 Given that the findings of this study showed that anxiety, depression, coping strategies,

415 and asthma control are variables that affect HRQoL independently, all of them should

416 be taken into account when considering HRQoL scores as an outcome measure in

417 asthma. It would be advisable to train healthcare professionals so that, when evaluating

418 asthmatic patients, they include screening for psychological variables and asthma

419 control estimated by the patient. Brief and easy to complete tools such as HADS and

420 ACT allow introducing the measurement of anxiety, depression and patient-rated

421 control in the routine clinical practice, in order to detect these characteristics in patients.

422 Effectively treating asthma symptoms improves asthma control and may reduce anxiety

423 and depression. A recent study has found that a significantly number of patients with

424 asthma improved anxiety and depression after 6 months of standardized treatment and

425 regular specialist care [58]. In cases where it is necessary, interventions specifically

426 focused on psychological factors should also be implemented in an attempt to improve

427 HRQoL in asthmatic patients.

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641

642 **Figure Legends**

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

644

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

Characteristics	N	%	95% CI
Sex			
Female	263	70.5	[65.74, 24.72]
Male	110	29.5	[75.27, 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: % FEV_1 = 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	*n*	M ± SD	Mdn	Min	Max
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 Depresion 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	*n*	M ± SD	Mdn	Mín	Max
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
PhysicalFunctioning				.37
	Female sex	-91.38 (-150.94 to -31.82)	.003	
	Age	1.64 (0.37 to 2.92)	.012	
	BMI ≥ 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	
BodilyPain				.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	
	Cognitiveavoidance	-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 ≥ 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 ≥ 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	
	Behavioralavoidance	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 ≥ 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 ≥ 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	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
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 ≥ 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	
	Age x Sex (female)	1.77 (0.28 to 3.26)	.020		1.72 (0.18 to 3.25)	.028	
Role Physical				.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	
	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	
Bodily Pain				.17			.11
	Uncontrolled asthma	-0.76 (-1.09 to -0.43)	<.001		- - -	- - -	
	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	
General Health				.34			.32
	Age	0.03 (0.02 to 0.04)	<.001		0.03 (0.02 to 0.04)	<.001	
	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	
Vitality				.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	
	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	
Social Functioning				.30			.29
	Age	0.32 (0.18 to 0.46)	<.001		0.30 (0.16 to 0.45)	<.001	
	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	
	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	
Mental Health				.48			.48
	Anxiety	-3.74 (-4.73 to -2.75)	<.001		-2.92 (-3.45 to -2.38)	<.001	
	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)*

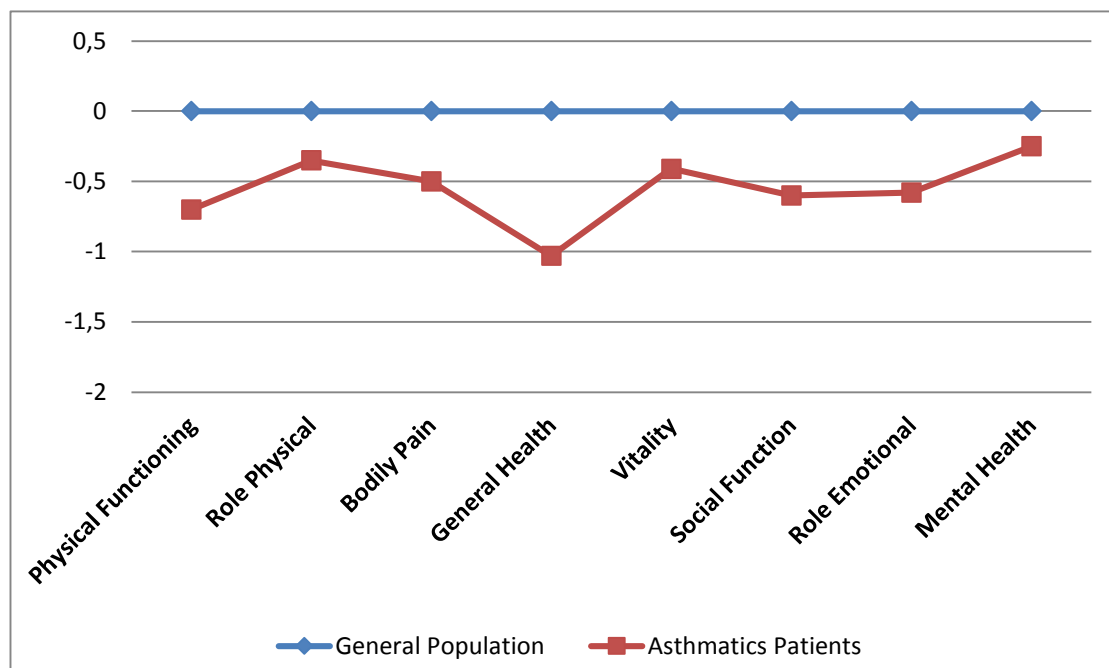| SGRQ	Predictors	M1 asthma control according to only ACT criteria			M2 asthma control according to only GINA criteria		
		B (95% CI)	p	R^2 corrected	B (95% CI)	p	R^2 corrected
Overall				.53			.47
	Female sex	1.40 (0.81 to 1.99)	<.001		1.49 (0.85 to 2.13)	<.001	
	Age	0.03 (0.02 to 0.05)	<.001		0.04 (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.