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Symptoms of anxiety and depression in patients with persistent asthma: a cross-sectional analysis of the INSPIRERS studies

Mafalda Simões Cunha,[1] Rita Amaral ,[2,3,4,5] Ana Margarida Pereira,[1,2,6] Rute Almeida,[3] Magna Alves-Correia,[1,2] Cláudia Chaves Loureiro,[7] Cristina Lopes,[8,9] Joana Carvalho,[10] Carmelita Ribeiro,[11] Carmen Vidal,[12] Dario Antolín-Amérigo,[13] Diana Pinto,[14] Manuel Ferreira-Magalhães,[3,14] Maria João Vasconcelos,[15] Carlos Lozoya,[16] Natacha Santos,[17] Francisca Cardia,[18] Luís Taborda-Barata ,[19,20] Rosário Ferreira,[21] Pedro Morais Silva,[22] Tania Monteiro Ferreira,[23] Raquel Câmara,[24] Eurico Silva,[25] Diana Bordalo,[26] Cristina Guimarães,[27] Maria José Calix,[28] Sofia da Silva,[29] Maria Luís Marques,[30] Ana Morete,[2,31] Carlos Nunes,[32] Cláudia Vieira,[33] Rosália Páscoa ,[1,6,34] Adelaide Alves,[35] José Varanda Marques,[36] Bruno Reis,[37] Luís Monteiro ,[1,38] Rosário Monteiro,[3,34] Margarida Cepa,[39] Bruno Valentim ,[40] Daniela Sousa Coelho,[41] Sara Fernandes,[42] Patrícia Meireles,[43] Margarida Abreu Aguiar,[44] Ana Rita Mourão,[45] Joao A Fonseca,[2,3,46] Cristina Jácome [3]

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For numbered affiliations see end of article.

Correspondence to
Dr Cristina Jácome;
cristinajacome.ft@gmail.com

ABSTRACT

Objectives Anxiety and depression are relevant comorbidities in asthma, but, in Portugal and Spain, data on this topic are scarce. We assessed, in patients with asthma, the frequency of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) and the European Quality of Life Five Dimension Questionnaire (EQ-5D); the level of agreement between these questionnaires, and the factors associated with these symptoms.

Methods This is a secondary analysis of the INSPIRERS studies. A total of 614 adolescents and adults with persistent asthma (32.6±16.9 years, 64.7% female) were recruited from 30 primary care centres and 32 allergy, pulmonology and paediatric clinics. Demographic and clinical characteristics, HADS and EQ-5D were collected. A score ≥8 on Hospital Anxiety and Depression Scale-Anxiety/Hospital Anxiety and Depression Scale-Depression or a positive answer to EQ-5D item 5 indicated the presence of these symptoms. Agreement was determined by Cohen's kappa. Two multivariable logistic regressions were built.

Results According to HADS, 36% of the participants had symptoms of anxiety and 12% of depression. According to EQ-5D, 36% of the participants had anxiety/depression. The agreement between questionnaires in identifying anxiety/depression was moderate (k=0.55, 95% CI 0.48 to 0.62). Late asthma diagnosis, comorbidities and female gender were predictors of anxiety/depression, while better asthma control, health-related quality of life and perception of health were associated with lower odds for anxiety/depression.

Conclusion At least 1/3 of the patients with persistent asthma experience symptoms of anxiety/depression, showing the relevance of screening these disorders in patients with asthma. EQ-5D and HADS questionnaires showed a moderate agreement in the identification of anxiety/depression symptoms. The identified associated factors need to be further investigated in long-term studies.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study is a secondary analysis of a multicentric study that recruited both adults and adolescents with asthma from primary and secondary care.
⇒ A comprehensive set of individual-level characteristics was analysed, which allowed us to explore the impact of sociodemographic factors and cofactors such as quality of life and asthma control on the presence of anxiety/depression symptoms.
⇒ A possible source of bias was the recruitment strategy based on convenience sampling.
⇒ The frequency of distressing symptoms and the relationships with associated factors could not be established overtime.

INTRODUCTION

Asthma affects approximately 300 million people worldwide.[1] In Portugal, asthma affects 695 000 Portuguese, with a general prevalence of 6.8%.[2] In Spain, asthma affects

more than 3 million people, with an estimated prevalence of 5% in adults.[3] Asthma is primarily related to chronic inflammation of the lower respiratory tract, variable airflow obstruction and bronchial hyper-responsiveness.[4] Yet, this disease is often accompanied by multiple associated comorbidities, such as chronic rhinosinusitis, nasal polyposis, allergic rhinitis, gastro-oesophageal reflux disease, obstructive sleep apnoea syndrome,[5] and also anxiety and depression.[6]

In two systematic reviews, the average reported prevalence of any anxiety disorder among patients with asthma was 24%[7] and 34%.[8] Regarding depression, a pragmatic literature review found that 1%–45% of patients with asthma suffer from depression or depressive symptoms.[9] In severe asthma, a study reported an average prevalence of 27% for emotional distress (mainly due to anxiety and depression).[10] Currently, most studies about emotional distress focus essentially on adult patients with more severe asthma.[11] There is a lack of data regarding other asthma subgroups, namely adolescents and those with mild or moderate persistent asthma.

Anxiety and depression are associated with significantly lower quality of life, poor asthma control, higher frequency of exacerbations and increased use of healthcare resources.[12] Moreover, anxiety is associated with greater perceived dyspnoea intensity and may shape the quality and intensity of this symptom at a given respiratory load.[13] However, it is still uncertain whether other factors can affect the patient's psychological state. It is important to have a more sophisticated understanding of the interplay between emotional distress and asthma.[14]

Despite these negative impacts, anxiety and depression in patients with asthma is not routinely assessed during clinical visits and thus there is a lack of information about its real-world frequency. One of the most used tools for psychological screening is the Hospital Anxiety and Depression Scale (HADS). HADS is a self-report questionnaire designed to screen anxiety and depression symptoms[15] and it was already used in adolescents and adults with asthma in previous studies.[16 17] However, this scale has 14 items and although it takes around 5 min to complete,[18] it is not always feasible to administer in a busy clinic setting.[19 20] European Quality of Life Five Dimension Questionnaire (EQ-5D) is a generic measure of health status that provides a simple descriptive profile and a single index value that can be used for the clinical and economic evaluation of healthcare,[21] but also emotional distress screening.[22] Currently, EQ-5D is being widely used in a variety of conditions, where asthma is integrated.[23] Some studies compared HADS and EQ-5D in patients with other diseases and showed that EQ-5D can be responsive to different degrees of HADS-assessed distress.[24] Yet, there is no published data comparing HADS and EQ-5D in patients with asthma.

With the present study, we aimed to assess (1) the frequency of symptoms of anxiety and depression in patients with asthma as assessed by HADS and EQ-5D questionnaires; (2) the level of agreement between the two questionnaires and (3) the factors associated with the presence of these symptoms.

METHODS

Patient and public involvement

No patient involved.

Study design

Data from the baseline face-to-face visit from five prospective observational studies of the INSPIRERS project were analysed.[25] This project addresses the topic of adherence to asthma inhalers among adolescents and adults with persistent asthma. Convenience samples were recruited between November 2017 and October 2020 at 32 allergy, pulmonology and paediatric secondary care outpatient clinics (30 from Portugal and 2 from Spain) and 30 primary care centres from Portugal. The studies were approved by the ethics committees of all participating centres. Eligible patients were approached by physicians during medical visits. Adult patients signed a consent form. Adolescents signed an assent form, and a parental consent form was also obtained. The studies had similar inclusion criteria and methods. The study is reported according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[26]

Patients

Patients were included in the analysis if they had a previous medical diagnosis of persistent asthma, were at least 13 years old (13–17 years adolescents; ≥18 years adults) and had an active prescription for an inhaled controller medication for asthma. All inhaled controller treatments were allowed, and there was no change in any prescribed medication regarding the participation in these studies. Patients were excluded if they had a diagnosis of a chronic lung disease other than asthma or a diagnosis of another significant chronic condition with possible interference with the study aims.

Data collection

During the baseline face-to-face visit, data were collected from both physicians and patients in an attempt to improve the quality of the information obtained. Physicians answered a questionnaire including the asthma treatment plan and comorbidities. Information about the healthcare setting (primary, secondary) was obtained based on the centre where patients were recruited.

Demographic data (age, gender, educational level, marital status and current occupation) and clinical data (weight, height, smoking habits and age of asthma diagnosis) were collected from patients.

Two asthma control questionnaires were used to gather the perspectives of the physician and the patient. Physicians answered the Global Initiative for Asthma (GINA) assessment of symptom control,[26] which is recommended to be used at every opportunity in adolescents and adults. Patients answered the Control of Allergic Rhinitis and

Asthma Test (CARAT). CARAT is a self-report questionnaire with a total score (CARAT-T) calculated by summing up the score of each of the 10 questions, resulting in a range of 0–30 points. A score >24 indicates good disease control.[27] This questionnaire has been widely used in clinical practice and in scientific research, being translated/culturally adapted in >27 languages and used in >15 different countries.[28]

The Portuguese version of the HADS was used to assess the presence of symptoms of anxiety and depression.[29] HADS contains 14 items related to the past week, 7 of which assess anxiety symptoms (HADS-A) and the other 7 depression symptoms (HADS-D). HADS-A and HADS-D are scored separately. The item response scale varies between 0 and 3 points, with total scores ranging from 0 (minimum symptomatic load) up to 21 (maximum symptomatic load) for HADS-A and HADS-D. A score ≥8 on HADS-A or HADS-D was considered as the presence of symptoms of anxiety or depression, respectively.[30]

The EQ-5D three-level version was filled in by the patients to assess their overall quality of life. The item 5 'Anxiety and Depression' could be a useful tool in screening for anxiety and depressive symptoms in hospital and community settings.[31] Therefore, this item, with its three response options ('I am not anxious or depressed', 'I am moderately anxious or depressed', 'I am extremely anxious or depressed') was additionally used to assess the presence of these symptoms.[32] Patients were considered to have anxiety/depression when answering 'I am moderately anxious or depressed' or 'I am extremely anxious or depressed'. The EQ-5D summary index score was calculated to characterise the sample. It ranges from less than 0 (where 0 is a health state equivalent to death) to 1 (perfect health).[33] The EQ-5D visual analogue scale (VAS) was also used to assess patients' perception of their general health (from 0 'the worst health you can imagine' to 100 'the best health you can imagine').

Statistical analyses

Descriptive statistics were used to characterise the sociodemographic variables, clinical characteristics, the HADS score and EQ-5D responses. Absolute and relative frequencies were used to characterise the categorical variables. Means and SD or medians and IQRs were used, according to data distribution, to characterise the numerical variables.

To determine the agreement between HADS and EQ-5D questionnaires for the presence of symptoms of anxiety/depression, the percentage of agreement and weighted Cohen's kappa were used. Cohen's kappa values were interpreted as follows: <0, no agreement; 0–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial and 0.81–1.0, almost perfect agreement.[34]

To explore associations between variables related to the presence of symptoms of anxiety and depression, patients with and without symptoms of anxiety and depression were compared using independent t-tests for normally distributed data, Mann-Whitney U tests for non-normally distributed continuous data and ordinal data, and χ^2 tests for categorical data. In the case of χ^2 tests, when a statistically significant difference was found for a categorical variable with more than two categories, χ^2 multiple comparison tests with Bonferroni correction were performed to explore which categories differed from each other. The variables that were statistically different ($p<0.05$) between the two groups were selected to further explore their relationship with the presence of anxiety and depression and to adjust for possible confounders in two stepwise multivariable logistic regression models. The dependent variable in each multivariable logistic regression was the presence of symptoms of anxiety or depression based on HADS (0=absent, 1=present). The overall models were evaluated using the goodness-of-fit tests and Nagelkerke's R^2 and the final model was selected based on the best combination of these results. The level of significance considered was 0.05. Statistical analyses were performed using IBM SPSS Statistics V.26.0 (IBM Corporation).

RESULTS

Patient's characteristics

A total of 614 participants with asthma (mean age 32.6±16.9 years) were included in this study. There were 447 (72.8%) adults and 397 (64.7%) women. Forty per cent of the participants had completed primary school (n=244), 47.4% were employed (n=289) and 65.1% were prescribed only one inhaler (n=396). According to the GINA assessment of symptom control, 296 (48.7%) patients had well-controlled asthma. Table 1 shows the sociodemographic and clinical characteristics of the study participants.

Symptoms of anxiety and depression

According to HADS, 221 (36.0%) participants had symptoms of anxiety, 73 (11.9%) had symptoms of depression, 59 (9.6%) both symptoms and 235 (38.3%) participants had symptoms of anxiety or depression. Both anxiety (41.4% vs 21.6%) and depression (14.1% vs 6%) symptoms were more frequent in adults than adolescents. According to EQ-5D, 223 (36.3%) participants had anxiety or depression problems, 32.6% were moderately anxious or depressed and 3.7% extremely anxious or depressed. The agreement between these two questionnaires was moderate for anxiety (k=0.54 (95% CI 0.47 to 0.61)); fair for depression (k=0.23 (95% CI 0.17 to 0.30)) and moderate for anxiety/depression (k=0.55 (95% CI 0.48 to 0.62)).

Predictors of anxiety and depression

In the multivariable logistic regression (table 2), being an adolescent (OR 0.43, 95% CI 0.27 to 0.68), having a better asthma control (CARAT-T score) (OR 0.98, 95% CI 0.94 to 1.00) and a perception of better health (OR 0.97, 95% CI 0.95 to 0.98) were significantly associated with lower odds for the presence of anxiety symptoms. In

Table 1 Sociodemographic and clinical characteristics of the participants (n=614)

Characteristics	
Age (years) M±SD*	32.6±16.9
Age group n (%)	
Adolescent	167 (27.2)
Adult	447 (72.8)
Gender n (%)	
Female	397 (64.7)
Male	217 (35.3)
Educational level n (%)†	
No education completed	4 (0.7)
Primary school	244 (40.4)
High school	177 (29.3)
Qualification above high school (but not university)	23 (3.8)
University	156 (25.4)
Other	1 (0.2)
Marital status n (%)‡	
Single	348 (56.7)
Married/living as a couple	223 (36.3)
Separated/divorced	33 (5.4)
Widowed	9 (1.5)
Current occupation n (%)§	
Employed	289 (47.1)
Student	235 (38.3)
Unemployed	41 (6.7)
Retired	36 (5.9)
Other	9 (1.5)
BMI Kg/m^2, M±SD¶	24.7 (5.3)
Smoking status n (%)§	
Never smoker	457 (74.4)
Ex-smoker	106 (17.3)
Current smoker	47 (7.7)
Setting	
Secondary care	475 (77.4)
Primary care	139 (22.6)
Age of asthma diagnosis (years) M±SD**	16.2±14.8
Number of prescribed inhalers n (%)††	
1	396 (64.5)
2	193 (31.4)
≥3	19 (3.1)
GINA assessment symptom control n (%)††	
Well controlled	296 (48.2)
Partly controlled	188 (30.6)
Uncontrolled	124 (20.2)
Number of physician-reported comorbidities median (P25–P75)	1 (0–2)
CARAT-T median (P25–P75)	21 (16–25)
CARAT-T classification	
Controlled n (%)	156 (25.4)
Uncontrolled n (%)	458 (74.6)
EQ-5D-3L median (P25–P75)	
Total	0.91 (0.81–1.0)
VAS	80.0 (70.0–90.0)

*Eight missing values.
†Nine missing values.
‡Missing value.
§Four missing values.
¶Twenty-eight missing values.
**Twenty-two missing values.
††Six missing values.
BMI, body mass index; CARAT-T, Control of Allergic Rhinitis and Asthma Test total score; EQ-5D-3L, European Quality of Life Five Dimension Questionnaire-three-level version; GINA, Global Initiative for Asthma; M, mean; P25, 25th percentile; P75, 75th percentile; VAS, visual analogue scale.

contrast, being a female was significantly associated with a higher odd for the presence of anxiety symptoms (OR 1.75, 95% CI 1.56 to 2.64). Having better health-related quality of life (OR 0.97, 95% CI 0.95 to 0.99) and perception of better health (OR 0.97, 95% CI 0.96 to 0.99) were associated with a lower odd for the presence of depression. While asthma diagnosis at a later age (OR 1.03, 95% CI 1.01 to 1.05) and the presence of a higher number of comorbidities (OR 1.31, 95% CI 1.05 to 1.64) were associated with an increase in the likelihood of exhibiting symptoms of depression. The univariate analyses are presented in online supplemental table 1.

DISCUSSION

This study showed that more than 1/3 of participants with asthma experienced symptoms of anxiety and/or depression. Asthma diagnosis at a later age, presence of comorbidities and female gender were predictors of anxiety/depression, while better asthma control, health-related quality of life and perception of better health were factors associated with lower odds for anxiety/depression. In this study, the agreement between HADS and EQ-5D questionnaires in identifying anxiety and depression was sufficient to moderate.

According to HADS and EQ-5D questionnaires, more than 1/3 of the patients with persistent asthma experience symptoms of anxiety/depression (38.3% and 36.3%, respectively). Therefore, the percentages of participants with one of these symptoms detected by HADS and EQ-5D were similar. With HADS, it was possible to detect the percentages of patients with persistent asthma that

Table 2 Multivariable logistic regression analyses to explain anxiety and depression

	Anxiety adjusted OR (95% CI)*	Depression adjusted OR (95% CI)†
Age group		
Adolescent	0.43 (0.27 to 0.68)	–
Adult	Reference	–
Gender		
Female	1.75 (1.56 to 2.64)	–
Male	Reference	–
Age of asthma diagnosis	–	1.03 (1.01 to 1.05)
Number of physician-reported comorbidities	1.17 (0.99 to 1.37)	1.31 (1.05 to 1.64)
CARAT T	0.98 (0.94 to 1.00)	–
Quality of life (EQ-5D total)	–	0.97 (0.95 to 0.99)
Perception of better health (EQ-5D VAS)	0.97 (0.95 to 0.98)	0.97 (0.96 to 0.99)
R^2	22%	23%
Hosmer-Lemeshow test—p value	0.435	0.449

*Age, current occupation, setting, age of asthma diagnosis, GINA assessment of symptom control and quality of life (EQ-5D total) were also tested but not included in the final adjusted model.
†Age, age group, educational level, marital status, current occupation, BMI, GINA assessment of symptom control and CARAT-T were also tested but not included in the final adjusted model.
BMI, body mass index; CARAT-T, Control of Allergic Rhinitis and Asthma Test total score; EQ-5D, European Quality of Life Five Dimension Questionnaire; VAS, visual analogue scale.

had only symptoms of anxiety (36.0%) or had only symptoms of depression (11.9%). The proportions found in the present study were similar to the ones found among patients with asthma in previous reviews,[8 9] analysing studies that included only, or mostly, adults with asthma. A study from the UK found similar frequencies of anxiety and depression using HADS, although a slightly higher cut-off has been used (HADS-A/HADS-D≥10).[35] We found a lower frequency for depression as compared with a study in patients with severe asthma, where 25% reported depression.[36] This difference might be explained by the role of poorer physical functioning on symptoms of depression.[37] Patients with severe asthma experience more physical disability. Other studies reported that patients with severe asthma have more often emotional distress as compared with patients with mild-moderate asthma.[38 39]

This study includes both adolescents and adults with persistent asthma, which is rarely found in previous articles. However, anxiety and depression were only assessed at one time point. Analysing emotional distress in the long run could be important as suggested in previous cohort studies that followed adolescents with asthma to young adulthood, showing that there was a persistence or recurrence of anxiety and depression in adulthood.[40 41] In our study, adults with persistent asthma presented an increased frequency of anxiety/depression symptoms (vs adolescents), which is in accordance with a population-based study that reported that having asthma and older age were independent risk factors for the presence of anxiety disorders, in participants above the age of 15 years.[42] Therefore, emotional distress seems to be associated with age differences in patients with persistent asthma.

Age at asthma onset has emerged as a critical factor in distinguishing the phenotypes of asthma.[43] Adult-onset asthma differs from asthma that first occurs in childhood since it usually is less well controlled, is associated with a faster decline in lung function and with more comorbidities.[44 45] Moreover, worse asthma control and the presence of more comorbidities might be associated with an increased risk of emotional distress.[46] These results contribute to explaining our finding that asthma diagnosis at a later age and number of physician-reported comorbidities were associated with a higher frequency of depression. Female patients were more likely to have anxiety symptoms. This was previously observed in other studies in asthma but also other respiratory diseases, such as chronic obstructive pulmonary disease (COPD). Possibly these gender differences are more than a specificity of respiratory diseases, but a reflection of the known gender differences in the general population.[47 48]

In our study, the perception of better health was associated with a lower odd for the presence of anxiety symptoms. In a previous study with patients with COPD, the perceived severity of COPD symptoms was predictive of depression and anxiety.[49] These findings are in line with our study, although coming from a different disease. The close correlation between asthma control, quality of life, anxiety and depression has been also confirmed in other studies.[50 51] Consequently, in patients with poor asthma control, physicians should ask about the symptoms of anxiety/depression or screen it using simple tools like

EQ-5D or HADS before making adjustments on asthma treatment strategy.[17]

EQ-5D questionnaire could be useful in clinical practice.[52] The EQ-5D anxiety or depression domain had a greater agreement with the HADS score in identifying cases with both symptoms, as expected, than in identifying anxiety or depressive symptoms. In general, the percentages of patients with anxiety/depression detected by HADS and EQ-5D were similar. Furthermore, it is expected that remarkably less time consumption is needed for the EQ-5D item 5 assessment compared with HADS.[18 53] Therefore, EQ-5D score appears to have value as a screening tool for anxiety or depression in patients with asthma. In a previous study, this questionnaire also seemed to be reasonably valid and moderately responsive in patients with anxiety disorders.[54] This could be important in clinical practice because a generic health instrument like the EQ-5D, with few and quick questions, could be used to easily raise awareness of a possible emotional distress in patients with asthma. A limitation of EQ-5D is that anxiety and depression are two separate emotional disorders and their combination in a single item in this questionnaire could lead to inconsistencies in responses.[55] Nevertheless, EQ-5D could be used as a first screening questionnaire and, in patients reporting anxiety or depression symptoms, a more specific questionnaire, such as HADS, could be used to better characterise their symptoms. Actually, emotional distress screening is very important in clinical practice because physicians can use targeted interventions to improve patients' symptoms.[56] Studies about psychological interventions in adults with asthma suggest that education and simple psychological interventions namely relaxation techniques and biofeedback or a stepped care approach could produce significant positive healthcare outcomes.[57 58]

This study has some strengths that should be acknowledged: it is a multicentric study that recruited both adults and adolescents with asthma from primary and secondary care. A comprehensive set of individual-level characteristics was collected and analysed, which allowed us to explore the impact of a range of sociodemographic factors, health literacy and cofactors such as quality of life and asthma control. Therefore, includes a sample from different healthcare contexts and with different clinical presentations, contributing to the robustness of these findings.

Nevertheless, it also has some limitations. A possible source of bias was the recruitment strategy of using a convenience sampling. Future studies using other sampling strategies could be important to generalise the results of our study. A control group of healthy individuals with similar sociodemographic characteristics should also be included in further research to increase the validity of these findings. In the absence of a control group it would have been useful to compare anxiety/depression frequencies with normative data from Portugal and Spain, but we did not find it neither for HADS nor EQ-5D. Moreover, the impact of the presence of specific comorbidities, such as rhinitis, which is closely associated both with asthma and anxiety/depression, was not assessed.[59] Another limitation of the present study is related to its cross-sectional nature. The frequency of distressing symptoms and the relationships with associated factors could not be established along the progression of the disease. Also, patients were not recruited at the same time point, as recruitment in the INSPIRERS studies occurred across four different years (from 2017 to 2020), and the last 15% of the sample was recruited during COVID-19 pandemic. Longitudinal studies following a cohort of patients with asthma would address these issues and identify other predictors of symptoms of anxiety and depression.

This study shows that more than 30% of the patients with persistent asthma experience symptoms of anxiety/depression, which supports the relevance of emotional distress screening in patients with asthma. EQ-5D and HADS questionnaires showed a moderate agreement in the identification of anxiety/depression symptoms. Late asthma diagnosis, presence of comorbidities and female gender were positively associated with the presence of emotional distress, while better asthma control, health-related quality of life and perception of better health presented a negative association. These factors need to be further investigated in future long-term studies.

Author affiliations
[1]Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal
[2]Allergy Unit, Instituto and Hospital CUF, Porto, Portugal
[3]CINTESIS@RISE, MEDCIDS, Faculty of Medicine of the University of Porto, Porto, Portugal
[4]Department of Cardiovascular and Respiratory Sciences, Porto Health School, Polytechnic Institute of Porto, Porto, Portugal
[5]Department of Women's and Children's Health, Paediatric Research, Uppsala University, Uppsala, Sweden
[6]Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS), Faculty of Medicine of the University of Porto, Porto, Portugal
[7]Pulmonology Department, Hospitais da Universidade de Coimbra, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
[8]Basic and Clinic Immunology, Faculty of Medicine of the University of Porto, Porto, Portugal
[9]Immuno-allergology, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal
[10]Serviço de Pediatria, Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Matosinhos, Portugal
[11]Serviço de Imunoalergologia, Hospital Universitário de Coimbra, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
[12]Servicio de Alergia, Complejo Hospitalario Universitario de Santiago, Santiago de Compostella, Spain
[13]Servicio de Alergia, Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain
[14]Serviço de Pediatria, Centro Materno Infantil do Norte, Centro Hospitalar Universitário do Porto, Porto, Portugal
[15]Serviço de Imunoalergologia, Centro Hospitalar Universitário de São João, Porto, Portugal
[16]Allergy, Hospital Amato Lusitano, Unidade Local de Saúde de Castelo Branco, Castelo Branco, Portugal
[17]Serviço de Imunoalergologia, Centro Hospitalar Universitário do Algarve, Portimão, Portugal
[18]Unidade de Saúde Familiar Terras de Azurara, Agrupamento de Centros de Saúde Dão Lafões, Mangualde, Portugal

[19]CICS-UBI Centro de Investigação em Ciências da Saúde - Health Sciences Research Centre & UBIAir – Clinical & Experimental Lung Centre, University of Beira Interior, Covilha, Portugal
[20]Department of Allergy & Clinical Immunology, Cova da Beira University Hospital Centre, Covilhã, Portugal
[21]Departamento de Pediatria, Hospital de Santa Maria, Centro Hospitalar de Lisboa Norte, Lisboa, Portugal
[22]Immuno-Allergology, Grupo HPA Saúde, Portimao, Portugal
[23]Unidade de Saúde Familiar Progresso e Saúde, Agrupamento de Centros de Saúde Baixo Mondego, Tocha, Portugal
[24]Serviço de Pneumologia, Hospital Nossa Senhora do Rosário, Centro Hospitalar Barreiro Montijo, Barreiro, Portugal
[25]Unidade de Saúde Familiar João Semana, Agrupamento de Centros de Saúde de Baixo Vouga, Ovar, Portugal
[26]Serviço de Pediatria, Unidade Hospitalar de Famalicão, Centro Hospitalar do Médio Ave, Vila Nova de Famalicão, Portugal
[27]Unidade de Cuidados de Saúde Personalizados Norte (Arnaldo Sampaio), Agrupamento de Centros de Saúde Pinhal Litoral, Monte Redondo, Portugal
[28]Serviço de Pediatria, Hospital de São Teotónio, Centro Hospitalar Tondela Viseu, Viseu, Portugal
[29]Unidade de Saúde Familiar Cuidarte, Unidade Local de Saúde do Alto Minho, Portuzelo, Portugal
[30]Serviço de Imunoalergologia, Hospital da Senhora da Oliveira, Guimarães, Guimaraes, Portugal
[31]Serviço de Imunoalergologia, Hospital Infante D Pedro, Centro Hospitalar Baixo Vouga, Aveiro, Portugal
[32]Centro de Imunoalergologia do Algarve, Portimão, Portugal
[33]Unidade de Saúde Familiar Corgo, Agrupamento de Centros de Saúde Douro I - Marão e Douro Norte, Vila Real, Portugal
[34]Unidade de Saúde Familiar Homem do Leme, ACeS Porto Ocidental, Porto, Portugal
[35]Serviço de Pneumologia, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal
[36]Unidade de Saúde Familiar Viseu-Cidade, Agrupamento de Centros de Saúde do Dão Lafões, Viseu, Portugal
[37]Unidade de Cuidados Saúde Personalizados Sicó, Agrupamento de Centros de Saúde Pinhal Litoral, Leiria, Portugal
[38]USF Esgueira +, ACES Baixo Vouga, Esgueira, Portugal
[39]Unidade de Saúde Familiar Marquês, ACES Pinhal Litoral, Pombal, Portugal
[40]Unidade de Saúde Familiar Condeixa, ACES Baixo Mondego, Condeixa-a-Nova, Portugal
[41]Unidade de Cuidados de Saúde Personalizados de Amarante, ACES Tâmega I - Baixo Tâmega, Amarante, Portugal
[42]Unidade de Saúde Familiar Bracara Augusta, ACES Cávado I, Braga, Portugal
[43]Unidade de Saúde Familiar Almedina, ACES Douro II - Douro Sul, Lamego, Portugal
[44]Unidade de Saúde Familiar Valongo, ACES Grande Porto III - Maia / Valongo, Valongo, Portugal
[45]Unidade de Saúde Familiar Canelas, ACES Grande Porto VIII - Espinho / Gaia, Vila Nova de Gaia, Portugal
[46]MEDIDA – Medicina, Educação, Investigação, Desenvolvimento e Avaliação, Porto, Portugal

Twitter Luís Monteiro @luismonteiro140 and Daniela Sousa Coelho @Daniela

Contributors All authors contributed to the selection of bibliography, revision and final approval of the manuscript. AMP, RAmaral, MA-C, RAlmeida, JAF and CJ were responsible for study conception and design. RAmaral, AMP, RAlmeida, MA-C, CCL, CLopes, JC, CR, CVidal, DA-A, DP, MF-M, MJV, CLozoya, NS, FC, LT-B, RF, PMS, TMF, RC, ES, DB, CG, MJC, SdS, MLM, AM, CN, CVieira, RP, AA, JVM, BR, LM, RM, MC, BV, DSC, SF, PM, MAA, ARM, JAF and CJ participated in the data collection. CJ and AMP performed the data analysis and MSC prepared the first draft. All authors contributed to the interpretation of data, to the critical revision of the manuscript for important intellectual content. JAF and CJ act as guarantors for study.

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ORCID iDs
Rita Amaral http://orcid.org/0000-0002-0233-830X
Luís Taborda-Barata http://orcid.org/0000-0001-6649-8890
Rosália Páscoa http://orcid.org/0000-0001-8782-0260
Luís Monteiro http://orcid.org/0000-0003-0784-5770
Bruno Valentim http://orcid.org/0000-0001-8216-5949
Cristina Jácome http://orcid.org/0000-0002-1151-8791

REFERENCES

1 Nanda A, Wasan AN. The medical clinics of North America. Asthma Adults 2020;104:95–108.
2 Sa-Sousa A, Morais-Almeida M, Azevedo LF, *et al*. Prevalence of asthma in Portugal-the Portuguese national asthma survey. *Clin Transl Allergy* 2012;2:15.
3 Cisneros C, Díaz-Campos RM, Marina N, *et al*. Accreditation of specialized asthma units for adults in Spain: an applicable experience for the management of difficult-to-control asthma. *J Asthma Allergy* 2017;10:163–9.
4 Mims JW. Asthma: definitions and pathophysiology. *Int Forum Allergy Rhinol* 2015;5 Suppl 1:S2–6.
5 Porsbjerg C, Menzies-Gow A. Co-Morbidities in severe asthma: Clinical impact and management. Respirology (Carlton, Vic.) 2017;22:651–61.
6 Homętowska H, Klekowski J, Świątoniowska-Lonc N, *et al*. Fatigue, depression, and anxiety in patients with COPD, asthma and asthma-COPD overlap. J Clin Med 2022;11:7466.
7 Ye G, Baldwin DS, Hou R. Anxiety in asthma: a systematic review and meta-analysis. *Psychol Med* 2021;51:11–20.
8 Weiser EB. The prevalence of anxiety disorders among adults with asthma: a meta-analytic review. *J Clin Psychol Med Settings* 2007;14:297–307.
9 Opolski M, Wilson I. Asthma and depression: a pragmatic review of the literature and recommendations for future research. *Clin Pract Epidemiol Ment Health* 2005;1:18.
10 Clark VL, Gibson PG, Genn G, *et al*. Multidimensional assessment of severe asthma: a systematic review and meta-analysis. *Respirology* 2017;22:1262–75.
11 Lomper K, Chudiak A, Uchmanowicz I, *et al*. Effects of depression and anxiety on asthma-related quality of life. *Pneumonol Alergol Pol* 2016;84:212–21.
12 Sastre J, Crespo A, Fernandez-Sanchez A, *et al*. Anxiety, depression, and asthma control: Changes after standardized treatment. J allergy Clin Immunol 2018;6:1953–9.

13 Li HL, He XL, Liang BM, *et al*. Anxiety but not depression symptoms are associated with greater perceived dyspnea in asthma during bronchoconstriction. *Allergy Asthma Proc* 2015;36:447–57.
14 McCauley E, Katon W, Russo J, *et al*. Impact of anxiety and depression on functional impairment in adolescents with asthma. *Gen Hosp Psychiatry* 2007;29:214–22.
15 Annunziata MA, Muzzatti B, Bidoli E, *et al*. Hospital anxiety and depression scale (HADS) accuracy in cancer patients. *Support Care Cancer* 2020;28:3921–6.
16 Licari A, Castagnoli R, Ciprandi R, *et al*. Anxiety and depression in adolescents with asthma: A study in clinical practice. Acta bio-Medica 2022;93:e2022021.
17 Labor M, Labor S, Jurić I, *et al*. Long-Term predictors of anxiety and depression in adult patients with asthma. *Wien Klin Wochenschr* 2017;129:665–73.
18 Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes* 2003;1:29.
19 Mitchell AJ. Screening for cancer-related distress: when is implementation successful and when is it unsuccessful? *Acta Oncol* 2013;52:216–24.
20 Turon H, Carey M, Boyes A, *et al*. Agreement between a single-item measure of anxiety and depression and the hospital anxiety and depression scale: a cross-sectional study. *PLoS One* 2019;14:e0210111.
21 Rabin R, de Charro F. EQ-5D: a measure of health status from the euroqol group. *Ann Med* 2001;33:337–43.
22 Chotai S, Khan I, Nian H, *et al*. Utility of anxiety/depression domain of EQ-5D to define psychological distress in spine surgery. *World Neurosurg* 2019;126:e1075–80.
23 Afshari S, Ameri H, Daroudi RA, *et al*. Health related quality of life in adults with asthma: a systematic review to identify the values of EQ-5D-5L instrument. *J Asthma* 2022;59:1203–12.
24 Whynes DK, TOMBOLA Group. Responsiveness of the EQ-5D to HADS-identified anxiety and depression. *J Eval Clin Pract* 2009;15:820–5.
25 Jácome C*et al*. MINSPIRERS – feasibility of a mobile application to measure and improve adherence to Inhaled Controller medications among adolescents and adults with persistent asthma: Protocol for a Multicentre observational study. Revista Portuguesa de Imunoalergologia 2018;26:47–61.
26 Vandenbroucke JP, von Elm E, Altman DG, *et al*. Strengthening the reporting of observational studies in epidemiology (STROBE): Explanation and elaboration. Int J sur 2014;12:1500–24.
27 Fonseca JA, Nogueira-Silva L, Morais-Almeida M, *et al*. Validation of a questionnaire (CARAT10) to assess rhinitis and asthma in patients with asthma. *Allergy* 2010;65:1042–8.
28 Vieira RJ, Sousa-Pinto B, Cardoso-Fernandes A, *et al*. Control of allergic rhinitis and asthma test: a systematic review of measurement properties and COSMIN analysis. *Clin Transl Allergy* 2022;12:e12194.
29 Pais-Ribeiro J, Silva I, Ferreira T, *et al*. Validation study of a Portuguese version of the hospital anxiety and depression scale. *Psychol Health Med* 2007;12:225–35.
30 Bjelland I, Dahl AA, Haug TT, *et al*. The validity of the hospital anxiety and depression scale. An updated literature review. *J Psychosom Res* 2002;52:69–77.
31 Short H, Al Sayah F, Ohinmaa A, *et al*. The performance of the EQ-5D-3L in screening for anxiety and depressive symptoms in hospital and community settings. *Health Qual Life Outcomes* 2021;19:96.
32 Ferreira PL, Ferreira LN, Pereira LN. Contribution for the validation of the Portuguese version of EQ-5D. *Acta Med Port* 2013;26:664–75.
33 Azevedo L*et al*. Validity and reliability of eq5d questionnaire in critically ill patients. *Crit Care Med* 2007;35:619.
34 Gabbe BJ, McDermott E, Simpson PM, *et al*. Level of agreement between patient-reported EQ-5D responses and EQ-5D responses mapped from the SF-12 in an injury population. *Popul Health Metr* 2015;13:14.
35 Cooper CL, Parry GD, Saul C, *et al*. Anxiety and panic fear in adults with asthma: prevalence in primary care. *BMC Fam Pract* 2007;8:62.
36 McDonald VM, Hiles SA, Godbout K, *et al*. Treatable traits can be identified in a severe asthma registry and predict future exacerbations. *Respirology* 2019;24:37–47.
5 Gellman MD, Turner JR. Encyclopedia of behavioral medicine. New York, NY, 2013.
38 Akula M, Kulikova A, Khan DA, *et al*. The relationship between asthma and depression in a community-based sample. *J Asthma* 2018;55:1271–7.
39 Amelink M, Hashimoto S, Spinhoven P, *et al*. Anxiety, depression and personality traits in severe, prednisone-dependent asthma. Resp MED 2014;108:438–44.
40 Goodwin RD, Fergusson DM, Horwood LJ. Asthma and depressive and anxiety disorders among young persons in the community. *Psychol Med* 2004;34:1465–74.
41 Ferro MA, Van Lieshout RJ, Scott JG, *et al*. Condition-specific associations of symptoms of depression and anxiety in adolescents and young adults with asthma and food allergy. *J Asthma* 2016;53:282–8.
42 Lee Y-C, Lee C-C, Lai Y-R, *et al*. Association of asthma and anxiety: A nationwide population-based study in Taiwan. J affect DIS 2016;189:98–105.
43 Ilmarinen P, Tuomisto LE, Kankaanranta H. Phenotypes, risk factors, and mechanisms of adult-onset asthma. *Mediators Inflamm* 2015;2015:514868.
44 Burdon J. Adult-onset asthma. *Aust Fam Physician* 2015;44:554–7.
45 Dunn RM, Busse PJ, Wechsler ME. Asthma in the elderly and late-onset adult asthma. *Allergy* 2018;73:284–94.
46 Katz PP, Morris A, Julian L, *et al*. Onset of depressive symptoms among adults with asthma: results from a longitudinal observational cohort. *Prim Care Respir J* 2010;19:223–30.
47 Altemus M. Sex differences in depression and anxiety disorders: potential biological determinants. *Horm Behav* 2006;50:534–8.
48 Baxter AJ, Scott KM, Vos T, *et al*. Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychol Med* 2013;43:897–910.
49 Cleland JA, Lee AJ, Hall S. Associations of depression and anxiety with gender, age, health-related quality of life and symptoms in primary care COPD patients. *Fam Pract* 2007;24:217–23.
50 Di Marco F, Verga M, Santus P, *et al*. Close correlation between anxiety, depression, and asthma control. *Respir Med* 2010;104:22–8.
51 Laforest L, Van Ganse E, Devouassoux G, *et al*. Influence of patients' characteristics and disease management on asthma control. *J Allergy Clin Immunol* 2006;117:1404–10.
52 Szentes BL, Schultz K, Nowak D, *et al*. How does the EQ-5D-5L perform in asthma patients compared with an asthma-specific quality of life questionnaire? BMC Pulmon Med 2020;20:.:168.
53 Jin X, Al Sayah F, Ohinmaa A, *et al*. The EQ-5D-5L is superior to the -3L version in measuring health-related quality of life in patients awaiting THA or TKA. *Clin Orthop Relat Res* 2019;477:1632–44.
54 König H-H, Born A, Günther O, *et al*. Validity and responsiveness of the EQ-5D in assessing and valuing health status in patients with anxiety disorders. Health Qual Life Outcome 2010;8:47.
55 Whalley D, Globe G, Crawford R, *et al*. Is the eq-5d fit for purpose in asthma? acceptability and content validity from the patient perspective. *Health Qual Life Outcomes* 2018;16:160.
56 Cooley C, Park Y, Ajilore O, *et al*. Impact of interventions targeting anxiety and depression in adults with asthma. *J Asthma* 2022;59:273–87.
57 Yorke J, Fleming SL, Shuldham C. Psychological interventions for adults with asthma: a systematic review. *Respir Med* 2007;101:1–14.
58 Stoop CH, Nefs G, Pommer AM, *et al*. Effectiveness of a stepped care intervention for anxiety and depression in people with diabetes, asthma or COPD in primary care: A randomized controlled trial. J affect DIS 2015;184:269–76.
59 Rodrigues J, Pinto JV, Alexandre PL, *et al*. Allergic rhinitis Seasonality, severity, and disease control influence anxiety and depression. The Laryngoscope 2022.