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Article type : Letter to the Editor

Anxiety and depression may associate with poorer control and quality of life in adults with asthma

A brief title: Psychological comorbidity in asthmatics

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ALL.14189](#)

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To the Editor:

Asthma is a major cause of global health problems and affects more than 300 million individuals worldwide. Furthermore, the global burden of asthma has increased by almost 30% in the past 20 years (1). Recent studies in different populations have shown that people with asthma have a higher prevalence of anxiety and depression than the general population (2). A recent national cross-sectional study reported that there were approximately 45 million adults with asthma in China, but co-existing mental health conditions in asthma are often overlooked during the clinical treatment (3). The impact of psychological disorders in people with asthma, especially those with uncontrolled symptoms, has not been fully elucidated(4). Therefore, in this study, we aimed to investigate the prevalence of anxiety and depression in people with asthma in China. We also sought to examine associations between psychological conditions and patient-centered outcomes, including disease control and quality of life among adults with asthma.

The study protocol was approved by the Ethics Committee of Ningbo First Hospital and all the participants provided written informed consent. Details for recruitment and methods are provided in this article's online supporting information (Data S1, Figure S1).

Results

Patient characteristics

105 male and 151 female participants were recruited in this study, with a mean age of 50.2 ± 15.2 years old, mean BMI of 23.6 ± 4.0 , and mean asthma duration of 14.5 ± 17.9 years. Using the Hospital Anxiety and Depression Scale (HADS), 35 (13.7%) patients were found to have symptoms of anxiety and 26 (10.2%) to have symptoms of depression. Characteristics of subjects and significant comparisons are summarized in Table 1.

Associations between asthma, anxiety and depression

Lower lung functions were found in people with higher anxiety symptoms from the HADS score (Table1). In terms of quality of life, the Asthma Quality of Life Questionnaire (AQLQ) scores decreased with increasing HADS-A score in all domains (Table 2). The Asthma Control Questionnaire (ACQ) score was positively associated with the HADS-A score (Table 2). Patients with high levels of anxiety symptoms were more likely to have uncontrolled asthma than patients with low levels of anxiety (85.7% vs 51.1%). Similarly, lower FEV₁, PEF, MMEF_{75/25} and

MMEF_{75/25}% were found in patients with higher depression scores. The AQLQ scores were inversely associated with the HADS-D score in domains of the total, activity limitation, asthma symptoms, psychological status and self-health care (Table 2). The ACQ score was higher in patients with higher HADS-D score (Table 2).

To find determinants that could best predict asthma control, AQLQ, anxiety and depression, stepwise multiple regression analysis was employed. FEV₁%, anxiety, AQLQ (subscales of activity limitations, psychological status, exposure to environmental stimuli and self-health care) accounted for 47.2% of asthma control. The allergic rhinitis, asthma control, anxiety, FEV₁ and MMEF_{75/25}% accounted for 29.2% of the variance in total score for the AQLQ. Asthma control, depression, and AQLQ (psychological status subscale) accounted for 46.0% of anxiety. MMEF_{75/25}%, FEV₁/FVC, anxiety and AQLQ (self-health care subscale) accounted for 44.1% of depression. All these findings implied that presence of anxiety and depression were both associated with reduced lung function, poor asthma control and lower quality of life.

Discussion

In this study, a high prevalence of anxiety (13.7%) and depression (10.2%) was observed in patients with asthma. Results suggested that higher levels of anxiety symptoms and depression symptoms are associated with lower lung function, poor asthma control and lower quality of life. Moreover, we further analyzed our data in three different severity levels (well-controlled, partially controlled and uncontrolled). Symptoms of anxiety and depression were more severe in patients with asthma who had uncontrolled disease, when comparing with those with well or partially controlled disease.

Patients with asthma in other developed countries, such as in Europe and the USA, have a higher prevalence of anxiety and depression than the levels found in our study within a Chinese population. For anxiety, prevalence in other countries is at 11-37% and prevalence of depression has been evidenced at 18% (4, 5). This difference in prevalence of anxiety and depression may be attributable to variance in socioeconomic status between different populations (6). A recent national cross-sectional study reported that there were approximately 45 million adults with asthma in China, but this disease remains largely undiagnosed (72.8%) and undertreated (94.4%) (3). Another potential reason for the lower prevalence of asthma found in our study, is that some

patients in China with symptoms of asthma are being treated for symptoms of anxiety and depression, bypassing asthma diagnosis and treatment (7). It is therefore essential to increase the awareness of psychological comorbidities in asthma in China.

Our study demonstrated that patients with asthma who had symptoms of either anxiety or depression, were likely to have lower quality of life. Moreover, this study observed a potential association between anxiety, depression and poor asthma control. In the regression model, anxiety was confirmed as a predictor of asthma control. Reasons for these findings may be that presence of mental disorders can reduce capability to self-manage asthma symptoms; impacting medication concordance and therefore increasing the risk of hospitalization (4, 8, 9).

One limitation of this study should be acknowledged. Our results implied that presence of anxiety and depression were both associated with reduced lung function, poor asthma control and lower quality of life, but the cross-sectional design made it impossible to explore the direction of associations between anxiety, depression and poor asthma control. A prospective, multi-centered clinical trial is needed to explore if treating anxiety and depression in patients with asthma can improve clinical outcomes, such as disease control and quality of life. Furthermore, further research is needed to evaluate the anxiety and depression in patients with asthma who have other comorbidities, especially chronic respiratory diseases and other chronic disorders that induce dyspnea.

In summary, our study found that presence of anxiety and depression is associated with poor asthma control and reduced quality of life. Such evidence will help physicians to focus on the psychological health of patients with asthma, especially in those with uncontrolled disease.

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Keyword: Anxiety; Asthma; Depression; Quality of life; Psychosomatic medicine

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Transparency:

Declaration of funding: This study was supported by the program for the National Natural Science Foundation of China (81700025), Medical and Health Science and Technology Project of Zhejiang (2018245859), and the Natural Science Foundation of Ningbo (2018A610269).

Authors' contributions: CC and YJ designed research; YL and QJ conducted research and analyzed data; YL and CC wrote the paper; CC had primary responsibility for final content. All authors read and approved the final manuscript.

Conflict of interest: The author has no conflicts of interest to declare.

Abbreviations: BMI, body-mass index; FEV₁/L, one-second forced expiratory volume; FEV₁ (%), predicted one-second forced expiratory volume; PEF/L, peak expiratory flow; PEF (%), predicted peak expiratory flow; MMEF_{75/25}/L, maximal mid-expiratory flow; MMEF_{75/25} (%), predicted maximal mid-expiratory flow; FVC/L, forced vital capacity; FVC (%), predicted forced vital capacity; FEV₁/FVC, forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) ratio; AQLQ, the Asthma Quality of Life Questionnaire; HADS, the Hospital Anxiety and Depression Scale; HADS-A, the anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, the depression subscale of the Hospital Anxiety and Depression Scale.

Table 1. Differences between asthmatics with anxiety/depression or not.

Feature	HADS-anxiety subscale			HADS-depression subscale		
	0-7 (N=221)	≥ 8 (N=35)	<i>P</i> Value	0-7 (N=228)	≥ 8 (N=26)	<i>P</i> Value
Gender:			0.384			0.780
Male	93 (88.6%)	12 (11.4%)		95 (90.5%)	10 (9.5%)	
Female	128 (84.8%)	23 (15.2%)		135 (89.4%)	16 (10.6%)	
Age (years)	52.0 (22.0)	50.0 (24.0)	0.483	52.0 (22.0)	52.5 (19.8)	0.320
BMI (kg/m²)	22.9 (4.9)	23.8 (4.4)	0.071	22.9 (4.9)	23.7 (4.3)	0.170
Asthma duration (years)	5.0 (19.0)	7.0 (35.0)	0.621	5.0 (18.8)	4.0 (36.0)	0.723
FEV₁/L	2.0 (1.0)	1.4 (1.0)	0.007	2.0 (1.0)	1.5 (1.0)	0.049
FEV₁ (%)	72.7±21.4	64.6±18.9	0.035	72.3±21.4	65.8±18.2	0.139
PEF/L	5.2 (2.9)	3.7 (2.4)	0.005	5.1 (2.9)	4.0 (3.3)	0.085
PEF (%)	75.3±25.5	65.3±25.9	0.033	74.6±25.6	68.3±26.1	0.241
MMEF_{75/25}/L	1.1 (1.2)	0.7 (0.8)	0.002	1.1 (1.2)	0.7 (0.8)	0.015
MMEF_{75/25} (%)	33.2 (30.0)	20.5 (22.8)	0.002	32.7 (31.0)	21.8 (25.4)	0.010
FVC/L	2.7 (1.1)	2.6 (1.1)	0.037	2.7 (1.1)	2.5 (1.1)	0.163
FVC (%)	85.1 (23.7)	84.2 (15.3)	0.247	84.8 (22.3)	84.0 (15.3)	0.422
FEV₁/FVC	73.4 (19.1)	69.6 (21.1)	0.180	73.5 (19.5)	69.6 (20.2)	0.096
Asthma control:			<0.001			0.146

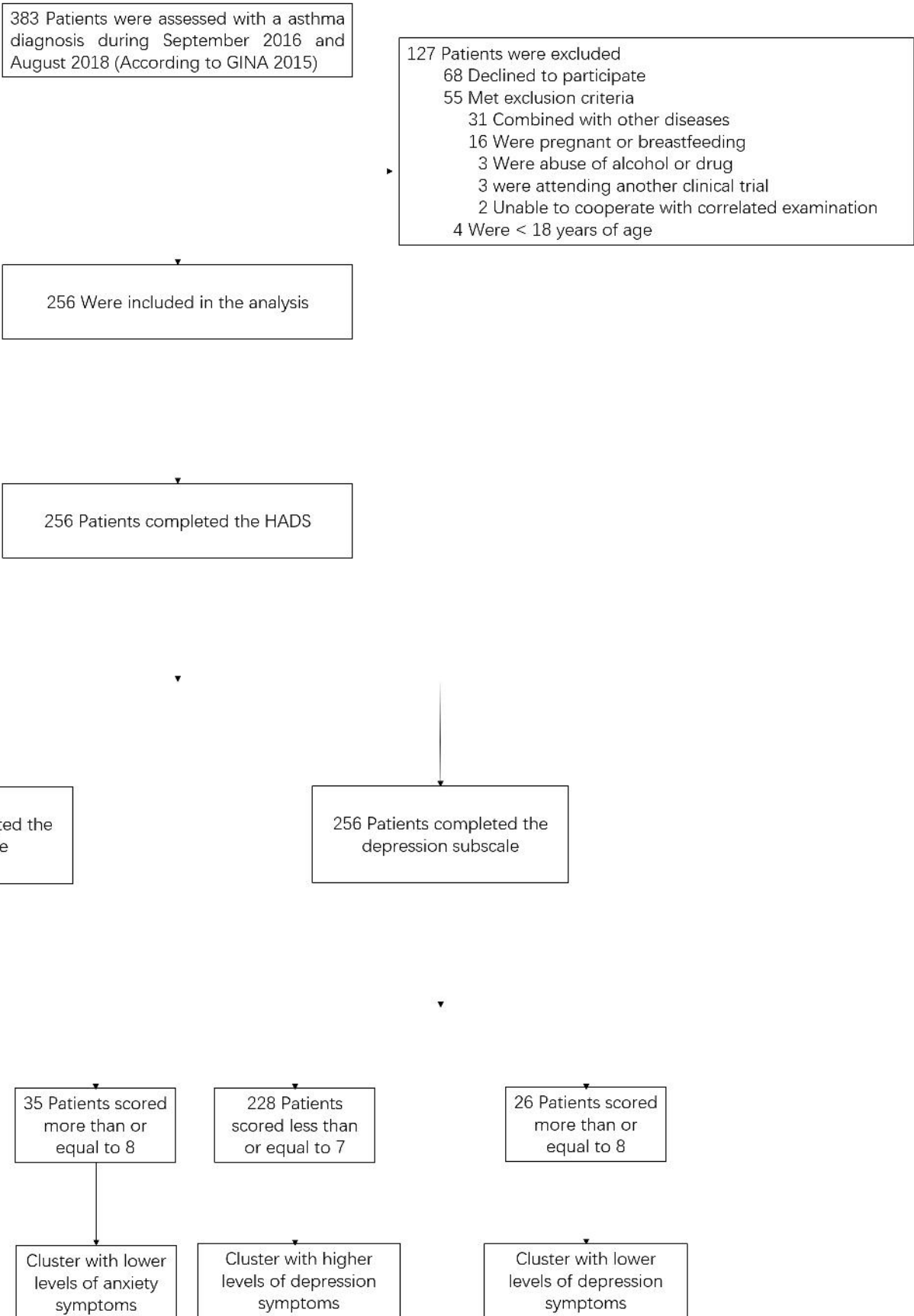
Well-controlled	48 (96.0%)	2 (4.0%)		46 (92.0%)	4 (8.0%)	
Partially controlled	60 (95.2%)	3 (4.8%)		60 (95.2%)	3 (4.8%)	
Uncontrolled	113 (79.0%)	30 (21.0%)		124 (86.7%)	19 (13.3%)	
AQLQ Score						
The total score	5.54 (1.09)	5.1 (1.4)	<0.001	5.5 (1.1)	5.2 (1.6)	0.121
Activity limitations	4.9±1.1	4.5±1.2	0.036	4.9±1.1	4.7±1.3	0.496
Asthma symptoms	5.9 (1.6)	4.8 (2.0)	<0.001	5.8 (1.4)	5.1 (2.0)	0.041
Psychological status	6.4 (1.0)	5.4 (1.2)	<0.001	6.4 (1.2)	5.4 (1.1)	<0.001
Exposure to environmental stimuli	6.0 (2.3)	6.0 (2.0)	0.619	6.0 (2.4)	6.2 (2.1)	0.529
Self-health care	6.0 (1.8)	4.8 (1.5)	<0.001	6.0 (1.8)	4.8 (1.8)	<0.001

BMI, body-mass index; FEV₁/L, one-second forced expiratory volume; FEV₁ (%), predicted one-second forced expiratory volume; PEF/L, peak expiratory flow; PEF (%), predicted peak expiratory flow; MMEF_{75/25}/L, maximal mid-expiratory flow; MMEF_{75/25} (%), predicted maximal mid-expiratory flow; FVC/L, forced vital capacity; FVC (%), predicted forced vital capacity; FEV₁/FVC, forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) ratio; AQLQ, the Asthma Quality of Life Questionnaire; HADS-A, the anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, the depression subscale of the Hospital Anxiety and Depression Scale.

Table 2. Associations between the mental status and asthma control, asthma-related quality of life.

	The score of ACQ	AQLQ domains					
		The total score	Activity limitations	Asthma symptoms	Psychological status	Exposure to environmental stimuli	Self-health care
HADS-A							
<i>P</i> value	<0.001	<0.001	0.002	<0.001	<0.001	0.039	<0.001
<i>r</i>	0.297	-0.385	-0.195	-0.345	-0.453	-0.129	-0.464
HADS-D							
<i>P</i> value	<0.001	<0.001	0.001	<0.001	<0.001	0.188	<0.001
<i>r</i>	0.258	-0.324	-0.208	-0.297	-0.428	-0.083	-0.35

ACQ, Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; HADS-A, the anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, the depression subscale of the Hospital Anxiety and Depression Scale.



Supporting information

Recruitment of Patients:

Patients were recruited between September 2016 and August 2018 from adult respiratory clinics at Ningbo First Hospital. The flow chart of study population was shown in the Figure S1. Diagnosis of asthma was confirmed by specialists in agreement with the Global Initiative for Asthma (GINA) guidelines(1). Patients who met all the inclusion criteria were enrolled: 1) age between 18 and 79 years; 2) with at least one respiratory symptom(wheeze, chest tightness, shortness of breath, or cough that vary over time and intensity); 3) airway hyperresponsiveness to methacholine, evidenced by a provocative concentration of methacholine (no more than 16 mg/ml) or the degree of reversibility in forced expiratory volume in one second (FEV₁) is more than 12% and more than 200 ml after bronchodilator administration; 4) confirmation of an over 10% improvement in the daily variation rate of peak expiratory flow (PEF) within one week; 5) no abnormality in chest high resolution computed tomography.

The following exclusion criteria were used: 1) patients are unable to cooperate with correlated examination; 2) patients with other conditions (ie, interstitial pneumonia, active pulmonary tuberculosis, community-acquired pneumonia, bronchiectasis, pulmonary heart disease, pulmonary embolism) or severe chronic comorbidities (ie, malignancies, hepatic or renal failure, neuromuscular disease, active autoimmune diseases); 3) patients with alcohol or drug abuse; 4) patients who are attending

another clinical trial; 5) women who are pregnant or breastfeeding. These criteria were adopted from previous researches and made carefully(2, 3).

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Figure legends

Figure S1. Flow chart of study population.