

Analysis of the role of selected demographic and psychological variables (anxiety and depression) as risk factors of inadequate control of bronchial asthma

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Abstract

Objective: The aim of the study was to analyze selected potential demographic and psychological variables (anxiety and depression) as risk factors of inadequate control of bronchial asthma.

Materials and method: The study consisted a group of 223 randomly selected asthma patients with varying degrees of asthma control. The study was designed as a diagnostic survey using the asthma control test (ACT), Beck's Depression Inventory (BDI), State- and Trait-Anxiety Inventory (STAI questionnaires X-1 and X-2), and the questionnaire for demographic data collection developed for the purposes of the presented study.

Results: Inadequate control of asthma was significantly more frequent amongst females ($p=0.008$) who were rural inhabitants ($p=0.020$) and professionally active ($p=0.000$) patients diagnosed with any grade of depression with an aid of BDI ($p=0.000$). Patients with inadequate control of asthma were characterized by a significantly higher level of depression, compared to patients controlling this condition adequately ($p=0.001$).

Conclusions: The female gender, living in a rural environment, professional activity, and even a slight degree of depression can promote inadequate control of asthma. Consequently, asthma patients with such characteristics should be provided with careful allergological surveillance. Since none of the abovementioned variables represents an independent risk factor of inadequate asthma control, it is not possible to classify asthma patients into risk groups on the basis of single parameter assessment. The risk of inadequate asthma control involves also individuals with a low severity of depression (more than 9 points on BDI), i.e. the patients who would not be diagnosed with even mild depression based on the existing criteria.

Key words

bronchial asthma, asthma test control, demographic factors, anxiety, depression

INTRODUCTION

Globally, bronchial asthma is one of the most frequently occurring chronic conditions. According to Global Initiative for Asthma (GINA) 2011 report, the estimated number of asthma patients comprises 300 million individuals worldwide; another 100 million individuals are expected to develop this condition by 2025 [1]. A large, international epidemiological study conducted in the early 1990s revealed that depending on the place of residence bronchial asthma affects between 1.6%–36.8% of children aged 13–14-years-old [2]. Between 5%–20% of individuals in Europe suffer from bronchial asthma [3, 4]. According to the Epidemiology of Allergic Conditions in Poland (EACP) project, 4.72% of Poles declare being affected by this condition [5]. According to other research, the prevalence of bronchial asthma in

Poland is estimated at 8.6% in 3- to 16-year-old children, and up to 4.8–5.4% in adults [6, 7, 8]. Under 14 years of age, asthma occurs in boys twice as frequently as in girls [9]. This difference diminishes with age; additionally, a different proportion is observed in adulthood, when females are affected more frequently [10, 11, 12]. Bronchial asthma is more common in urban than in rural inhabitants (10.8–16.42% vs. 1.97–6.2%) [13, 14]. Both the incidence and severity of asthma have increased, beginning from the 1960s [15]. Also, the co-existence of mental disorders and asthma is not infrequent. Studies conducted between 1980–2002 unambiguously indicate that a considerable proportion of asthma patients suffer from anxiety and mood disorders; in fact, as many as 41–52% of bronchial asthma patients have exhibited various psychological pathologies [16]. The chronic character of the condition impairs the patient's life physically, as well as emotionally and socially.

The factors modulating the risk of bronchial asthma are well established and include: genetic predisposition, obesity, and male or female gender in the case of childhood or adult asthma, respectively. Also, the agents able to induce the clinical

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signs of asthma are well known; this group comprises tobacco smoke, allergens, and specific occupational hazards [17]. The influence of the above-mentioned factors on the course of asthma is complex, and their underlying mechanisms are frequently interrelated. The involvement of some of these factors in the development and manifestations of asthma does not raise any questions, while the others, although associated with asthma, do not represent the true causative factors.

Since the international guidelines of the Global Initiative for Asthma (GINA) were published in 2006, adequate control of asthma is considered as the most important therapeutic objective in the case of this condition [1]. Furthermore, the degree of asthma control constitutes the basis for the clinical classification of this condition, as well as the selection criterion for its correct treatment.

While the factors influencing the development of bronchial asthma and those inducing its clinical manifestations are well understood, less is known about the potential factors modulating the degree of asthma control (according to the ACT). Therefore, the presented study addresses this question.

Objective: The aim of this study was to analyze selected potential demographic and psychological variables as risk factors of inadequate control of bronchial asthma.

MATERIALS AND METHOD

The study consisted of a group of 223 randomly selected asthma patients with varying degrees of asthma control. The patients were followed-up by allergology outpatient clinics in the Kujawsko-Pomorskie province in northern-central Poland between October 2008 – November 2011. The study was designed as a diagnostic survey using the asthma control test (ACT) [18], Beck's Depression Inventory (BDI) [19], State- and Trait-Anxiety Inventory (STAI questionnaires X-1 and X-2) [20], and the questionnaire for demographic data collection developed for the purposes of this study. The patients completed the questionnaires during a single follow-up visit. The protocol of the study was approved by a Bioethics Committee.

The following independent variables were analyzed: a) continuous variables: patients' age, level of state- and trait-anxiety, and severity of depression; b) discrete variables: gender, place of residence, pet ownership, marital status, professional activity, occurrence of depression (at least 12 points on the examination with BDI). Inadequate control of asthma (no more than 19 points on the examination with ACT) was considered to constitute a dependent variable.

The normality of continuous variables distribution was verified with the Shapiro-Wilk test. Statistical characteristics of continuous variables were presented as arithmetic means and their standard deviations (SD), medians, and lower (q25) and upper quartiles (q75). The Mann-Whitney U test was used for intergroup comparisons of the continuous variables. The statistical characteristics of discrete variables were presented as number and percentage distributions. The distributions of discrete variables in various groups of patients were compared with Pearson's chi-square test or Fisher's exact test.

The role of independent variables as the risk factors of inadequate asthma control was verified by univariate and multivariate analysis of logistic regression. The odds ratios (ORs) of inadequate asthma control were calculated, together

with their 95% confidence intervals (95% CIs). Variables with $OR > 1$ and $p \leq 0.05$ were considered as significant risk factors of inadequate asthma control; higher values of OR corresponded to the higher risk associated with a given variable. Variables with $OR < 1$ and $p \leq 0.05$ were considered as significant protective factors against inadequate control of asthma; lower values of OR corresponded to the stronger protective effect in this case. Variables which proved significant or close to significant ($p < 0.1$) risk or protective factors on univariate analysis were analyzed collectively in a multivariate model of logistic regression. Variables with $p \leq 0.05$ on multivariate analysis were considered significant for independent risk or protective factors.

In the case of continuous variables which proved to constitute risk or protective factors on logistic regression analysis, the cut-off value used to distinguish between patients with inadequate and adequate control of asthma was defined on ROC analysis. The following characteristics of the ROC curve were determined for the optimal cut-off point selected by statistical software:

- 1) sensitivity – the fraction of patients with inadequate control of asthma and the value of analyzed variable exceeding the defined cut-off point;
- 2) specificity – the fraction of patients with adequately controlled asthma, in whom the level of analyzed variable did not exceed the identified cut-off point;
- 3) positive predictive value (PPV) – the probability of inadequate control of asthma in individuals in whom the value of analyzed variable exceeded the identified cut-off point;
- 4) negative predictive value (NPV) – the probability of adequate asthma control in individuals with the value of analyzed variable not exceeding the identified cut-off point.

The maximal value of all the above-mentioned parameters was 1 (i.e. 100%). Additionally, the area under the ROC curve (AUC) was calculated together with its 95% confidence interval (95% CI). This value was used to assess the fraction of variance between patients with inadequate and adequate control of asthma, based on the result of diagnostic test. The maximal possible value of AUC was 1 (i.e. 100%), describing the situation in which inadequate control of asthma pertained to all patients in whom the values of analyzed variables exceeded the identified cut-off point, and did not occur in any individual with the value below the same threshold.

All statistical calculations were carried out using Statistica 10 package (StatSoft, Tulsa OK, USA), with the level of statistical significance set at $p \leq 0.05$.

RESULTS

Compared to individuals characterized by adequate asthma control, the group of patients with inadequate control of asthma included significantly more females ($p=0.008$), rural inhabitants ($p=0.020$), professionally active individuals ($p=0.000$), and patients diagnosed with any grade of depression with the aid of BDI ($p=0.000$). In contrast, the compared groups did not differ significantly in terms of the frequency of pet ownership ($p=0.230$) or the distribution of marital status ($p=0.810$) (Tab. 1).

Individuals with inadequate control of asthma were characterized by a significantly higher level of depression,

Table 1. Distribution of demographic, social, and clinical characteristics of patients with inadequate and adequate asthma control

Variable	Lack of asthma control		Control of asthma		p
	n	%	n	%	
Gender					
male	39	30.0	44	47.3	0.008
female	91	70.0	49	52.7	
Place of residence					
countryside	91	70.0	51	54.8	0.020
city	39	30.0	42	45.2	
Pet ownership					
yes	49	37.7	45	48.4	0.230
no	81	62.3	48	51.6	
Marital status					
single	72	55.4	50	53.8	0.810
married	58	44.6	43	46.2	
Professional activity					
employed	107	82.3	55	59.1	0.000
unemployed	23	17.7	38	40.9	
Depression					
yes	86	66.2	14	15.1	0.000
no	44	33.8	79	84.9	

compared to patients controlling this condition adequately ($p=0.001$). In contrast, there were no significant intergroup differences with regards to patients' age ($p=0.119$), or the level of state- ($p=0.324$) and trait-anxiety ($p=0.621$) (Tab. 2).

Table 2. Statistical characteristics of age and the scores of psychological tests in patients with inadequate and adequate asthma control

Variable	Control of asthma	mean	SD	median	q25	q75	p
Age	no	44.08	13.07	47	32	54	0.119
	yes	39.96	14.73	39.5	25	53	
STAI-1	no	47.98	4.37	49	44	50	0.324
	yes	47.61	4.65	47	45	50	
STAI-2	no	46.94	4.53	47	44	50	0.621
	yes	46.71	4.58	47	43	49	
BDI	no	13.13	10.22	10	4	19	0.001
	yes	7.56	8.01	5.5	3	9	

The following were identified as the risk factors of inadequate asthma control on univariate analysis of logistic regression (ranked in descending order of power):

- 1) the occurrence of depression of any grade;
- 2) professional activity;
- 3) living in a rural environment;
- 4) increasing BDI score by 1 point.

Male gender was the only significant protective factor against inadequate control of asthma (Tab. 3).

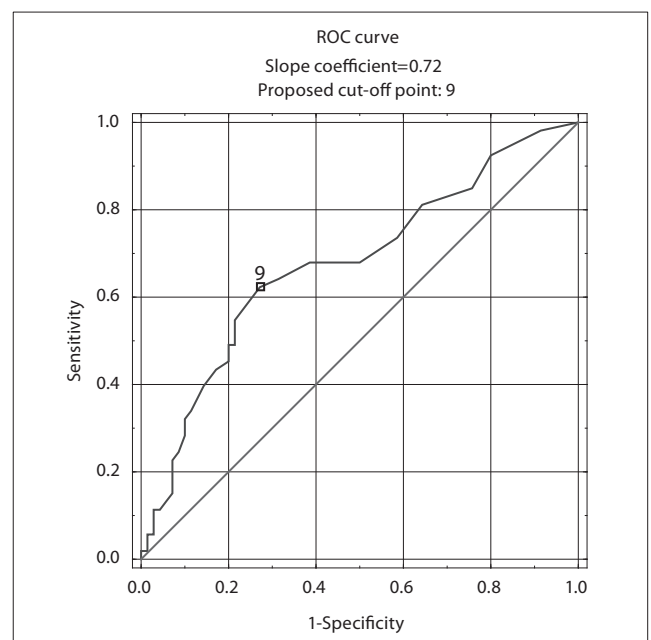
Since the BDI-determined severity of depression proved to be the only continuous variable constituting the risk factor of inadequate asthma control, the appropriate cut-off value that would enable discriminating the risk group were sought. ROC analysis identified this value as a 9-point BDI score. Analysis of the parameters of ROC curve (Tab. 4, Fig. 1)

Table 3. Effect of demographic, social, and clinical characteristics of patients on the risk of inadequate asthma control – the results of univariate analysis

Variable	OR	95%CI	p
Depression	11.03	5.60–21.73	0.000
Professional activity	3.21	1.74–5.94	0.000
Living in the countryside	1.92	1.1–3.35	0.021
Single marital status	1.07	0.62–1.83	0.811
BDI	1.07	1.02–1.12	0.001
Age	1.02	0.99–1.05	0.107
STAI-1	1.02	0.94–1.10	0.655
STAI-2	1.01	0.93–1.09	0.781
Pet ownership	0.64	0.31–1.34	0.229
Male gender	0.48	0.27–0.83	0.008

Table 4. Characteristics of the ROC curve for the level of BDI as the risk factor of inadequate asthma control

Factor	Cut-off point	Sensitivity	Specificity	PPV	NPV	AUC	(-95%CI)	(+95%CI)
BDI	9	0.623	0.729	0.271	0.377	0.677	0.580	0.775

**Figure 1.** ROC curve for BDI severity of depression equal to 9 points as a variable distinguishing between patients with adequate and inadequate control of asthma

revealed a relatively high sensitivity and specificity of this cut-off point (62.3% and 72.9%, respectively), together with a relatively low predictive value (PPV=27.1% and NPV=37.7%). Based on AUC analysis, the defined cut-off value explained nearly 70% of variance between patients with adequate and inadequate asthma control.

None of significant risk or protective factors of inadequate asthma control proved to be independent on multivariate analysis of logistic regression (Tab. 5).

Table 5. Effect of demographic, social, and clinical characteristics of patients on the risk of inadequate asthma control – the results of multivariate analysis

Variable	OR	95%CI	p
Male gender	0.55	0.22–1.36	0.189
Living in the countryside	0.87	0.39–1.95	0.736
Professional activity	1.46	0.66–3.23	0.350
BDI	1.03	0.96–1.12	0.380
Depression	2.43	0.55–10.78	0.236

DISCUSSION

The minimum of good control of asthma (ACT \geq 20) exerts a positive effect in the context of reduced use of healthcare resources, and is associated with better quality of life and work efficiency [21]. This evidence points to the important role of the ACT score in the evaluation of this condition.

According to a study conducted in 2008 in a large group of patients from five European countries, asthma was poorly controlled (ACT $<$ 20) in 56.6% of the subjects [22]. The presented study revealed lack of asthma control in 58.3% of patients. Urban inhabitants were characterized by a better degree of asthma control. In a study with urban dwellers representing the great majority of the subjects, a low level of asthma control was observed in 45.5% of cases [23]. The presented study confirmed poorer control of asthma in rural inhabitants. This finding confirms widely established worldwide evidence of the inferior health status of individuals living in the rural environment [24]. One of the reasons behind this situation may be lower access to healthcare resources by rural inhabitants, compared to urban dwellers. This may result from the lower income of rural inhabitants, bigger distances to healthcare practices, and poorer health awareness [25]. Furthermore, rural inhabitants suffer from inferior availability of specialist care.

It is widely known that particular occupations are associated with an increased risk of clinical signs of bronchial asthma. The number of identified substances that can potentially induce asthma exceeds 800 [1]. The presented study reveals that professionally active individuals were characterized by a lesser degree of asthma control. This probably resulted from their continuous exposure to the factors inducing the signs of asthma. However, lack of information on the type of occupation performed by the participants, or substances to which they may be exposed in the course of their occupation, precludes an objective interpretation of this finding.

An interesting relationship was observed between a patient's gender and poor control of asthma. Male gender was revealed as the only significant protective factor against inadequate control of asthma. The reasons behind this finding cannot be explained unambiguously. It could result partially from the small size of the sample, uneven distribution of gender (females represented more than 60% of the group), and higher prevalence of asthma in females.

The studies by Lavoie and Trzcinska revealed a relationship between the occurrence of depressive states in asthma patients and poorer control of this latter condition. However, a similar relationship was not confirmed in the case of co-occurrence of anxiety disorders [23, 26]. Similar findings were reported by Wang, who observed that the degree of asthma control

correlates solely with depression [27]. In contrast, other studies revealed that the degree of asthma control is related solely to the level of anxiety [28, 29] or, at the same time, to depression and anxiety [30, 31]. Therefore, the character of the above-mentioned relationships cannot be unambiguously verified on the basis of international studies.

The presented study, however, unambiguously confirmed that individuals suffering from depressive disorders are characterized by poorer control of bronchial asthma. Furthermore, it was observed that the more severe the depression, the poorer the degree of asthma control. These findings confirm the results of previous studies [23, 30]. Importantly, the risk of lack of asthma control was documented in patients who scored at least 9 points on the BDI, i.e. below the established cut-off level for depression.

Obviously, the condition which limits one's functioning can predispose to the development of psychopathologies. Perhaps more comprehensive analyses of the components of the mood of depression will be able to determine whether some of them are asthma-specific. Moreover, it should be remembered that depression can directly exacerbate the signs of asthma; according to Allen [32] it can impair voluntary activation of the diaphragm, thus impairing the respiratory drive [32]. Additionally, depression can indirectly affect the severity of asthma, e.g. through a decreased motivation to obtain adequate control of asthma or employing inferior coping mechanisms. Consequently, possible synergy, e.g. mutual exacerbation of asthma and depression, has been postulated [33].

The results of the presented study should be of interest for clinicians and stimulate them to actively seek individuals at risk of inadequate asthma control, particularly amongst females who are rural inhabitants and professionally active. Patients with established depression, as well as those at risk of depression, should be taken into consideration.

Further multi-centre studies on the risk factors associated with lack of asthma control should serve to enable the identification of patients who require particular support in managing this condition.

CONCLUSIONS

Female gender, living in a rural environment, professional activity, and even a slight degree of depression can promote inadequate control of asthma. Consequently, asthma patients with such characteristics should be provided with careful allergological surveillance.

Since none of the above-mentioned variables represents an independent risk factor for inadequate asthma control, it is not possible to classify asthma patients into risk groups on the basis of single parameter assessment.

The risk of inadequate asthma control also involves individuals with a low severity of depression (more than 9 points on the BDI), i.e. the patients who would not be diagnosed with even mild depression based on existing criteria.

REFERENCES

1. From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2011. Available from: <http://www.ginasthma.org> (access: 23.11.2012).

2. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; 351: 1225–32.
3. European Community Respiratory Health Survey: Variations in the prevalence of respiratory symptoms, self-reported asthma, and use of asthma medication in the European Community Respiratory Health Survey. *Eur Respir J*. 1996; 9: 687–695.
4. European Community Respiratory Health Survey II Steering Committee. The European Community Respiratory Health Survey II. *Eur Respir J* 2002; 20: 1071–1079.
5. Samoliński B, Sybilski AJ, Raciborski F, Tomaszewska A, Samel-Kowalik P, Walkiewicz A, et al. Występowanie astmy oskrzelowej u dzieci, młodzieży i młodych dorosłych w Polsce w świetle badania ECAP. *Alerg Astma Immunol*. 2009; 14: 27–34.
6. Samoliński B, Hałat Z, Samolińska-Zawisza U, Raciborski F, Tomaszewska A, Jakubik N, et al. Epidemiologia nieżytych nosa, astmy i AZS na podstawie badań ECRHS i ISAAC w Polsce. *Alergia* 2007; 3: 10–12.
7. Liebhard J, Małolepszy J, Wojtyniak B, Pisiewicz K, Plusa T, Gładysz U. Prevalence and risk factors for asthma in Poland: Results from the PMSEAD Study. *J Investig Allergol Clin Immunol*. 2007; 17: 367–374.
8. Trzcinska H, Dziedziczko A. Allergic diseases among high school students with Sick building syndrome in the background. *Int Rev Allergol Clin Immunol*. 2005; 3: 99–103.
9. Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. *Pediatrics* 1985; 75: 859–868.
10. Leynaert B, Sunyer J, Garcia-Esteban R, Svanes C, Jarvis D, Cerveri I, et al. Gender differences in prevalence, diagnosis and incidence of allergic and non-allergic asthma: a population-based cohort. *Thorax*. 2012; 67: 625–631.
11. Torén K, Ekerljung L, Kim JL, Hillström J, Wennergren G, Rönmark E, et al. Adult onset asthma in west Sweden – incidence, sex differences and impact of occupational exposures. *Respir Med*. 2011; 105: 1622–1628.
12. Antó JM, Sunyer J, Basagaña X, Garcia-Esteban R, Cerveri I, de Marco R, et al. Risk factors of new-onset asthma in adults: a population based international cohort study. *Allergy* 2010; 65: 1021–1030.
13. Majkowska-Wojciechowska B, Pełka J, Korzon L, Kozłowska A, Kaczała M, Jarzebska M, et al. Prevalence of allergy, patterns of allergic sensitization and allergy risk factors in rural and urban children. *Allergy* 2007; 62: 1044–1050.
14. Ekici A, Ekici M, Kocyigit P, Karlidag A. Prevalence of self-reported asthma in Urban and rural areas of Turkey. *J Asthma* 2012; 49: 522–526.
15. Beasley R, Crane J, Lai CK, Neil P. Prevalence and etiology of asthma. *J Allergy Clin Immunol*. 2000; 105: 466–472.
16. Baumeister H, Korinthenberg K, Bengel J, Harter M. Bronchial asthma and mental disorders – a systematic review of empirical studies. *Psychother Psychosom Med Psychol*. 2005; 55: 247–255.
17. Busse W, Lemanske RF. Jr. Asthma. *N Eng J Med*. 2001; 344: 350–262.
18. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol*. 2004; 113: 59–65.
19. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961; 4: 53–63.
20. Spielberger CD, Gorsuch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press; 1970.
21. Wang L, Mo ZC, Ji YL. The study on relationship between negative mood states and asthma control and quality of life. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2009; 40(3): 544–547.
22. Demoly P, Gueron B, Annunziata K, Adamek L, Walters RD. Update on asthma control in five European countries: results of a 2008 survey. *Eur Respir Rev*. 2010; 19: 150–157.
23. Trzcinska H, Przybyłski G, Kozłowski B, Derdowski S. Analysis of the relation between the level of asthma control and depression and anxiety. *Med Sci Monit*. 2012; 18: CR 190–194.
24. Mainous AG III, Kohrs FP. A comparison of health status between rural and urban adults. *J Comm Health*. 1995; 20: 423–431.
25. Morgan A. A national call to action: CDC's 2001 urban and rural health chartbook. *J Rural Health*. 2002; 18:382–383.
26. Lavoie KL, Bacon SL, Barone S, Cartier A, Ditto B, Labrecque M. What is Worse for Asthma Control and Quality of Life: Depressive Disorders, Anxiety Disorders, or Both? *Chest*. 2006; 130: 1039–1047.
27. Wang L, Mo ZC, Ji YL. The study on relationship between negative mood states and asthma control and quality of life. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2009; 40: 544–547.
28. Wang G, Wang L, Szczepaniak WS, Xiong ZY, Wang L, Zhou T, et al. Psychological status in uncontrolled asthma is not related to airway hyperresponsiveness. *J Asthma*. 2010; 47: 93–99.
29. Vieira AA, Santoro IL, Dracoulakis S, Caetano LB, Fernandes ALG. Anxiety and depression in asthma patients: impact on asthma control. *J Bras Pneumol*. 2011; 37: 13–18.
30. Di Marco F, Verga M, Santus P, Giovannelli F, Busatto P, Neri M, et al. Close correlation between anxiety, depression, and asthma control. *Respir Med*. 2010; 104: 22–28.
31. Strine TW, Mokdad AH, Balluz LS, Berry JT, Gonzalez O. Impact of depression and anxiety on quality of life, health behaviors, and asthma control among adults in the United States with asthma, 2006. *J Asthma*. 2008; 45: 123–133.
32. Allen GM, Hickie I, Gandevia SC, McKenzie DK. Impaired voluntary drive to breathe: a possible link between depression and unexplained ventilatory failure in asthmatic patients. *Thorax*. 1994; 49: 881–884.
33. Rubin NJ. Severe asthma and depression. *Arch Fam Med*. 1993; 2: 433–440.