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Asthma in men and women: Treatment adherence, anxiety, and quality of sleep

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Summary
The aim of this study was to compare female and male asthmatics with special emphasis on reported adherence, anxiety, and quality of sleep.

The study included 470 subjects with current asthma from the Nordic countries, who took part in the European Community Respiratory Health Survey (ECRHS) II. Subjects were investigated with a structured clinical interview, including questions on the presence of respiratory symptoms and therapy. They were also asked to fill in the self-reported Hospital Anxiety Depression scale and the Basic Nordic Sleep Questionnaire.

Inhaled corticosteroids (OR = 0.55) and a doctor's appointment in the last 12 months (OR = 0.54) implied a significantly reduced risk for non-adherence in normal situations. At exacerbation in asthma, women had a significantly decreased risk for non-adherence (OR = 0.46). Female gender and anxiety were independent risk factors for both insomnia (OR = 3.67 and 2.53, respectively) and daytime sleepiness (OR = 2.53 and 2.04, respectively).

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Women with asthma have a more positive attitude towards their medication, have a higher reported adherence, and use inhaled corticosteroids more often than men. At the same time women report more often anxiety and insomnia than men. Awareness of sex differences in the manifestations and attitudes towards treatment of asthma is important in order to improve asthma management.

Introduction

In early childhood, asthma is more common among males, but after puberty the incidence increases in females[1–3] and decreases in males.[4] In addition, asthma after childhood is more severe in females than in males, and is more frequently under-diagnosed and undertreated in females.[5] In general, there is a large sex difference among adults presenting to emergency departments with acute asthma.[6] The female majority present with specific and important pathophysiological features; however the observed differences may also represent sex differences in use of health care.[6] Several studies suggest that men and women respond differently to their asthma disease, and that gender differences in various measures of asthma such as symptoms, hospital admissions, and quality of life may be explained by this response to disease, rather than to real differences in disease characteristics between men and women.[1–8]

Patients with chronic diseases are in general more at risk for mental disorder.[9] Feldman et al. found that mood and anxiety disorder were the most common psychiatric diagnoses in a patient sample of 85 adult asthma patients. However, patients with and without mental disorders did not differ with regard to asthma severity[10]. Feldman et al. concluded in another study of 21 asthma patients with panic disorder and 27 asthma patients without that the initial treatment goal should be to distinguish between anxiety mobilizing appropriate asthma self-management versus panic anxiety that is often mistaken as an asthma exacerbation[11].

Depression among those with asthma is associated with poor adherence to medication regimens, more severe asthma, and poorer disease outcomes[12,13]. Cluley et al. showed that the highest psychiatric morbidity was found among those asthma patients who were poorly controlled, were less adherent to their medication, and more frequently dropped out from clinic visits.[14]

The presence of psychological problems along with attitudes, feelings and beliefs about asthma and its treatment may affect patient behavior. Characteristics which adversely affect self-care, including compliance with treatment, should be identified and addressed so that morbidity due to asthma can be reduced.[15] The literature contains particularly strong evidence regarding the effects of anxiety on asthma. Along with the heightened prevalence rates of anxiety disorders, in particular panic disorder, this points to the important role of psychopathology in asthma.[16]

The aim of this study was to compare female and male subjects with asthma with special emphasis on reported adherence, anxiety, and quality of sleep.

Methods

Study design

The first European Community Respiratory Health Survey (ECRHS I) documented treatment and self-reported adherence,[17,18] while in the follow-up study (ECRHS II) gave the opportunity to study the factors affecting adherence to asthma treatment.

ECRHS I[19] was a multicentre study on the prevalence, determinants, and management of asthma performed in 48 study centres during 1991–1993. ECRHS II[20] was a follow-up study, performed between 1999 and 2002, of the participants in the second stage of ECRHS. The following analyses include data from Sweden, Iceland, and Norway covering 470 subjects with current asthma in the ECRHS II.

Ethics approval

Local ethics committees at each centre approved the study protocols.

Questionnaires

Each participant underwent a structured clinical interview including questions on the presence of asthma, respiratory symptoms, and therapy. The full questionnaire can be found at www.ecrhs.org/quests. Participants were also asked to fill in the self-reported Hospital Anxiety Depression (HAD) scale[21] and the Basic Nordic Sleep Questionnaire (BNSQ) on sleep disturbances.[22] The HAD questionnaire consists of 14 questions 7 related to anxiety and 7 related to depression. Each item is rated on a 4-pointscale: 0, not at all: 1, sometimes: 2, often: 3, all the time, giving maximum subscale scores of 21 for anxiety and depression, respectively. The participants were asked to describe their feelings during the last week. In the validation of the questionnaire, a score of 0–7 in the two subscales has been found to discriminate non cases, from doubtful cases with a score of 8–10 and scores of 11 or more for definite cases of anxiety and depression, respectively.[21] There is also a third cutoff of 14/15 for severe disorder.[23] The HAD questionnaire gives clinically meaningful results as a psychological screening tool, in clinical group comparisons and correlation studies with several aspects of disease and quality of life.[24] The questionnaire was found to perform well in assessing the symptom severity and caseness of anxiety disorders and depression in both somatic, psychiatric and primary care patients and in the general population.[25] The seven questions on sleep disorders were derived from the Basic Nordic Sleep Questionnaire and had

been used previously in the Respiratory Health in Northern Europe (RHINE) study.[26] Participants were asked to estimate the frequency of different symptoms during the last months on a five point scale: 1, never; 2, less than once a week; 3, 1–2 nights per week; 4, 3–5 nights per week; and 5, almost every night.

Definitions

Asthma-related variables

Physician-diagnosed asthma was defined as a positive answer to both of the questions ''Have you ever had asthma?'' and ''Was this confirmed by a doctor?''[27] Asthma-related symptoms were classified as wheezing, nocturnal chest tightness, and attacks of breathlessness following activity, at rest or at night during the previous 12 months. *Symptomatic asthma* was defined as physician-diagnosed asthma and asthma-related symptoms or attacks of asthma in the previous 12 months.[28] *Age of asthma onset* was estimated from the answer to the question: ''How old were you when you had your first attack of asthma?''

Blood samples were collected for measurement of total and specific serum IgE using the Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden). Specific IgE was measured against *Dermatophagoides pteronyssinus*, cat, timothy grass and *Cladosporium herbarum*. *Atopy* was defined as sensitisation to at least one of the allergens investigated (≥ 0.35 kU/l)

Adherence

Adherence in normal situations was assessed by the question: ''When you have been prescribed medicine for your breathing, do you normally take: all the medicine, most of the medicine, some of the medicine, or none of the medicine?'' *Adherence during exacerbations* was assessed by the question: ''When your breathing gets worse, and you are prescribed medicine for your breathing, do you normally take all of the medicine, most of the medicine, some of the medicine or none of the medicine?'' Patients answering ''all of the medicine'' were defined as being adherent.[18,29]

The attitude to therapy was defined as a positive answer to the questions: ''Do you think it is bad for you to take medicines all the time to help your breathing'' and ''Do you think you should take as much medicines as you need to get rid of all your breathing problems''?[18]

The following adherence-related variables were considered: smoking habits, having taken inhaled corticosteroids in the previous 12 months, having regular appointments for asthma with a doctor or a nurse, having written instructions from a doctor, having a personal peak expiratory flow (PEF) meter, and having had spirometry during the previous 12 months.[29]

Asthma control

Table 1. Definition of asthma control[30,31]

Anxiety and depression

The definition of anxiety and depression was a cutoff point of 8 for the two sub-scales.

Table 1 Definition of asthma control.[30,31]

Asthma was considered controlled if all the following features were present:

asthmasymptoms	less than once a week
no astma attacks	in the last 3 months
no activity limitations	in the last 12 months
no nocturnal symptoms	in the last 3 months
short-acting beta-2agonists twice or less per week	in the last 3 months
no use of oral steroids	in the last 12 months
FEV$_1$ of 80 % of predicted value or greater	

Asthma was considered partly controlled if 1 or 2of the above features were absent
Asthma was considered uncontrolled if more than 2 features were absent or:

if asthma, shortness of breath, or wheezing had caused hospital/emergency department admission	in the last 12 months
oral steroids were used	in the last 12 months
more than 12 asthma attacks	in the last 3 months

Insomnia and excessive daytime sleepiness

Three aspects of insomnia were assessed: difficulty inducing sleep as ''difficulty in falling asleep at night'', difficulty maintaining sleep as ''waking up repeatedly during the night'', and early morning awakenings as ''waking up too early and having difficulty in getting to sleep again''. Insomnia was defined as reporting at least one of the three aspects with a frequency of at least 3 nights a week.[26] Excessive daytime sleepiness was defined as reported problems with daytime sleepiness at least 3 days/week.[32]

Statistical analysis

Statistical analyses were performed using the STATA 9 software (Stata Corp.,College, Station, Texas, USA). Chi-squared tests and unpaired *t*-test were used to compare characteristics between men and women. Multiple logistic regression model was used to analyse determinants for adherence, insomnia and daytime sleepiness. A *p*-value < 0.05 was considered to be statistically significant.

Results

Descriptive results

In total 40 % of the participants ($n = 189$) were men and 60 % ($n = 281$) were women. There were no differences in age and body mass index between the sexes. Men were more to be sensitised to mite, cat, timothy and *C. herbarum* than women, and also had a lower age of asthma onset (Table 2).

Women with asthma were more likely than men to be smokers, have a PEF-meter, use inhaled corticosteroids and have seen a doctor in the last 12 months. There was no difference in asthma control between men and women (Table 2).

Factors associated with adherence, insomnia and daytime sleepiness

Women with asthma had a higher self reported adherence and a less negative attitude towards their medication than men (Table 3).

The results of the logistic regression analysis on risk factors for non-adherence are summarized in Table 4. Inhaled corticosteroids and an appointment with a doctor in the last 12 months implied a significantly reduced risk for non-adherence in normal situations. No significant association was found for age, nocturnal attacks of breathlessness, smoking, anxiety and non-adherence in normal situations. Women had a significantly reduced risk for non adherence in exacerbations. Subjects with anxiety were more likely to report being non-adherent in exacerbations (Table 4). No significant sex difference was found in the association between risk factors and reported non-adherence ($p_{interaction} > 0.1$ for all independent variables).

In this study women had a higher prevalence of anxiety, insomnia, and daytime sleepiness compared to men (Fig. 1). Female gender was an independent risk factor for insomnia and daytime sleepiness when this was analysed in a multiple logistic model (Table 5). Older asthmatics were more likely to report insomnia than their younger counterparts. Anxiety was an independent risk factor for both insomnia and with excessive daytime sleepiness (Table 5), No significant sex difference was found in the association between risk factors and sleep- related variables ($p_{interaction} > 0.1$ for all independent variables). No significant association was found between sensitisation to allergens and adherence, insomnia or daytime sleepiness.

Discussion

The main finding of this study was that in comparison to men, women with asthma had a higher self - reported adherence and a less negative attitude towards their medication than men and were more likely to have used inhaled corticosteroids and had appointments with a doctor in the last 12 months. Women had a higher prevalence of anxiety, insomnia, and daytime sleepiness than men. No significant sex difference was found in asthma control.

In the present study women with asthma were more adherent than their male counterparts in both in normal and in exacerbation. The main finding of ECRHS II, (the follow-up study of the international cohort) compared to ECRSH I was that adherence to asthma treatment remained low worldwide; although it increased significantly in Continental and extra-European areas, and subjects living in Nordic countries were less likely to be compliant.[29] The major predictors of increased or persistent adherence were regular appointment with health care professionals, and positive beliefs about medication. Adherence is a complex, multidimensional, and dynamic phenomenon that is influenced by many factors related to the patients, doctors, disease, and therapy. To achieve optimal asthma control, it is important to identify factors that contribute to non-adherence.[33,34]

Table 2 Characteristic of patients with asthma in the Nordic centres of ECHRS II (mean±SD and %).

	Men (n = 189)	Women (n = 281)	p-value
Age (year)	42.0 ± 7.4	42.3 ± 7.2	0.62
BMI	26.1 ± 3.2	26.7 ± 5.7	0.23
Age of asthma onset	17.1 ± 13.7	21.9 ± 13.3	0.0002
Atopy	68.0	43.6	<0.0001
Dermatophagoides pteronyssinus	23.4	14.9	0.04
cat	49.4	33.5	0.002
timothy	49.4	26.7	<0.0001
Cladosporium herbarum	12.3	2.7	<0.0001
Nocturnal attacks of breathlessness	18.6	25.7	0.07
Personal peak expiratory flow meter	21.9	31.6	0.02
Smoking history			0.002
never-smokers	51.6	43.2	
ex-smokers	33.5	27.9	
current smokers	14.9	28.9	
Inhaled corticosteroids	41.6	52.2	0.03
Seen a physician last 12 months	33.6	46.2	0.02
Regular appointments hospital doctor	4.8	6.6	0.44
Regular appointments GP	7.4	9.1	0.53
Regular appointments nurse	0	2.9	0.02
Emergency room treatment last 12 months	6.9	9.7	0.28
Asthma control			0.54
Controlled	33.5	36.1	
Partly controlled	39.5	34.2	
Uncontrolled	27.0	29.7	

Table 3 Medication in the cohort (%).

	Men ($n = 189$)	Women ($n = 281$)	p-value
Use of medication normally			0.08
all of the medicine	46.2	57.3	
most of the medicine	23.4	18.1	
some of the medicine	30.4	23.8	
none of the medicine	0	0.8	
Adherent in normal situations	46.2	57.3	0.02
Use of medication during exacerbations			0.002
all of the medicine	55.3	73.5	
most of the medicine	20.0	12.6	
some of the medicine	24.0	13.9	
none of the medicine	0.7	0	
Adherent during exacerbations	55.3	73.5	<0.0001
Medicine all the time considered harmful	48.2	35.3	0.009
Should take as much medication as needed to get rid of all symptoms	35.6	39.5	0.43
Adherence in normal and exacerbations			<0.0001
adherent only in normal situations	11.7	6.2	
adherent only at exacerbations	14.0	17.7	
adherent in both situations	34.5	51.2	

Previous studies have shown that the prevalence of anxiety is higher in women than in men, and increases with age.[15,35] The opposite was found about depression in Norway, the prevalence of depression is higher in men than in women.[36] The relationship between psychological manifestation and respiratory symptoms is a point to consider in the management of asthma.[37] Neuman et al. found that symptoms related to anxiety and especially depression are important determinants for the development of dyspnea, while there was less evidences that dyspnea induces psychological symptoms.[38] Bonala et al. reported a positive correlation between both increased anxiety and depression and higher dose of corticosteroids in asthmatics.[39] Depression and anxiety among people with asthma are also associated with an increased level of impaired health related quality of life.[40]

Our results are differ in some respects from those of Lee et al. who found that female asthma patients reported significantly greater health care utilisation, more unscheduled office contact, more asthma control problems, and had more allergic manifestations than men.[41]

Conversely we found no sex differences in asthma control, and atopy was more common in male asthmatics than in female asthmatics.

In our study female asthmatics were much more likely to have problems with insomnia and excessive daytime sleepiness. The significance of insomnia and daytime sleepiness should be taken into consideration in the search for optimal asthma control. Krouse et al. concluded that asthma is a chronic inflammatory disease that can significantly affect the individual's physical and psychosocial functioning, for example in terms of daytime wakefulness and sleep quality.[42] The increased insomnia seen in adult women may begin to manifest in early adolescence as excessive daytime sleepiness.[43] Improvement in sleep quality has been shown to correlate with improvement in asthma control, even in individuals without a specific history of asthma-related nocturnal awakenings.[44]

To some extent the reported sex differences could be related to differences in asthma phenotypes between men and women. Women had a later asthma onset and were less likely to have allergic asthma. Non-allergic asthma may be

Table 4 Independent determinants for non-adherence in normal and acute situations: adjusted OR (95% CI)[a]

	Non-adherence in normal situations	Non-adherence in exacerbations
Women	0.64 (0.37–1.10)	0.46 (0.25–0.85)
Age per 10 year	0.85 (0.59–1.24)	1.00 (0.66–1.53)
Nocturnal attacks of breathlessness	0.92 (0.47–1.82)	0.67 (0.30–1.46)
Smoking history		
never-smokers	1	1
ex-smokers	1.34 (0.72–2.49)	1.16 (0.59–2.30)
current smokers	1.34 (0.65–2.78)	1.37 (0.60–3.14)
Inhaled corticosteroids	0.55 (0.31–0.97)	0.74 (0.40–1.38)
Seen a physician in the last 12 months	0.54 (0.31–0.94)	0.61 (0.32–1.16)
Anxiety	1.17 (0.61–2.24)	2.35 (1.18–4.69)

[a] Adjusted for the variables in the table and centre.
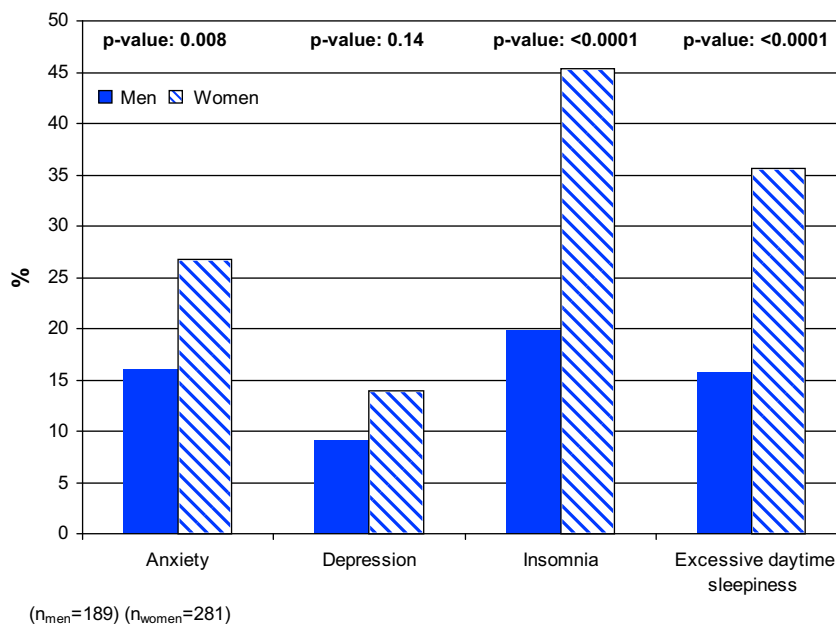
Figure 1   Anxiety, depression, insomnia and excessive daytime sleepiness in the study.

Table 5   Independent determinants for insomnia and excessive daytime sleepiness adjusted OR (95% CI)[a]

	Insomnia	Excessive daytime sleepiness
Women	3.67 (1.94—6.95)	2.53 (1.32—4.86)
Age per 10 year	1.62 (1.07—2.45)	0.80 (0.52—1.22)
Nocturnal attacks of breathlessness	1.85 (0.91—3.79)	1.87 (0.91—3.59)
Smoking history		
never-smokers	1	1
ex-smokers	1.29 (0.66—2.52)	1.40 (0.69—2.81)
current smokers	0.97 (0.46—2.07)	1.86 (0.87—3.95)
Inhaled corticosteroids	1.43 (0.76—2.67)	0.85 (0.44—1.65)
Seen a physician in the last 12 months	1.22 (0.66—2.28)	1.08 (0.57—2.06)
Anxiety	2.53 (1.32—4.85)	2.04 (1.54—5.60)

[a] Adjusted for the variables in the table and study centre.

less responsive to inhaled corticosteroid treatment[45] and thus more difficult to treat.

Women with asthma have a more positive attitude towards their medication, have a higher reported adherence, and use inhaled corticosteroids more often than men. At the same time women report more often anxiety and insomnia than men. Awareness of sex differences in the manifestations and attitudes towards treatment of asthma is important in order to improve asthma management.

Conflict of interest

None of the authors have a conflict of interest to declare in relation to this work.

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References

1. Osborne ML, Vollmer WM, Linton KLP, Buist AS. Characteristics of patients with asthma within a large HMO. A comparison by age and gender. *Am J Respir Crit Care Med* 1998;**157**:123—8.
2. Nicolai T, Pereszlenyiova-Bliznakova L, Illis S, Reinhardt D, von Mutius E. Longitudinal follow-up of the changing gender ratio in asthma from childhood to adulthood: role of delayed manifestation in girls. *Pediatr Allergy Immunol* 2003;**14**:280—3.
3. Torén K, Gislason T, Omenaas E, Svanes C, Jögi R, Forsberg B, Olin A-C, Janson C. A prospective study of asthma incidence and its predictors: the RHINE study. *Eur Respir J* 2004;**24**:942—6.
4. de Marco R, Locatelli F, Sunyer J, Burney Pthe European Community Respiratory Health Survey Study Group.

Differences in incidence of reported asthma related to age in men and women. *Am J Respir Crit Care Med* 2000;**162**:68–74.

5. Almqvist C, Worm M, Leynaert Bfor the working group of GA2LEN WP 2.5 'Gender'. Impact of gender on asthma in childhood and adolescen: a GA2LEN review. *Allergy* 2008;**63**:47–57.

6. Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CAfor the multicenter asthma research collaboration investigators. Sex differences among adults presenting to the emergency department with acute asthma. *Arch intern Med* 1999;**159**:1237–43.

7. Naleway AL, Vollmer WM, Frazier A, O'Connor E, Magid DJ. Gender differences in asthma management and quality of life. *J Asthma* 2006;**43**:549–52.

8. Prescott E, Lange P, Vestbo JThe Copenhagen City Heart Study Group. Effect of gender on hospital admissions for asthma and prevalence of self-reported asthma: a prospective study based on a sample of the general population. *Thorax* 1997;**52**:287–9.

9. Verhaak PFM, Heijmans JWM, Peters L, Rijken M. Chronic disease and mental disorder. *Soc Sci Med* 2005;**60**:789–97.

10. Feldman JM, Siddique MI, Morales E, Kaminski B, Lu S-E, Lehrer PM. Psychiatric disorders and asthma outcomes among high-risk inner-city patients. *Psychosom Med* 2005;**76**:989–96.

11. Feldman JM, Siddique MI, Thompson NS, Lehrer PM. The role of panic-fear in comorbid asthma and panic disorder. *J Anxiety Disord* 2009;**23**:178–84.

12. Goldney RD, Ruffin R, Fisher LJ, Wilson DH. Asthma symptoms associated with depression and lower quality of life: a population survey. *MJA* 2003;**178**:437–41.

13. Mancuso CA, Rincon M, McCulloch CE, Sharlson ME. Self-efficacy, depressive symptoms, and patient' expectations predict outcomes in asthma. *Med Care* 2001;**39**:1326–38.

14. Cluley S, Cochrane GM. Psychological disorder in asthma is associated with poor control and poor adherence to inhaled steroids. *Respir Med* 2001;**95**:37–9.

15. Bosley CM, Fosbury JA, Cochrane GM. The psychological factors associated with poor compliance with treatment in asthma. *Eur Respir J* 1995;**8**:899–904.

16. Kullowatz A, Kanniess F, Dahme B, Magnussen H, Ritz T. Association of depression and anxiety with health care use and quality of life in asthma patients. *Respir Med* 2007;**101**:638–44.

17. Janson C, Chinn S, Jarvis D, Burney P. Physician-diagnosed asthma and drug utilization in the European Community Respiratory Health Survey. *Eur Respir J* 1997;**10**:1795–802.

18. Cerveri I, Locatelli F, Zoia MC, Corsico A, Accordini S, de Marco Ron behalf of the ECRHS. International variations in asthma treatment compliance. The results of the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1999;**14**:288–94.

19. Burney PG, Lyczynska C, Chinn S, Jarvis D. The European Community Respiratory Health survey II. *Eur Respir J* 1994;**7**:954–60.

20. European Community Respiratory Health Survey II Steering Committee. The European Community Respiratory Health Survey II. *Eur Respir J* 2002;**20**:1071–9.

21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**. 361–37.

22. Partinen M, Gislason T. Basic Nordic Sleep Qustionnaire (BNSQ): a quantitated measure of subjective sleep complaints. *J Sleep Res* 1995;**4**:361–70.

23. Snaith RP, Zigmond AS. *HADS: Hospital Anxiety and Depression Scale*. Windsor: NFER Nelson; 1994.

24. Herrman C. International experiences with the hospital anxiety and depression scale – A review of validation data and clinical results. *J Psychosom Res* 1997;**42**:17–41.

25. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the hospital anxiety and depression scale. An updated literature review. *J Psychosom Res*. 2002 Feb;**52**(2):69–77.

26. Janson C, Norbäck D, Omenaas E, et al. Insomnia is more common among subjects living in damp buildings. *Occup Environ Med* 2005;**62**:113–8.

27. Torén K, Palmqvist M, Löwhagen O, Balder B, Tunsäter A. Self-reported asthma was biased in relation to disease severity while reported year of asthma onset was accurate. *J Clin Epidemiol* 2006;**59**:90–3.

28. Janson C, de Marco R, Accordini S, et al. Changes in the use of anti-asthmatic medication in an international cohort. *Eur Respir J* 2005;**26**:1047–55.

29. Corsico AG, Cazzoletti L, de Marco R, et al. Factors affecting adherence to asthma treatment in an international cohort of young and middle-aged adults. *Respir Med* 2007;**101**:1363–7.

30. National Heart Lung and Blood Institute. *Global initiative for asthma. Global strategy for asthma management and prevention. NHLBI/WHO workshop report*. Bethesda (MD): National Institutes of Health; 2006. National Heart lung and Blood Institute publication no. 02-3659.

31. Cazzoletti L, Marcon A, Janson C, et alfor the Therapy and Health Economics group of the European Community Respiratory Health Survey. Asthma control in Europe: a real-world evaluation based on an international population-based study. *J Allergy Clin Immunol* 2007;**120**:1360–7.

32. Janson C, De Backer W, Gislason T, Plaschke P, Björnsson E, Hetta J, Kristbjarnason H, Vermeire P, Boman G. Increased prevalence of sleep disturbances and daytime sleepiness in subjects with bronchial asthma: a population study of young adults in three European countries. *Eur Respir J* 1996;**9**:2132–8.

33. Baiardini I, Braido F, Giardini A, et al. Adherence to treatment: assesment of an unmet need in asthma. *J Investig Allergol Clin Immunol* 2006;**16**:218–23.

34. Janson SL, Earnest G, Wong KP, Blanc PD. Predictors of asthma medication nonadherence. *Heart Lung* 2008;**37**:211–8.

35. Cooper CL, Parry GD, Saul C, Morice AH, et al. Anxiety and panic fear in adults with asthma: prevalence in primary care. *BMC Fam Pract* 2007;**8**:62.

36. Nortvedt MW, Riise T, Sanne B. Are men more depressed than women in Norway? Validity of the hospital anxiety and depression scale. *J Psychosom Res*. 2006 Feb;**60**(2):195–8.

37. Rimington LD, Davies DH, Lowe D, Pearson MG. Relationship between anxiety, depression, and morbidity in adult asthma patients. *Thorax* 2001;**56**:266–71.

38. Neuman Å, Gunnbjörnsdottir M, Tunsäter A, et al. Dyspnea in relation to symptoms of anxiety and depression: a prospective population study. *Respir Med* 2006;**100**:1843–9.

39. Bonala SB, Pina D, Silverman A, Amara S, Bassett CW, Schnaider AT. Asthma severity, psychiatric morbidity, and quality of life: correlation with inhaled corticosteroid dose. *J Asthma* 2003;**40**:691–9.

40. 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 adult in the United States with asthma, 2006. *J Asthma* 2008;**45**:123–33.

41. Lee JH, Haselkorn T, Chipps BE, Miller DP, Wenzel SE. Gender differences in IgE- mediated allergic asthma in the epidemiology and natural history of asthma: outcomes and treatment regimens (Tenor) study. *J Asthma* 2006;**43**:179–84.

42. Krouse HJ, Yarandi H, McIntosh J, Cowen C, Selim V. Assessing sleep quality and daytime wakefulness in asthma using wrist actigraphy. *J asthma* 2008;**45**:389–95.

43. Camhi SL, Morgan WJ, Pernisco N, Quan SF. Factors affecting sleep disturbances in children and adolescents. *Sleep Med* 2000;**1**:117–23.

44. Mastronarde JG, Wise RA, Shade DM, Olopade CO, Scharf SMfor the American lung association and asthma clinical research centers. Sleep quality in asthma: results of a large prospective clinical trial. *J Asthma* 2008;**45**:183—9.

45. De Marco R, Marcon A, Jarvis D, Accordini S, Bugiani M, Cazzoletti L, Cerveri I, Corsico A, Gislason D, Gulsvik A, Jõgi R, Marinez-Mortalla J, Pin I, Janson C. Inhaled steroids and lung function decline in asthma. *J Allergy Clin Immunol* 2007;**119**:611—7.