Uncontrolled asthma and its risk factors in adult Chinese asthma patients

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Abstract

Background: Asthma affects a large number of patients in China, but relatively little is known about asthma management among Chinese patients. This study aims to estimate asthma control rate among adult Chinese patients and to identify predictors associated with uncontrolled asthma.

Methods: A total of 4125 asthma patients aged ⩾17 years and representing all regions of mainland China except Tibet were surveyed. Asthma control status was assessed using the Asthma Control Test (ACT) and classified as controlled (ACT score ⩾ 20) and uncontrolled (ACT score ⩽ 19). A multivariate logistic regression model was used to identify predictors associated with uncontrolled asthma from the factors including demographics, rhinitis, allergic rhinitis, and treatment adherence.

Results: Asthma was controlled in 44.9%, and uncontrolled in 55.1% of the study participants. High rates of uncontrolled asthma were found in patients with treatment nonadherence (77.3%), poor adherence (66.2%), no schooling (64.8%), or obesity (62.9%). The risk of uncontrolled asthma was much higher in the treatment nonadherence group than the complete adherence group [odds ratio (OR) = 4.55 (3.68–5.62), $p < 0.001$]. Other predictors for uncontrolled asthma included concomitant rhinitis [OR = 1.31 (1.14–1.50), $p < 0.001$], obesity [OR = 1.31 (1.05–1.64), $p = 0.019$], asthma duration > 3 years [OR = 1.22 (1.07–1.39), $p = 0.004$] and age ⩾ 45 years [OR = 1.23 (1.07–1.41), $p = 0.004$].

Conclusions: About half of the participants in this study had uncontrolled asthma. Treatment nonadherence is one of the significant predictors, which is very strongly associated with uncontrolled asthma. Efforts should be prioritized to promote patients' treatment adherence to improve asthma control while attention is needed on rhinitis or obesity.

Keywords: adult, asthma, cross-sectional studies, risk factors

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Introduction

Asthma is a severe chronic disease which induces airway hyper-responsiveness and results in recurrent symptoms such as wheezing, dyspnea and cough [GAN, 2014]. The prevalence of asthma has been increasing in recent years, and now affects as many as 334 million people worldwide [GAN, 2014; GINA, 2015]. A survey of 164,215 residents over the age of 14 years in eight Chinese provinces from February 2010 to August 2011 found the overall prevalence of asthma to be 1.2% [Feng *et al.* 2014]. The number of asthmatic patients in China has been estimated to be roughly 30 million [Lin *et al.* 2013].

Although asthma is not curable, many studies have shown that correct diagnosis, proper treatment and long-term management of asthma can improve the level of asthma control and enhance the quality of life [CTS, 2008]. Good management of asthma is also essential to reduce the economic burden of asthma. If not controlled properly, asthma can affect daily activities and result in physical, emotional and social limitations which can impair quality of life and even be fatal [Van Lieshout and MacQueen, 2012; Likhar *et al.* 2015]. According to the Global Initiative for Asthma (GINA), the long-term goals of asthma control are symptom control and risk reduction [GINA, 2015].

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Only limited information is available on the state of asthma management in Chinese patients, especially adult patients. A survey conducted in eight Asia-Pacific countries in 2011 reported that asthma was uncontrolled for a large proportion of patients, and that 98% of the 402 surveyed patients from mainland China were either uncontrolled or only partly controlled [Thompson *et al.* 2013]. However, a survey of 2034 asthma patients from eight Chinese provinces found that 15.6% were completely controlled and 49.5% were partly controlled, as evaluated by the Asthma Control Test (ACT) [Su *et al.* 2014]. The discrepancy between the findings of these two studies may be due to limitations in geographic distribution and sample size.

Asthma control is related to many factors. Medication adherence is an important determinant of asthma control, though nonadherence to asthma controllers among asthma patients is prevalent and maybe is an important reason for poor asthma control in many countries including China [Davidsen, 2012; Murphy *et al.* 2012; Ahmedani *et al.* 2013; Makela *et al.* 2013; Wang *et al.* 2013]. Allergic rhinitis (AR) is also a widely reported risk factor for asthma control. A study showed that 69.9% of Chinese asthma patients over the age of 14 years reported AR symptoms and that the presence and severity of AR were negatively associated with asthma control [Lin *et al.* 2014]. Studies also reported obesity is associated with subsequent poor asthma control [Schatz *et al.* 2015; Ulrik, 2016]. However, studies to comprehensively evaluate risks associated with poor asthma control in Chinese patients were still very limited.

This study aims to provide a comprehensive estimate of asthma control across mainland China and to identify predictors associated with uncontrolled asthma in Chinese asthma patients.

Methods

Study design and patients

This nationwide cross-sectional observational study was conducted in China between November 2012 and June 2013. It involved patients aged ⩾2 years who visited outpatient clinics of respiratory disease for treatment, prescription refill and consultation during the study period. A total of 8873 asthma patients were enrolled in this study. Here we report only the results from the 4125 participants aged 17 and older. The results from the 4223 participants aged 2–16 years will be reported separately.

The asthma patients ⩾17 years old were consecutively enrolled from 48 tertiary general hospitals in 34 cities of different provinces across China, covering all territories and regions of mainland China except Tibet. All participants had confirmed asthma for at least 3 months and had symptoms or took asthma medication during the past 12 months.

Asthma diagnosis was confirmed by medical chart review at the enrollment visit. The diagnosis of asthma was defined as the presence of relevant clinical history (i.e. history of recurrent dyspnea, wheezing or cough episodes) and pulmonary function tests demonstrating variable airflow limitation by means of airway responsiveness testing or airway reversibility testing, which satisfied those of GINA [GINA, 2015]. Asthma duration and treatment were also confirmed by medical chart review. Eligible patients were requested to sign the informed consent. Patients who had mild asthma, intermittent asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis, bronchitis, cystic fibrosis, lung cancer or pneumonia or who were not able to fill in the questionnaires were excluded.

The study protocol was originally approved by the Independent Ethics Committee of China–Japan Friendship Hospital. Other participating hospitals either accepted the decision of that committee or conducted a further independent ethics review, according to their own institutional policy.

Data collection

Sociodemographic and clinical information, including family history of allergic disease, concomitant disease (e.g. rhinitis and AR), asthma symptoms, asthma duration since diagnosis, asthma-related treatments and tests, and asthma treatment adherence, was collected from participants' medical charts during their visits. Any identifier to an individual patient, such as social security number, identification number and full name, was not collected. Body mass index (BMI) was measured and classified as normal ($18.5 \leqslant$ BMI <24), lean (BMI < 18.5), overweight ($24 \leqslant$ BMI < 28), and obesity (BMI $\geqslant 28$) based on Criteria Of Weight for Adults issued by National

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Health and Family Planning Commission (NHFPC) of China in 2013 [NHFPC, 2013]. Rhinitis was defined as nasal symptoms including sneezing, nasal blockage, itching of the nose occurring during multiple consecutive days for more than 1 hour on most days and not caused by cold or flu [Bousquet *et al.* 2008]. AR was defined as rhinitis associated with immunoglobulin (Ig) E-mediated immune response confirmed by serum specific IgE or skin prick test [Bousquet *et al.* 2008]. Asthma treatment adherence was assessed by physicians through review of prescription refill in the past 3 months and was classified into four levels: complete adherence (⩾90%), good adherence (70–89%), poor adherence (50–69%) and nonadherence (<50%).

The five-item ACT questionnaire was used to assess the level of asthma control [Zhou *et al.* 2009; Nguyen *et al.* 2012]. Asthma control was classified into controlled (ACT ⩾ 20) and uncontrolled (ACT ⩽ 19) [NIH, 2007]. Mini Asthma Quality-of-Life Questionnaire (Mini-AQLQ) was used to measure quality of life [Juniper *et al.* 1999]. Both questionnaires were completed by participants during the interview and reviewed by physicians for completeness.

Quality control

All data were collected using a uniform data collection form. All investigators were trained on the standardized study protocol and data collection form before initiation of the study. A clinical research organization (CRO) was employed to monitor the quality of data collection and to manage the data. All data were inputted into a programmed database by two people independently for statistical analysis.

Statistical analysis

Since the study was not testing any hypothesis, we calculated sample size based on the estimation of uncontrolled asthma rate. A sample size of 1500 was necessary (5% level of significance, two-sided) when we estimated uncontrolled asthma rate was 42% according to the result of the Asia Pacific Asthma Insights and Management study [Thompson *et al.* 2013]. With consideration of stratification analysis on AR comorbidity and other risk factors, we amplified the sample size to 4000. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were displayed by mean, median, standard deviation (SD), and first and third quartiles (Q1 and Q3). Categorical variables were summarized by frequency and percentage. Continuous variables were compared using two-sample Student's *t*-test. To explore the potential risk factors associated with uncontrolled asthma, the level of asthma control was summarized into two categories: controlled asthma (ACT ⩾ 20) and uncontrolled asthma (ACT ⩽ 19). The proportion of uncontrolled asthma in patients among two different characteristics groups was calculated and compared using a Chi-square test. A Cochran–Armitage test was used to detect the trend of proportions of uncontrolled asthma in patients among more than two ordinal categories. Factors of statistical significance ($p < 0.1$) were analyzed using multivariate logistic regression models to identify the risk factors associated with uncontrolled asthma. Odds ratio (OR) and the 95% confidence interval (CI) of each factor from the multivariate logistic regression models was estimated and presented. A two-tailed p value < 0.05 was considered to be statistically significant.

Statistical analyses were performed using the SAS® System for Windows™ 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Demographic and clinical characteristics of study participants

A total of 4125 asthma patients aged ⩾17 years were enrolled in the study. The average age was 46.4 (±14.0), with a range of 17–94 years old. Female patients constituted 60.7% of the study population. A total of 67.7% of the participants (2793/4125) lived in cities and 7.0% (288/4125) were current smokers.

A total of 37.1% (1531/4124) of the participants had rhinitis in addition to asthma; overall, 15.2% (625/4124) had AR, and 6.9% (286/4125) reported medical history of allergic eczema. There were 21.0% of the participants (868/4125) with at least one first-degree relative with asthma.

The median duration of asthma since diagnosis was 3 years (Q1–Q3: 1.0–9.0). Cough (72.7%, 2999/4125) and wheeze (70.4%, 2904/4125) were the most common asthma symptoms reported. Overall, 51.0% of the participants (2105/4124) reported seasonal changes in asthma

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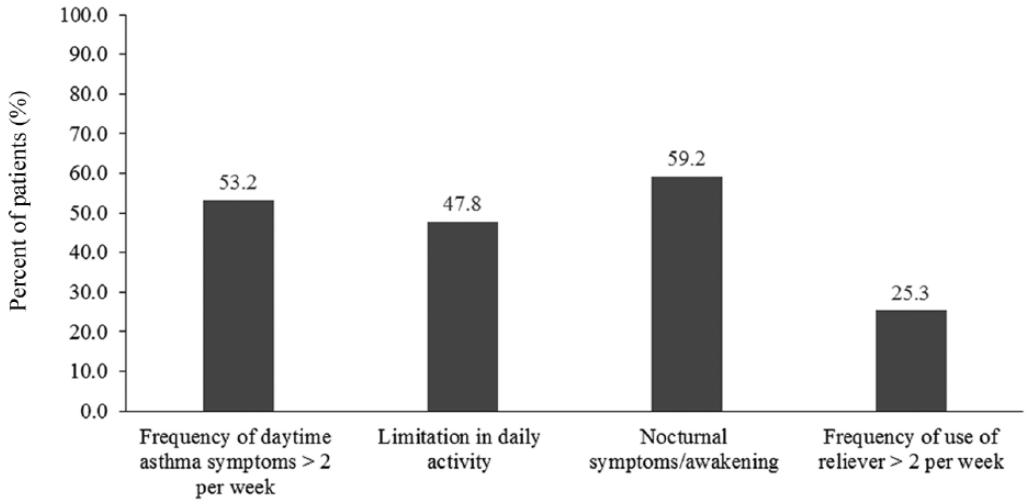

Figure 1. Asthma symptoms during the previous 4 weeks.

symptoms. A total of 12.1% (500/4124) were diagnosed with cough-variant asthma. Overall, 70.4% of the participants (2902/4123) reported having asthma symptoms during the previous 4 weeks. Detailed characteristics of the symptoms are shown in Figure 1. More than half of the participants (57.6%, 2374/4119) had asthma acute exacerbation during the past 3 months.

Management of asthma control

A total of 78.7% (3245/4125) of the study participants had taken asthma controllers during the previous 4 weeks. Most of them (88.4%, 2867/3245) used combination therapies. Inhaled corticosteroids (ICSs) plus long-acting β-agonists (LABAs) fixed dose combination (FDC) was the most common combined therapy, followed by ICS/LABA FDC plus a leukotriene receptor antagonist (LTRA). The distribution of combination therapies used by study participants is shown in Figure 2A. A small portion of the patients (11.6%, 378/3245) used monotherapies, with ICSs being the most frequently used monotherapy. The distribution of monotherapy drugs used by study participants is shown in Figure 2B.

A total of 21.3% (880/4125) of the participants had not taken any asthma controller during the previous 4 weeks. Of these, 88.4% (775/877) stopped taking controllers on their own, of which 53.3% (413/775) stopped because they thought their asthma symptoms had been relieved. Only 39.0% (1607/4116) of all patients maintained complete asthma controller adherence. In addition, among all study participants, only 31.9% (1314/4125) had undergone skin prick testing and 11.7% (483/4125) had serum-specific IgE testing.

Uncontrolled asthma and its impact on quality of life

According to ACT criteria, asthma was controlled (ACT $\geqslant$ 20) in 44.9% of the participants and remain uncontrolled (ACT $\leqslant$ 19) in 55.1% of them. The frequency of uncontrolled asthma in groups with different characteristics is shown in Table 1. High frequencies of uncontrolled asthma were found in participants with poor asthma treatment adherence (66.2%) or nonadherence (77.3%). Participants with rhinitis had a higher frequency of uncontrolled asthma than those without rhinitis (57.5% *versus* 53.6%, $p = 0.016$). The frequency of uncontrolled asthma in those with or without AR was almost the same (54.9% *versus* 55.1%, $p > 0.05$). The frequency of uncontrolled asthma among the participants with concomitant AR was significantly lower in those with corresponding AR treatment than without it, but this difference was not statistically significant (previous AR treatment: 52.2% *versus* 58.6%, current AR treatment: 51.2% *versus* 56.8%, both $p > 0.05$).

Participants with uncontrolled asthma had significantly lower total scores and individual domain scores on the Mini AQLQ compared with those with controlled asthma (all $p < 0.001$)

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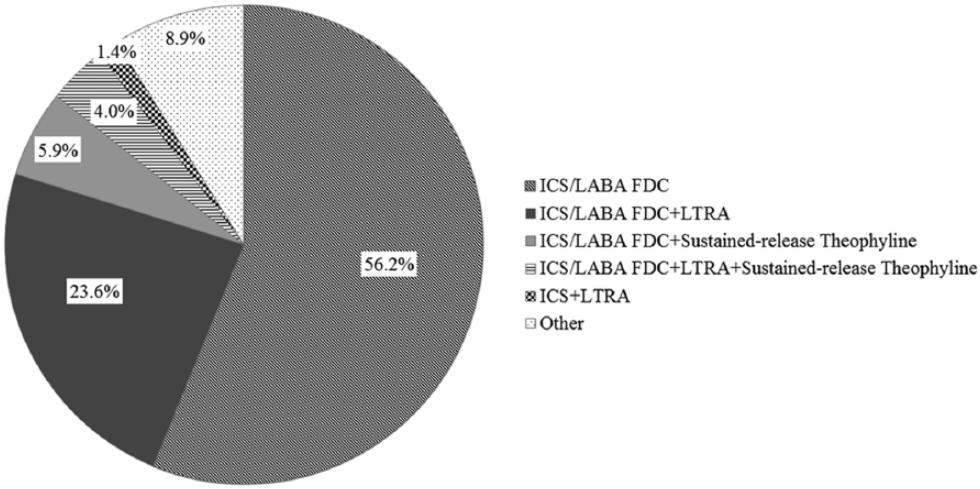

Figure 2A. Distribution of combination therapies for asthma control.
FDC, fixed dose combination; ICS, inhaled corticosteroids; LABA, long-acting β-agonists; LTRA, leukotriene receptor antagonist.

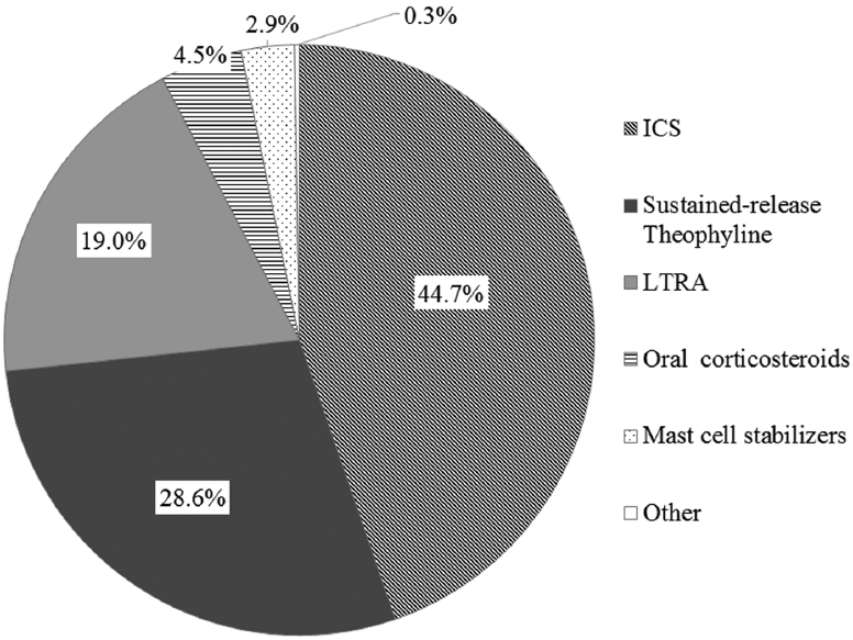

Figure 2B. Distribution of monotherapy medicines for asthma control.
ICS, inhaled corticosteroids; LTRA, leukotriene receptor antagonist.

(Figure 3), showing that the quality of life of patients with uncontrolled asthma is significantly affected in terms of symptoms, activity, emotions and environment.

Risk factors of uncontrolled asthma

As shown in Table 1, several factors were associated with level of asthma control. BMI was related to level of asthma control. Participants with normal BMI had a lower frequency of uncontrolled asthma compared with those in overweight and obese groups (52.6% *versus* 57.0% and 62.9%, $p < 0.05$). Education level was negatively related to uncontrolled asthma. The frequency of uncontrolled asthma decreased from 64.8% to 44.5% as education level increased from 'no schooling' to 'college and above' ($p < 0.001$). Asthma treatment adherence was also important contributor in asthma control. The frequency of uncontrolled

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Table 1. Uncontrolled asthma in various patient groups.

Factor	*N* (%*)	Uncontrolled asthma *n* (%$)	*p*-value‡
Overall	4125	2271 (55.1%)	
Age group (years)			
17–29	565 (13.7%)	238 (42.1%)	<0.001
30–44	1299 (31.5%)	698 (53.7%)	
45–59	1511 (36.6%)	910 (60.2%)	
60–70	572 (13.9%)	325 (56.8%)	
>70	178 (4.3%)	100 (56.2%)	
Sex			
Male	1620 (39.3%)	867 (53.5%)	0.111
Female	2505 (60.7%)	1404 (56.0%)	
BMI (kg/m^2)			
18.5 ⩽ BMI <24 (normal)	2134 (51.9%)	1122 (52.6%)	<0.001
BMI < 18.5 (lean)	230 (5.6%)	123 (53.5%)	
24 ⩽ BMI < 28 (overweight)	1327 (32.3%)	756 (57.0%)	
BMI ⩾ 28 (obese)	423 (10.3%)	266 (62.9%)	
Smoking status			
Never smoked	3270 (79.3%)	1781 (54.5%)	0.111
Exsmoker	567 (13.7%)	321 (56.6%)	
Current smoker	288 (7.0%)	169 (58.7%)	
Education			
No schooling	145 (3.5%)	94 (64.8%)	<0.001
Primary school	555 (13.5%)	338 (60.9%)	
Junior high school	1091 (26.4%)	653 (59.9%)	
Senior high school	1097 (26.6%)	635 (57.9%)	
College and above	1237 (30.0%)	551 (44.5%)	
First-degree relative(s) with asthma			
Yes	868 (21.0%)	500 (57.6%)	0.089
No	3257 (79.0%)	1771 (54.4%)	
Concomitant rhinitis			
Yes	1531 (37.1%)	880 (57.5%)	0.016
No	2593 (62.9%)	1390 (53.6%)	
Concomitant AR			
Yes	625 (15.2%)	343 (54.9%)	0.929
AR treated previously			
Yes	458 (86.7%)	239 (52.2%)	0.319
No	70 (13.3%)	41 (58.6%)	
Current AR treatment			
Yes	377 (82.3%)	193 (51.2%)	0.360
No	81 (17.7%)	46 (56.8%)	
No	3499 (84.8%)	1927 (55.1%)	
Asthma duration > 3 years since diagnosis			
Yes	1812 (44.0%)	1064 (58.7%)	<0.001
No	2309 (56.0%)	1204 (52.1%)	
Asthma treatment adherence			
Complete adherence	1607 (39.0%)	664 (41.3%)	<0.001
Good adherence	1115 (27.1%)	606 (54.3%)	
Poor adherence	739 (18.0%)	489 (66.2%)	
Nonadherence	655 (15.9%)	506 (77.3%)	

*Percentage of total number of patients who answered each question.
$ Percentage of total number of patients in each category.
‡For factors of two categories, *p*-value was calculated using Chi-square test comparing proportions of uncontrolled asthma between the two categories. For factors of more than two categories, *p*-value was calculated using Cochran–Armitage test on the trend of proportions of uncontrolled asthma across the ordinal categories.
AR, allergic rhinitis; BMI, body mass index.

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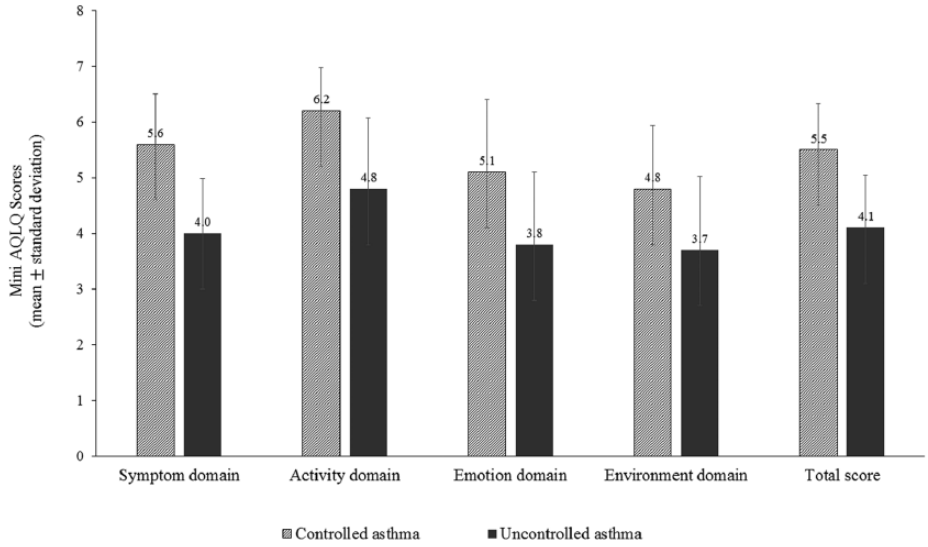

Figure 3. Mini AQLQ scores among patients with controlled and uncontrolled asthma.
AQLQ, asthma quality-of-life questionnaire.

Table 2. Risk factors of uncontrolled asthma.

Factor	Odds ratio (95% CI)*	*p*-value*
Age ⩾ 45 years	1.23 (1.07–1.41)	0.004
Female (*versus* 'male')	1.10 (0.93–1.30)	0.263
BMI (*versus* 'normal')		
<18.5 (lean)	1.06 (0.79–1.41)	0.703
24–27.9 (overweight)	1.08 (0.93–1.25)	0.296
⩾28 (obese)	1.31 (1.05–1.64)	0.019
Current or previous smoking	1.12 (0.92–1.37)	0.247
Education (*versus* 'no schooling')		
Primary school	0.97 (0.65–1.45)	0.865
Junior high school	1.00 (0.68–1.48)	0.989
Senior high school	0.93 (0.63–1.37)	0.730
College and above	0.58 (0.39–0.85)	0.006
First-degree relative(s) with asthma	1.08 (0.92–1.27)	0.332
Concomitant rhinitis	1.31 (1.14–1.50)	<0.001
Asthma duration > 3 years since diagnosis	1.22 (1.07–1.39)	0.004
Asthma treatment adherence (*versus* 'complete adherence')		
Good adherence	1.62 (1.39–1.90)	<0.001
Poor adherence	2.73 (2.27–3.28)	<0.001
Nonadherence	4.55 (3.68–5.62)	<0.001

*Odds ratio and *p*-value were from a multivariate logistic regression model with uncontrolled asthma as the event and all factors listed in this table as the predictors.
BMI, body mass index; CI, confidence interval.

asthma increased dramatically as treatment adherence decreased from complete adherence to nonadherence (41.3% *versus* 77.3%, $p < 0.001$). Additional factors were positively related to uncontrolled asthma including asthma duration since diagnosis >3 years and concomitant rhinitis.

Multivariate logistic regression analysis (Table 2) confirmed that the risk of uncontrolled asthma

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increased significantly as asthma treatment adherence decreased ($p < 0.001$). Compared with patients with complete adherence, the OR of uncontrolled asthma was 1.62 ($p < 0.001$) among patients with good adherence, 2.73 and 4.55 (both $p < 0.001$) for those with poor adherence and nonadherence, respectively. In addition, concomitant rhinitis (OR = 1.31, $p < 0.001$), obesity (OR = 1.31, $p = 0.019$), asthma duration since diagnosis > 3 years (OR = 1.22, $p = 0.004$) and age ⩾ 45 years (OR = 1.23, $p = 0.004$) were all found to significantly increase the risk of uncontrolled asthma. Patient education level above 'college' is a protective factor and negatively related to uncontrolled asthma (OR = 0.58, $p = 0.006$), compared with those with no schooling.

Discussion

More than half (55.1%) of the 4125 adult Chinese asthma patients surveyed in this study had uncontrolled asthma, indicating that asthma management in China is still a major challenge. Several risk factors for uncontrolled asthma were identified, including poor treatment adherence, concomitant rhinitis, asthma duration since diagnosis > 3 years, age ⩾ 45 years and obesity.

Previous studies have found that insufficient treatment is prevalent among asthma patients [Davidsen, 2012; Murphy *et al.* 2012; Ahmedani *et al.* 2013; Makela *et al.* 2013; Wang *et al.* 2013]. In the present study, asthma treatment adherence was low in most of the study participants, and 21.3% of the participants had not taken any asthma medication during the previous 4 weeks. Only 39.0% of them had complete asthma treatment adherence. The frequency of uncontrolled asthma was particularly high in patients with poorer asthma controller adherence. Multivariate logistic regression analysis showed that poor asthma treatment adherence was a significant risk factor associated with uncontrolled asthma. The risk of uncontrolled asthma in patients with nonadherence was 4.55 times of that for patients with complete adherence. All these results show that poor treatment adherence is a very important factor contributing to the high proportion of uncontrolled asthma among Chinese patients.

Among the participants who had not used asthma controllers during the previous 4 weeks, most stopped taking asthma controllers on their own and 53.3% stopped taking them because they thought their asthma symptoms had been relieved. These patients probably overestimated the level of asthma control they had achieved. This finding is consistent with a previous survey in the Asia–Pacific area which reported that one third of responders with severe persistent asthma thought their disease was either well or completely controlled [Thompson *et al.* 2013]. Differences between patient perceptions of asthma control and clinically defined asthma control is an important factor for low asthma treatment adherence in Chinese patients. Efforts should be made to improve patients' understanding of asthma control and of the importance of good treatment adherence.

Rhinitis was identified as predictor associated with uncontrolled asthma (OR = 1.31, $p < 0.001$) in this study. This was different from many studies where concomitant AR was usually reported as predictor for asthma control. The prevalence of rhinitis in this study was 37.1% and it was higher than the prevalence of AR 15.2% we found. A previous study showed that over 50% of patients with asthma or rhinitis in China had identifiable sensitivity to aeroallergens, as detected by a skin prick test [Li *et al.* 2009]. But there was insufficient use of a skin prick test (31.6%) or serum IgE test (11.7%) in this study population, which might have resulted in underdiagnosed AR among those with rhinitis. This might be the reason why the prevalence of AR is lower than the other study [Hojo *et al.* 2015]. Lin and colleagues also reported a higher prevalence of AR 69.9% in Chinese asthma patients [Lin *et al.* 2014], however, the definition of AR they adopted was only based on typical nasal symptoms without the evidence of an IgE-mediated immune response, which may have led to the overestimation of prevalence. Since AR was not identified as a contributor to uncontrolled asthma with statistical significance in the univariate analysis and both AR and rhinitis were moderately correlated (Spearman correlation coefficient = 0.55, $p < 0.001$), AR was not included in the multivariate logistic regression model for risk analysis. Nevertheless, when we used it to replace rhinitis in the model, very similar results were observed and AR was still found to be associated with increased risk of uncontrolled asthma (OR = 1.22, $p = 0.035$). It proved that our finding did not conflict with previous studies but was a new complement in this study context. The finding was also consistent with the study by Powell and colleagues where rhinitis adversely affected asthma control [Powell *et al.* 2015]. All of these

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suggest that diagnosis and treatment of concomitant AR or rhinitis may help to maintain good control of asthma in China.

Obesity has been reported to be associated with poor asthma control [Pradeepan *et al.* 2013; Schatz *et al.* 2015; Ulrik, 2016]. In the present study, high frequency of uncontrolled asthma (62.9%) was found in obese participants (BMI $\geqslant$ 28) and they had a 1.31-fold risk of uncontrolled asthma compared with those with normal BMI. This finding was similar to previous studies [Pradeepan *et al.* 2013; Schatz *et al.* 2015]. Response to pharmacological asthma therapy in obese patients showed that obese patients altered, in general less favorable, response to both reliever and controller medication compared with normal weight patients [Ulrik, 2016]. Obesity increases airway hyperresponsiveness and restoring normal body weight is an appropriate strategy for reducing airway hyperresponsiveness and controlling inflammation that may help improve asthma control [Kim *et al.* 2015]. Therefore, in addition to good treatment adherence, options such as weight loss and dietary intervention should be considered in asthma management.

A study conducted in China reported that children with asthma with a longer disease course and regular follow up had better treatment compliance and fewer asthma attacks [Thomas *et al.* 2010]. Those finding implied that patients with a longer duration of asthma tended to have better drug adherence and better control of asthma. However, a study conducted in Warsaw in Polish reported that a longer duration of the disease was associated with worse asthma control [Krasnodebska *et al.* 2012]. All those studies indicated that a longer duration of asthma does not necessarily mean better drug adherence and asthma control. In this study, we found that patients with a duration of asthma more than 3 years had a higher risk of uncontrolled asthma (OR = 1.22, p = 0.004). This implied that patients with a longer duration of asthma in China may still not be well trained in terms of following standard asthma management and correct perception of asthma control. This study also revealed that having 'college and above' education was a protective factor for asthma control (OR = 0.58, p = 0.006), which was consistent with other studies' common findings that higher socioeconomic status or health literacy have been associated with good asthma control [Cope *et al.* 2008; Sheehan and Phipatanakul, 2015]. All the above implies that patient educational intervention should be included in asthma management to increase treatment adherence and also improve asthma control.

Since this study was a cross-sectional survey, no definite conclusion can be drawn about the causal relationship between risk factors and uncontrolled asthma. The enrollment of study participants depends on patient clinical visits and their willingness to be surveyed which might result in selection bias. Patients willing to attend the study might be prone to follow physician advice or their prescription during previous treatment, which may cause better adherence for them than those not in the study. Therefore, the proportion of patients with poor or nonadherence may be underestimated. Additionally, the judgment of adherence in this study was based on outpatient prescription refill during the past 3 months rather than actual dosage that the patients took, which may have led to complete or good adherence to have been overestimated to some extent. There was still a possibility that outpatients hospitalized due to an asthma attack during the past 3 months before the study and all related inpatient treatments for asthma could not be included in their records of outpatient clinics, which also jeopardized the accuracy of judgment of adherence. Also, since the participants all came from tertiary general hospitals, it is possible that the symptoms of asthma among these patients were more severe than in ordinary asthma patients such as patients visiting lower-grade hospitals. This may be a reason for the high proportion of uncontrolled asthma among surveyed patients. We excluded intermittent asthma because it does not necessarily need controller treatment and has limited negative impacts on patient's daily activity and sleep due to a symptom duration of less than once a week. We also excluded mild asthma. Therefore, interpreting the results needs caution that the uncontrolled rate of asthma might be overestimated for overall asthmatic patients. The study was carried out between November and June of the following year when the impact of rhinitis/AR on asthma control could be modified by the season. This could be another explanation for the high rates of uncontrolled asthma in this study [Hojo *et al.* 2015]. Our study found that patient education level was positively related to asthma control, however it might be confounded by socioeconomic class. Although people with higher education are very likely to have better or competitive earnings, meanwhile it could not be

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denied that the rich could purchase better healthcare than the poor. Future studies should exclude such confounding effects to generate more solid evidence. Nevertheless, this study provided a comprehensive profile of the most recent asthma control status in Chinese adult patients. The results should serve as a valuable reference to guide further management of asthma control in China.

The long-term goals of asthma control, as defined by GINA, are symptom control and risk reduction. The results of this study revealed that the level of asthma control in China is still far below the goal. Poor asthma treatment adherence was the most important risk factor contributing to uncontrolled asthma. Patients' lack of knowledge of standard asthma control might be an underlying reason for poor treatment adherence. This may be improved through educating patients about asthma control and improving the awareness of asthma management. Diagnosis and appropriate treatment of AR or rhinitis are also important.

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