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# A multicenter, cross-sectional, observational study of budesonide/formoterol maintenance and reliever therapy in real-world settings

Jiangtao Lin [a, *], Jing Li [b], Wencheng Yu [c], Yuejian Liu [d], Chuntao Liu [e], Ping Chen [f], Huijie He [g], Bei He [h], Shuang Liu [i], Xiangdong Zhou [j]

[a] Department of Respiratory Diseases, China-Japan Friendship Hospital, Peking University, Beijing 100029, China
[b] State Key Laboratory of Respiratory Disease, Department of Allergy and Clinical Immunology, Guangzhou Institute of Respiratory Disease, First Affiliated Hospital of Guangzhou Medical University, Guangzhou 510120, China
[c] Department of Respiratory Medicine, Affiliated Hospital of Qingdao Medical College, Qingdao 266071, China
[d] Department of Respiratory Medicine, Sichuan Provincial People's Hospital, Chengdu 610072, China
[e] Department of Respiratory Medicine, West China Hospital, Sichuan University, Chengdu 610041, China
[f] Department of Respiratory Medicine, The Second Xiangya Hospital of Central South University, Changsha 410011, China
[g] Department of Respiratory and Critical Care, The First Affiliated Hospital of Baotou Medical College, Baotou 014040, China
[h] Department of Respiratory Medicine, Peking University Third Hospital, Beijing 100191, China
[i] Department of Respiratory and Critical Care, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China
[j] Department of Respiratory Medicine, Southwest Hospital, 1st Affiliated Hospital of Third Military Medical University, Chongqing 400038, China

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ABSTRACT

*Background:* To assess the level of asthma control achieved with budesonide/formoterol in Chinese patients with asthma, based on the Global Initiative for Asthma (GINA) definition and Asthma Control Test (ACT) score.

*Methods:* This multicenter, cross-sectional study (NCT01785901) evaluated asthma control levels in Chinese patients receiving physician-prescribed budesonide/formoterol treatment. Adults with a diagnosis of asthma ≥6 months and receiving budesonide/formoterol treatment ≥3 months before screening were consecutively enrolled. Data including medical and medication history were collected using face-to-face questionnaires and physical examinations during a single visit.

*Results:* A total of 1483 asthma out-patients from 27 medical centers were enrolled; 217 (14.6%) were treated with budesonide/formoterol using a fixed-dose strategy and 1266 (85.4%) with the SMART (Symbicort® Maintenance And Reliever Therapy) strategy. According to GINA criteria, asthma was controlled in 58.6% (95% CI: 56.1%–61.1%) of patients and was either controlled or partly controlled in 94.1% (95% CI: 92.8%–95.3%) of patients. According to ACT score, asthma was completely controlled in 22.4% (95% CI: 20.3%–24.6%) of patients and was either completely or well controlled in 83.3% (95% CI: 81.4%–85.2%) of patients. Multivariate logistic regression analysis revealed that a >5-year history of asthma and an age of >50 years were factors associated with lower levels of asthma control.

*Conclusions:* This study demonstrated high levels of asthma control (GINA: controlled and partly controlled and ACT: completely and well controlled) in Chinese patients with asthma treated with budesonide/formoterol. Greater age and a longer disease history were associated with lower levels of asthma control.

*Trial registration:* ClinicalTrials.govNCT01785901. Registered February 5, 2013.



*Abbreviations:* ACT, Asthma Control Test; COPD, chronic obstructive pulmonary disease; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; LABA, long-acting inhaled $\beta_2$-agonist; SMART, Symbicort® Maintenance And Reliever Therapy.

* Corresponding author. Department of Respiratory Diseases, China-Japan Friendship Hospital, Peking University, No.2 Yinghua East Street, Chaoyang District, Beijing 100029, China.

*E-mail addresses:* jiangtao_l@263.net (J. Lin), jingli1016@vip.163.com (J. Li), qdyuwencheng@163.com (W. Yu), andyyjliu@163.com (Y. Liu), taosen666@vip.163.com (C. Liu), pingchen0731@sina.com (P. Chen), 2628191690@qq.com (H. He), puh3_hb@bjmu.edu.cn (B. He), liushuang862002@163.com (S. Liu), xiangdongzhou@126.com (X. Zhou).

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## 1. Introduction

Asthma is a chronic inflammatory airway disorder associated with a reduction in quality of life and work productivity, affecting more than 300 million people worldwide [1]. The disease is characterized by episodic symptoms and fluctuating levels of inflammation, which may culminate in an exacerbation [1]. The Global Initiative for Asthma (GINA) recommends the use of medications to control the underlying inflammation and symptoms, and to prevent exacerbations as part of an asthma management plan [1]. In current clinical practice, inhaled corticosteroids (ICS) are the most effective anti-inflammatory medication for treating asthma and are used in combination with long-acting inhaled $\beta_2$-agonists (LABA) for patients not controlled on ICS alone [1]. The use of an ICS combined with LABA has several advantages, including improvements in symptoms and lung function, and reductions in asthma-related hospitalizations and exacerbations [1].

Currently, several ICS/LABA combination agents are available in China, including salmeterol/fluticasone, budesonide/formoterol, and beclomethasone/formoterol. Of these combination agents, budesonide/formoterol is authorized for use in asthma as maintenance therapy (fixed dose) or as both maintenance and reliever therapy (SMART), providing greater flexibility in dosing. In at risk patients, SMART significantly reduces exacerbations while providing similar levels of symptom control at a relatively low dose of ICS in comparison to fixed-dose ICS/LABA regimens [1]. Multiple randomized, double-blind studies have shown that budesonide/formoterol treatment using a fixed dose or SMART strategy can achieve similar asthma control compared with other ICS/LABA combinations [2–4]. A real-world study of the budesonide/formoterol SMART strategy demonstrated that 86.5% of patients achieved asthma control, defined as an Asthma Control Test (ACT) score $\geq$20 [5]. However, there have been few studies of GINA-defined asthma control levels in patients receiving budesonide/formoterol in real-world settings.

In China, there are now 30 million people with asthma [6], which places an enormous burden on healthcare resources. Furthermore, a recent report showed that 57% of adults and 26% of children have poorly controlled asthma [7]. Understanding the level of asthma control achieved with ICS/LABA is important to inform treatment decisions. To date, few real-world data have been published on the level of asthma control achieved with budesonide/formoterol in China.

Therefore, this study aimed to determine the levels of, and factors associated with, asthma control achieved with budesonide/formoterol, in real-world settings at tertiary hospitals in mainland China.

## 2. Patients and methods

### 2.1. Study design

This was a multicenter, cross-sectional, observational study of asthma control in patients treated with budesonide/formoterol in mainland China (NCT01785901). The study was conducted between May 9, 2013, and October 14, 2014, at 27 tertiary hospitals. Patients were eligible if they were $\geq$18 years with a diagnosis of asthma $\geq$6 months, and receiving budesonide/formoterol (Symbicort® Turbuhaler®; AstraZeneca, UK) treatment for $\geq$3 months before enrollment (at a stable maintenance dose $\geq$4 weeks prior to enrollment). Patients were excluded if they met any of the following criteria: (a) participation in any other clinical studies in the 3 months prior to enrollment; (b) $\geq$10 pack years of smoking history; (c) chronic obstructive pulmonary disease (COPD) or suspected COPD; (d) the use of any other asthma maintenance medication in addition to budesonide/formoterol during the previous 3 months; (e) acute asthma exacerbation during the previous 4 weeks. Written informed consent was obtained from all patients. All study procedures, including informed consent forms, were approved by the ethics committee at each institution in accordance with laws and regulations.

### 2.2. Data collection and outcome measures

The primary outcome measure was the level of asthma control according to the GINA (2011) definition (controlled, partly controlled, and uncontrolled as summarized in Table S1, Additional File 1) [8]. Secondary outcome measures included the level of asthma control defined by ACT score (completely controlled asthma: overall ACT score of 25; well-controlled asthma: 20–24; and uncontrolled asthma: $\leq$19) and the frequency of reliever use in the week prior to enrollment.

Patients were interviewed by investigators and completed a face-to-face questionnaire and physical examination during a single visit. All patients were required to complete an ACT form to determine their level of asthma control during the previous 4 weeks.

### 2.3. Statistical analysis

Statistical analysis was performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA). Associations between categorical variables and asthma control were analyzed using the Chi square test or Fisher's exact test. Multivariate logistic regression was used to investigate the factors affecting asthma control. Significance was defined by a p-value <0.05.

## 3. Results

### 3.1. Patient characteristics

A total of 1502 patients from 27 medical centers in mainland China were enrolled and 1483 patients (98.7%) were included in the full analysis set (FAS; Table 1).

The average duration of illness was 6.2 ± 9.0 years. The mean treatment duration with budesonide/formoterol was 15.7 ± 18.2 months, and of the three available dosages (80 μg/4.5 μg, 160 μg/4.5 μg, and 320 μg/9 μg), 160 μg/4.5 μg was most commonly prescribed (97.0% of patients). All patients administered budesonide/formoterol via a dry-powder-inhaler and the most common regimen was one inhalation, twice daily (71.4% of patients). At enrollment, 217 patients (14.6%) were using fixed-dose budesonide/formoterol and 1266 patients (85.4%) were using the SMART strategy.

### 3.2. GINA-defined asthma control level

According to the GINA definition, asthma was controlled in 868 (58.6%) patients, partly controlled in 526 (35.5%) patients, and uncontrolled in 87 (5.9%) patients (Table 2).

Sub-analysis demonstrated that the factors associated with asthma control status included age ($p < 0.0001$), gender ($p = 0.0029$), asthma history ($p < 0.0001$), and education level ($p < 0.0001$; Table 3).

There was a significantly greater proportion of patients with controlled asthma among those with a disease course of <2 years (69.1%) compared with those with a disease course of 2–5 years and >5 years (55.8% and 44.2%, $p < 0.0001$). The proportion of patients with partly controlled and uncontrolled asthma followed a similar pattern: 28.3% and 2.6% in those with a disease course of <2