

Self-reported reasons for treatment non-adherence in Chinese asthma patients: A 24-week prospective telephone follow-up study

Qianli Ma¹ | Guangming Luo² | Xiangdong Zhou² | Ying Huang³ | Enmei Liu³ |
Xin Hong⁴ | Liangping Mao⁵ | Yamei Wu⁶ | Xumei Chen⁷ | Xiuqing Liao⁸ |
Guangmei Qin⁹ | Daoxin Wang¹⁰ | Lian Li¹¹ | Shifu Zhang¹² | Changzheng Wang¹

¹Institute of Respiratory Disease, Xinqiao Hospital, Third Military Medical University, Chongqing, China

²Department of Respiratory Medicine, Southwest Hospital, Third Military Medical University, Chongqing, China

³Department of Respiratory Medicine, Children's Hospital of Chongqing Medical University, Chongqing, China

⁴Department of Respiratory Medicine, Daping Hospital, Third Military Medical University, Chongqing, China

⁵Department of Respiratory Medicine, Chongqing Three Gorges Central Hospital, Chongqing, China

⁶Department of Respiratory Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

⁷Department of Respiratory Medicine, No.324 Hospital of Chinese PLA

⁸Department of Respiratory Medicine, Fuling Center Hospital of Chongqing, Chongqing, China

⁹Department of Respiratory Medicine, Yongchuan Hospital of Chongqing Medical University, Chongqing, China

¹⁰Department of Respiratory Medicine, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

¹¹Department of Respiratory Medicine, Jiangjin Central Hospital, Chongqing, China

Abstract

Background: Treatment non-adherence is a challenge to achieve asthma control. However, few prospective studies were done for exploring asthma patient adherence in real world.

Objectives: To evaluate treatment adherence and causes of non-adherence in a large asthma Chinese population. To analyze newly-diagnosed patients' adherence first time.

Methods: About 1582 asthma patients' data were collected from 12 study centers in China from February, 2012 to October, 2012. Disease and treatment information of subjects were collected were at first clinic visit, at 4, 12, and 24 weeks after that, follow-up phone calls were carried out for recording subjects' treatment adherence based on their self-reports. Subjects who reported non-adherence were additionally asked to choose the primary non-adherence cause from a list of nine potential causes.

Results: Treatment adherence rate of all subjects markedly decreased from 83.3% at week 4 to 42.0% at week 24 after the first clinic visit. Significantly, at week 24, good treatment adherence rate in newly-diagnosed patients was lower than those patients with asthma history (22.9% vs. 63.9%, $P < .001$). Newly-diagnosed patients were three times more likely to become non-adherence than those patients with asthma history. Female patients had lower treatment adherence rate than male patients (38.3% vs. 45.6%, $P = .006$). Subjects in 30-39 year age group had the worst treatment adherence (27.3%). The most commonly chosen cause for non-adherence was "relief of symptoms after short-term controller medication use" (43.8%).

Conclusions: Asthma patients' treatment adherence could be improved by improving patient education, doctor/patient partnership, and level of medical service in Chinese population.

KEYWORDS

doctor/patient communication, patient education, self-report, treatment adherence

¹²Department of Respiratory
Medicine, Chonggang Zong Hospital,
Chongqing, China

Correspondence

Changzheng Wang, No183 Xinqiao
Street, Xinqiao Hospital, Chongqing,
China, 400037.
Email: czwang@netease.com

1 | INTRODUCTION

Asthma is a common chronic respiratory disease, affecting more than 300 million people in the world.¹ With best evidence-based care, the majority of asthma patients can obtain satisfactory clinical benefit.² However, control of asthma is not achieved in many patients, particularly in the Asia-Pacific region. The Asthma Insights and Reality in Asia-Pacific Phase 2 (AIRIAP2) study indicates only 2.9% patients in that region achieve asthma control.³

Although there are many elements involved in good control of asthma, treatment adherence is perhaps the most important.¹ Improving treatment adherence in asthma patients is of significant value in improving asthma control,⁴ reducing mortality,⁵ and maximizing the utility of health resources.⁶ However, developing and implementing effective approaches to improve treatment adherence is challenging and requires long-term commitment from health care providers.

Treatment adherence rate in asthma patients ranges from 30% to 70%. The reported levels of adherence can be affected by a variety of factors, including location, study methods, and study periods.⁷ A study including more than 5500 patients indicated that in the United States only 22.2% asthma patients complied with treatment in a 1-year period.⁸ In developing countries, treatment adherence is even lower.⁷ The World Health Organization (WHO) proposed five interacting dimensions affecting adherence: social and economic factors; health care team and system-related factors; condition-related factors; therapy-related factors; and patient-related factors.⁷ Causes for treatment non-adherence are very complex and vary according to country and patients' cultural backgrounds. Health care providers must understand the main causes for treatment non-adherence in order to provide specific interventions.

So we designed this study to investigate treatment adherence and causes for non-adherence in asthma patients in Chongqing, a major city in Southwest China. Especially, which was focus on newly-diagnosed patients' adherence behaviors first time. This is the first large scale study addressing this issue in the Chinese population.

2 | METHODS

2.1 | Study design

This was a 24-week, prospective, telephone follow-up study conducted at 12 hospitals in Chongqing from February to October, 2012. This study included one clinic visit and three follow-up telephone calls, one each at 4, 12, and 24 weeks after the clinic visit. Information on gender, age, history of asthma diagnosis, and asthma control level were collected during the clinic visit. Self-reports on treatment adherence were collected during the follow-up phone calls, in which the details of physician prescription and actually using asthma medication (controller medication) were collected. Investigator calculated the ratio of actually using medication to expected medication consumption. For subjects under the age of 18, some reports were made by parents or guardians, and some reports were made by subject and parent/guardian together. Those patients reporting non-adherence were asked to choose one reason for their non-adherence from of list of nine potential reasons (see below). Once a patient reported non adherence, he or she received no further follow-up calls. A schematic representation of the study design is shown in Figure 1. This study was approved by the Medical Ethics Committee of Xinqiao Hospital at the Third Military Medical University. All patients, or, in the case of pediatric patients, parents, or guardians, gave written informed consent (Registration No:ChiCTR-OCH-12002744).

2.2 | Patients and measurements

Patients with a diagnosis of asthma and with the recommendation to use prescribed asthma "Controllers" (as defined by The Society of Paediatrics, Respiratory Diseases Subspecialty Group and the Chinese Medical Association Society of Respiratory Diseases Asthma Subspecialty Group) were consecutively recruited for this study. All recruited patients had been prescribed "controller" to control their symptoms, such as inhaled corticosteroids; a small number, primarily children, had also been prescribed anti-leukotriene as following doctor's advice in a short time. There was no

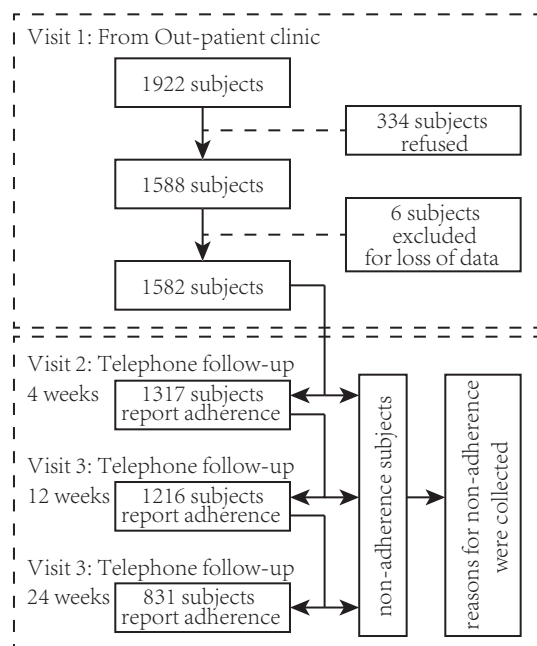


FIGURE 1 Study design. The schematic shows study design and numbers of subjects evaluated at the clinic visit and in the three subsequent follow-up telephone calls

limitation on gender or age. About 1922 eligible subjects were identified. And 334 were not included in the study due to refusal and 6 were excluded due to loss of data, leaving a total of 1582 subjects analyzed.

2.2.1 | Definition of treatment adherence

Adherence with medicine treatment was defined as a ratio of actual medication consumption to expected medication consumption in a specific time range before follow-up calls. The specific time ranges were 2 weeks before the week 4 call, 4 weeks before the week 12 call and 4 weeks before the week 24 call. Good adherence was defined to the rate between $\geq 80\%$ and $< 120\%$. Patients not meeting this definition of adherence with drug treatment were considered non-adherent.

2.3 | Causes for non-adherence

We defined nine potential causes for non-adherence, based on the WHO proposal,⁷ previous studies,⁹ and the authors' clinical experience: (1) high cost of medication, (2) diminished treatment effectiveness with long-term use, (3) poor self-efficacy, (4) relief of symptoms after short-term controller medication use, (5) occurrence/fear of side effects, (6) difficulty obtaining medication, (7) inconvenience of treatment, (8) preference for oral medication, and (9) other. We chose these causes in part because they are based on factors that can be addressed or changed, unlike inherent characteristics such as age or gender.

2.4 | Statistical analysis

Study data were managed using a clinical study database system at the center for Chronic Airway Disease Management, Department of Respiratory Diseases, Xinqiao Hospital. Active Server Page (ASP) was used to establish input interface and MySQL (a name of a relational database management system) database was used for recording. A Cox regression model was used in the analysis of the time to non-adherence. Chi-square test was used for comparison of proportions (adherence between different age groups, causes of non-adherence between different gender, time, diagnosis, age groups). Statistical significance was defined as a two-tailed *P* value of less than .05 by the use of software-assisted analysis of SPSS 12.

3 | RESULTS

3.1 | Subject characteristics

Of the 1922 eligible subjects identified, 334 were not included in the study due to refusal and six were excluded from the study due to loss of data, leaving 1582 participating subjects to be analyzed. About 728 of these subjects were men. The mean age was 40.92 ± 20.25 years old. About 848 participants were first diagnosed with asthma at the clinic visit which they joined this study. Table 1 shows patients' clinical characteristics.

3.2 | Treatment adherence

The results of this study revealed several factors that affect treatment adherence in asthma patients in west China. As shown in Figure 2A, treatment adherence of study subjects gradually decreased with prolongation of treatment from 83.3% at week 4 to 41.9% at week 24. Disease duration had a significant impact on adherence. Only 22.9% of newly diagnosed patients reported good treatment adherence at week 24 compared with 63.9% of patients with a history of asthma ($P < .001$). Cox regression analysis showed that newly diagnosed asthma patients were 3 times more likely to stop using their medication than patients with a history of asthma. Age was another important factor. At week 24, treatment adherence was particularly low among subjects young or middle age people. Treatment adherence in patients 30-39 old years was lower compared with the all other age groups except 20-29 old years (Figure 2B). Also, adherence among subjects aged 20-29 years was low as well, with significant differences when compared with subjects under 20 years of age ($P < .001$) and subjects 40-49 years of age ($P = .011$). Gender also played a role. Treatment adherence in female patients was significantly lower than male patients (38.8% vs. 45.6%, $P = .006$) at week 24.

TABLE 1 Patient characteristics

	Total	Newly diagnosed	History of asthma
Gender, females/males	854/728	467/381	387/347
Age, years (range)	45 (5-87)	47 (5-87)	42 (5-83)
Asthma control			
Well controlled, <i>n</i> (%)	99 (6.3%)	12 (1.4%)	87 (11.8%)
Partly controlled, <i>n</i> (%)	429 (27.1%)	54 (6.4%)	375 (51.1%)
Uncontrolled, <i>n</i> (%)	1054 (66.6%)	782 (92.2%)	272 (37.1%)

3.3 | Causes for non-adherence

Subjects reporting non-adherence were asked to choose the most relevant cause from a list of nine possible causes, as described in the Methods section. Overall the most frequently chosen cause was “relief of symptoms after short term controller medication use” (43.8%; Figure 3A). The next most frequently chosen cause was “poor self-efficacy” (14.8%), followed by “high cost of medication” (12.8%). Comparing frequencies at week 4, week 12 and week 24 showed that with prolongation of treatment the frequency of choosing “high cost of medication” and “poor self-efficacy” decreased, while frequency of choosing “difficulty obtaining medication” increased. While “relief of symptoms after short term controller medication use” was the most frequently chosen cause of non-adherence among both newly diagnosed asthma patients and those with history of asthma, there were significant differences between these groups in regard to other causes. “Poor self-efficacy” was chosen significantly more frequently by newly diagnosed patients ($P = .007$), while “diminished treatment effectiveness with long-term use” was chosen more frequently by those with a history of

asthma ($P < .001$; Figure 3B). Comparing responses from male and female subjects showed that male patients were significantly more likely to choose “difficulty obtaining medication” ($P = .002$) and “preference for oral medication” ($P = .004$) compared with female patients (Figure 3C). Responses also varied with age (Figure 3D). “High cost of medication” was more frequently chosen as the cause of treatment non-adherence by subjects aged 50 and older compared with younger subjects ($P = .019$). “Diminished treatment effectiveness with long-term use” was more frequently chosen by subjects under 20 years old compared with older subjects ($P < .05$), and less frequently chosen by subjects aged 50 and older compared with those aged 20-39 ($P < .05$).

4 | DISCUSSION

The results of this study show that, despite possible over estimation due to self-reporting, the level of treatment adherence in asthma patients in Chongqing, China is low, which is nearly 40% in the end of 24 week. It is noteworthy that

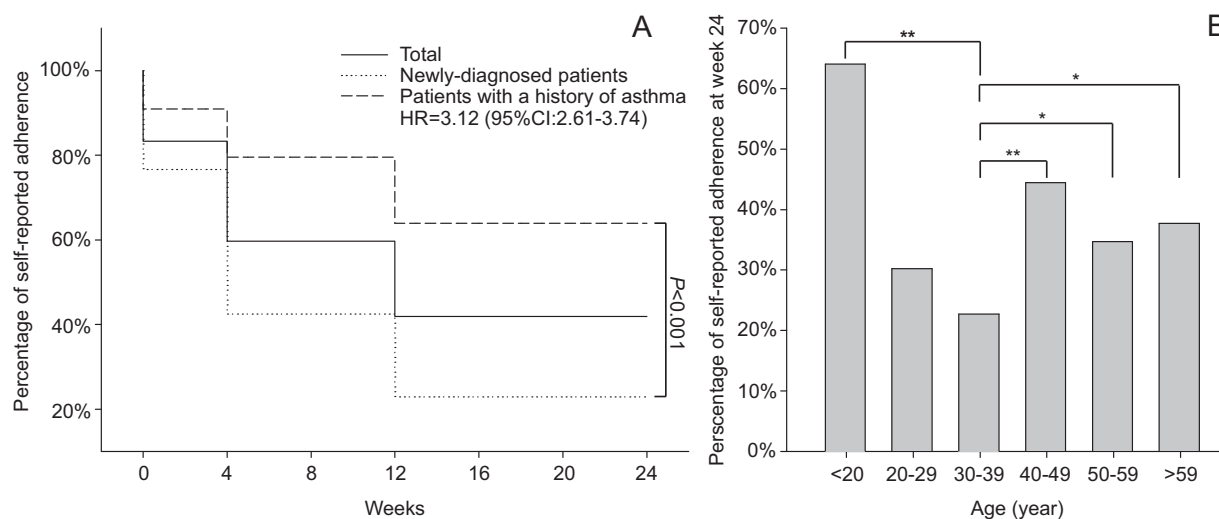


FIGURE 2 Effect of subject characteristics on treatment adherence. (A) Self-reported adherence of all subjects (total), newly diagnosed patients and patients with history of asthma. HR, hazard ratio. (B) Self-reported adherence of subjects at week 24 by age. * $P < .01$; ** $P < .001$

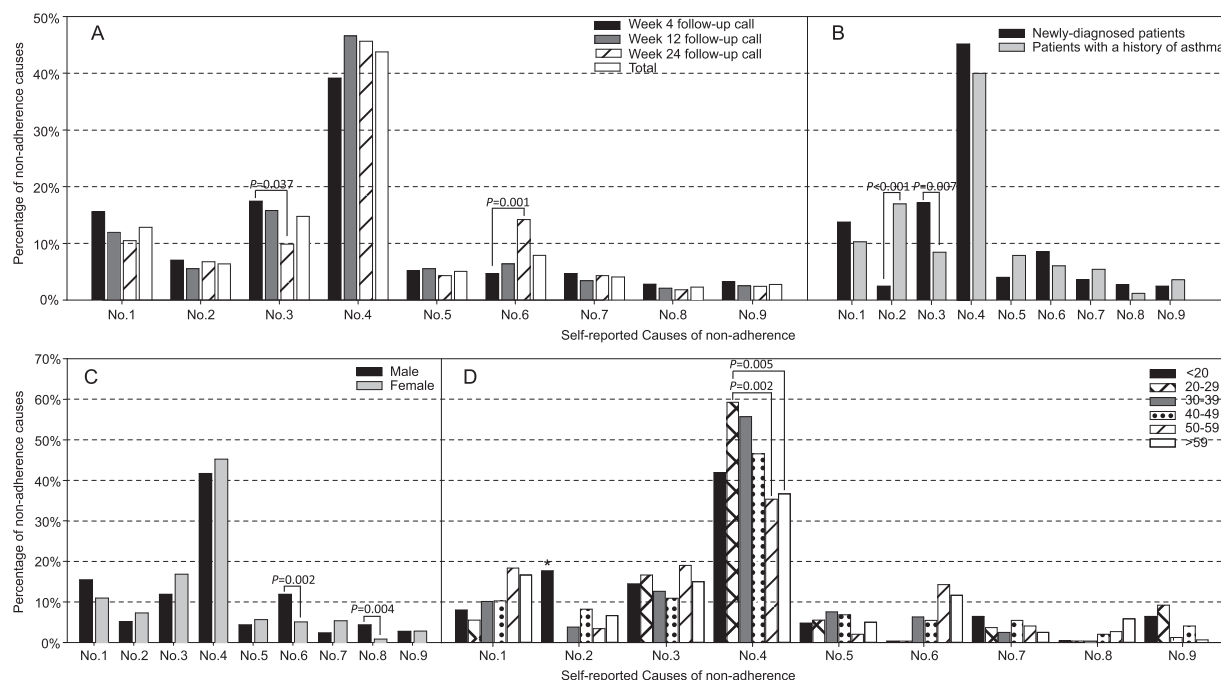


FIGURE 3 Causes of treatment non-adherence. (A) Self-reported causes of non-adherence at each of the three follow-up phone calls and in total. (B) Comparison of total self-reported causes of non-adherence between newly diagnosed patients and patients with a history of asthma. (C) Comparison of total self-reported causes of non-adherence between males and females. (D) Comparison of total self-reported causes of non-adherence between various age groups. * $P < .05$, compared with all other groups. No. 1: high cost of medication, No. 2: diminished treatment effectiveness with long-term use, No. 3: poor self-efficacy, No. 4: relief of symptoms after short-term medication use, No. 5: occurrence/fear of side effects, No. 6: difficulty obtaining medication, No. 7: inconvenience of treatment, No. 8: preference for oral medication, No. 9: other

newly diagnosed patients were with lower treatment adherence and were three times more likely to stop using their medication than patients with a history of asthma. This interesting result has not been reported before. Existing reports usually were focus on the patients with a history of asthma, not newly diagnosed patients. Therefore, maybe treatment adherence was been overestimated in most studies reported. Understanding these newly diagnosis patients' adherence behaviors and designed a special asthma management plan based on their characteristics may help then more. There are some similar findings such as treatment adherence in male patients is slightly higher than that in female patients which have been reported by Bender et al.⁸ And we also find that older adults have better adherence than younger adults.^{8,10-12} Although, Cruz et al., found that there were no difference in treatment adherence between different age groups.¹³ These conflicting results may be related to differences in the social environments of the various study populations. Treatment adherence is unlikely to be completely the individual's choice, but rather is probably the comprehensive outcome of interaction between social and environmental factors and personal choice.

Based on the self-reported feedback from the subjects in this study, the most common cause of treatment non-

adherence in asthma patients in Chongqing is "relief of symptoms after short-term controller medication use," with nearly 44% of the study subjects choosing that as the primary cause of no-adherence. "High cost of medication," previously assumed by most Chinese doctors to be the major reason for non-adherence,⁹ was only the third most common cause in this study population, chosen by approximately 13% of the subjects, lower than the 14.8% of the study subjects who identified "poor self-efficacy" as the cause of their non-adherence.

The fact that many asthma patients discontinue treatment because they experience relief of symptoms after short-term use of controller medication that may reflect the influence of variable asthma symptoms and deviation of patients' treatment expectations on patient adherence. With improving symptoms, some asthma patients may begin to doubt the original diagnosis of asthma and the value of regular treatment. Unfortunately, patient self-assessment of asthma symptoms is not always correct.¹⁴ In addition, poor communication between doctors and patients in China may aggravate this phenomenon.¹⁵ Poor doctor-patient communication and incomplete understanding of asthma as a chronic disease may also explain why some asthma patients discontinue treatment because of a feeling of low self-efficacy. There are

many ways to improve the doctor–patient relationship. For health care providers, an asthma management team which should consist of physicians, nurses, and other health actors, should be constructed in China. An evidence-based and practical asthma follow-up project is needed to be designed and to be performed in routine clinical practice. Especially, the details of every health actor's role, the content of asthma patient education are required to clarify. Reasons for asthma patients choosing to discontinue treatment because of high cost of medication probably have less to do with the doctor–patient relationship and more to do with medical insurance practices and the state of the economy. About 2013, the annual disposable income of residents in Chongqing was about 25,216 Yuan (RMB) (about 4000 dollars),¹⁶ while the direct annual cost of maintenance therapy for a typical asthma patient is about 3102 Yuan (about 492 dollars),¹⁷ accounting for 12.3% of disposable income. For patients supported by medical insurance (about 91% of the population in Chongqing are covered by basic medical insurance), personal cost is about 1260 Yuan (about 200 dollars)¹⁶ (Personal cost were calculated based on government-run insurance scheme.), accounting for 6.6% of disposable income. Better medical insurance support, cheaper drugs, or higher income would be needed to address this issue.

Our results suggest areas for improvement in patient education. “Relief of symptoms after short-term medication use” was the most commonly chosen cause for non-adherence, regardless of age, gender, disease duration, or treatment duration. To lower the frequency of non-adherence for this cause, all asthma patients should be educated on the benefits and risks of asthma treatment, and on ways to deal with the risks. Because “poor self-efficacy” was more frequently chosen as the cause of non-adherence by newly diagnosed patients, more effort should be made to teach newly diagnosed patients how to face unsatisfactory treatment efficacy and how to assess symptoms of asthma. And because “diminished treatment effect with long-term use” was more frequently chosen by patients under 20 years of age with a history of asthma, that issue should be routinely addressed with that patient population. However, because the cause for treatment non-adherence for some of the subjects in the less than 20 year group was actually chosen by adult parents or guardians, and because over all adherence among pediatric subjects is probably heavily influenced by adult parents or guardians, data from younger age groups need further analysis in the future. Our results also suggest areas for improvement in medical service. Strengthening communication and partnership between doctors and patients should decrease non-adherence due to almost all the causes considered in our study. Patients should feel comfortable asking help from medical service providers whenever they have questions or face challenges with their treatment regime. Development of

new medications that are less expensive, easier to use, and have fewer side effects would also be beneficial.

5 | CONCLUSIONS

Our results show that treatment adherence among asthma patients in Chongqing is low, particularly among newly diagnosed patients. The most commonly reported cause of non-adherence was “relief of symptoms after short-term controller medication use,” followed by “poor self-efficacy” and “high cost of medication.” These findings suggest that treatment adherence could be improved in this population by improving patient education, doctor/patient partnership and level of medical service.

ACKNOWLEDGMENTS

We thank all the patients who took part in this study. We acknowledge Dr. Qiao Zhang's assistance of draft the manuscript. We acknowledge Dr. Mary Chaiken's assistance of copy-editing. We acknowledge the valuable assistance of our colleagues, Min Wan, Hailin Li, Yin Wu. The study was funded by National Key Technology Support Program Numbers 2012BAI05B02 and 2014BAI08B05.

CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest in relation to this article.

AUTHOR CONTRIBUTIONS

QM draft the manuscript, participated in the design of the study, data management and statistical analysis. GL, XZ, YH, EL, XH, LM, YW, XC, XL, GQ, DW, LL, SZ and CW participated in subjects enroll, data collection, quality control and participated in the design of the study. All authors read and approved the final manuscript.

ETHICS

This study was approved by the Medical Ethics Committee of Xinqiao Hospital at the Third Military Medical University. All patients, or, in the case of pediatric patients, parents, or guardians, gave written informed consent (Registration No:ChiCTR-OCH-12002744).

Please cite this paper as: Ma Q, Luo G, Zhou X, Huang Y, Liu E, Hong X, Mao L, Wu Y, Chen X, Liao X, Qin G, Wang D, Li L, Zhang S and Wang C. Self-reported reasons for treatment non-adherence in Chinese asthma patients: A 24-week prospective telephone follow-up study. *Clin Respir J* 2016; 00:000–000. DOI:10.1111/crj.12525.

REFERENCES

- [1] Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA). 2014 [updated 2014; cited]. <http://www.ginasthma.org/>.
- [2] Bateman ED, Boushey HA, Bousquet J, et al. Can guideline-defined asthma control be achieved? the gaining optimal asthma Control study. *Am J Respir Crit Care Med*. 2004;170:836–844.
- [3] Lai CK, Ko FW, Bhome A, et al. Relationship between asthma control status, the asthma control test and urgent health-care utilization in Asia. *Respirology*. 2011;16:688–697.
- [4] Ying W, Qiao Z, Min W, et al. Status of asthma outpatient control and influencing factors for their revisit compliance. *J Third Mil Med Univ*. 2013;35:1305–1307.
- [5] Mohiuddin M, Zacharisen MC, Poulos C, Levy MB. Asthma deaths outside the hospital in an urban community from 2004 to 2008. *Ann Allergy Asthma Immunol*. 2012;108:412–417.
- [6] Makela MJ, Backer V, Hedegaard M, Larsson K. Adherence to inhaled therapies, health outcomes and costs in patients with asthma and COPD. *Respir Med*. 2013;107:1481–1490.
- [7] World Health Organization. *Adherence to Long-Term Therapies: Evidence for Action*. Geneva: WHO; 2003.
- [8] Bender BG, Pedan A, Varasteh LT. Adherence and persistence with fluticasone propionate/salmeterol combination therapy. *J Allergy Clin Immunol*. 2006;118:899–904.
- [9] Chiu KC, Boonsawat W, Cho SH, et al. Patients' beliefs and behaviors related to treatment adherence in patients with asthma requiring maintenance treatment in Asia. *J Asthma*. 2014;51:652–659.
- [10] Lacasse Y, Archibald H, Ernst P, Boulet LP. Patterns and determinants of compliance with inhaled steroids in adults with asthma. *Can Respir J*. 2005;12:211–217.
- [11] Bae YJ, Kim TB, Jee YK, et al. Severe asthma patients in Korea overestimate their adherence to inhaled corticosteroids. *J Asthma*. 2009;46:591–595.
- [12] Broder MS, Chang EY, Kamath T, Sapra S. Poor disease control among insured users of high-dose combination therapy for asthma. *Allergy Asthma Proc*. 2010;31:60–67.
- [13] Souza-Machado A, Santos PM, Cruz AA. Adherence to treatment in severe asthma: predicting factors in a program for asthma control in Brazil. *World Allergy Org J*. 2010;3:48–52.
- [14] Lai CK, De Guia TS, Kim YY, et al. Asthma control in the Asia-Pacific region: the asthma insights and reality in Asia-Pacific study. *J Allergy Clin Immunol* 2003;111:263–268.
- [15] Zhaofeng L, Xiaoyan W, Jian Z, et al. Typical investigation in ten cities of China: analytical on the status of doctor-patient relationship. *Chin Hosp*. 2008;12:7.
- [16] Government CMPs. Analysis of the development of social undertakings in Chongqing city in 2013. [www.cq.gov.cn: Bureau of Statistics of Chongqing](http://www.cq.gov.cn/Bureau of Statistics of Chongqing); 2014 [updated 2014; cited]; <http://www.cq.gov.cn/zwgk/qwfb/2014/9/1334605.shtml>.
- [17] Xiuli J. *Analysis of Economic Burden and Influence Factors of Bronchial Asthma in Jinan*. Shandong, China: Shandong University; 2012.