

# Prescription pattern of Chinese herbal products for adult-onset asthma in Taiwan: a population-based study

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## ABSTRACT

**Background:** Throughout the world, asthma can be a life-threatening disease. Traditional Chinese medicine (TCM) is commonly used among Taiwanese adults to control many diseases.

**Objective:** To analyze the use of Chinese herbal products (CHPs) among adults with asthma in Taiwan.

**Methods:** The use, frequency of service, and the type of CHP prescribed for asthma among adults with asthma were evaluated. The study group consisted of a randomly sampled cohort of 1,000,000 beneficiaries from the National Health Insurance Research Database. Logistic regression was used to estimate the odds ratios (ORs) for use of CHP.

**Results:** Overall, 20,627 asthma patients (85.7%) used TCM. Ding-chuan-tang (panting-stabilizing decoction) was the most frequently prescribed CHP, followed by xiao-qing-long-tang (minor green-blue dragon decoction) and ma-xing-gan-shi-tang (ephedra, apricot kernel, licorice, and gypsum decoction).

**Conclusion:** The use of CHPs among adults with asthma appears high. Ding-chuan-tang containing ma-huang is the most commonly prescribed and consumed among adults with asthma.

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## Introduction

The incidence and prevalence of asthma among adults, which is sometimes a life-threatening disease, appear to be increasing, and the disease now affects more than 8 million adults in the United States.<sup>1–4</sup> Although relief medication that quickly controls the bronchospasm and symptom controllers that prevent or diminish the inflammatory process and the consequent increase in airway hyperactivity are available for those with asthma,<sup>5</sup> there are a number of adverse effects of the steroids and  $\beta_2$ -adrenergic agonists in these medications, which may result in patients seeking alternatives.<sup>6–9</sup>

Traditional Chinese medicine (TCM) has been increasing in popularity and offers an important alternative or complementary medication in many countries. In contrast to the long history of use of TCMs for asthma, newer pharmacotherapeutic agents have been in use for a shorter period. Previous studies of TCMs have found that some Chinese herbs<sup>10–17</sup> may have antiasthmatic activity. TCM, which includes acupuncture, traumatology manipulative therapies, and Chinese herbal products (CHPs), has been an

important part of health care in Taiwan for hundreds of years and is fully reimbursed under the current National Health Insurance (NHI) system. Accordingly, the claims database part of the Taiwan National Health Insurance Research Database (NHIRD) provides a platform for understanding the use of TCM therapies by licensed TCM physicians. The aims of our study are to analyze a random sample from this comprehensive database and to determine CHP utilization patterns among Taiwanese adults newly diagnosed as having asthma. The results of this study should provide valuable information that will enable physicians to respond to patient use of TCMs in an informed way, which will, in turn, further strengthen the patient-physician relationship when treating asthma and asthma-related complications.

## Methods

### Data Resources

This study was conducted after approval by the review board of the Taipei City Hospital. It was designed as a population-based study analyzing a sample of 1 million individuals selected at random from the 22 million beneficiaries of the NHI scheme of Taiwan between January 1, 1997, and December 31, 2008. The data set was obtained from the NHIRD, which includes all the NHI reimbursement data with the identification numbers of all individuals encrypted and transformed; this database is maintained by the National Health Research Institutes of Taiwan.<sup>18,19</sup> The NHIRD contains the patient's sex, the patient's date of birth, all

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records of the patient's clinical visits and hospitalizations, and all drugs prescribed to the patient with dosages, including CHP, together with 3 major diagnoses coded using the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* format.<sup>20</sup>

### Study Participants

The selection of study participants from the random sample of 1 million individuals was performed as follows (Fig 1). First, we included all patients who had at least 3 outpatient visits with a diagnosis of asthma within 1 year ( $n = 50,955$ ) or having 1 or more hospital admission with an asthma diagnosis ( $n = 6,228$ ). A total of 53,251 study participants were obtained. Second, we excluded those with missing information on sex and age ( $n = 673$ ). Third, cases ( $n = 4,329$ ) that had been diagnosed before the end of 1997 and patients younger than 20 years ( $n = 24,187$ ) were also excluded to make sure that all the individuals included in the study were newly diagnosed as having asthma and to limit the study sample to adults. Finally, 24,062 study participants formed the study cohort.

### Traditional Chinese Medicine

CHPs composed of 1 or more herbs (the formula) are more widely adopted than other forms of TCM by patients in Taiwan.<sup>21–25</sup> To study the use of prescribed CHPs in the present study, we downloaded the detailed herbal content of all reimbursed CHPs from the website of the Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare, Taiwan, including the name of each CHP, the proportion of each constituent, the date and period of approval of use as a drug, the code, and the name of manufacturer.<sup>26</sup>

### Study Variables

To determine the key independent variables for use of CHP among adults with asthma, we selected a series of demographic factors based on previous studies.<sup>1,3,4,22–25</sup> Patients were classified, based on age, into 1 of 6 groups, as follows: 20 through 29 years, 30 through 39 years, 40 through 49 years, 50 through 59 years, 60 through 69 years, and 70 years or older. The geographic areas of Taiwan where patients resided were classified as 1 of the following 7 regions: Taipei City, Kaohsiung City, Northern region, Central region, Eastern region, Southern region and outlying islands. Patients' monthly income in New Taiwan dollars (NT\$) was categorized into 1 of the following 4 levels: \$0, \$1 through \$19,999, \$20,000 through \$39,999, and \$40,000 or more.

We also searched the NHIRD for diagnosis and treatment records related to asthma as independent variables. The clinical features associated with asthma may be classified as atopic (*ICD-9-CM* code, 493.0), nonatopic (*ICD-9-CM* code, 493.1), chronic obstructive (*ICD-9-CM* code, 493.2: asthma with chronic obstructive pulmonary disease, chronic asthmatic bronchitis), other forms of asthma (*ICD-9-CM* code, 493.8), and asthma unspecified (493.9). In addition, we categorized the types of medicines used for treating asthma according to clinical guidelines (Global Initiative for Asthma) into 2 groups: controllers (glucocorticosteroids, sodium cromoglycate, anti-leukotrienes, anti-IgE monoclonal antibody, and long-acting  $\beta_2$ -agonists) and relievers (short-acting  $\beta_2$ -agonists, anticholinergics, and epinephrine). Because the use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been associated with an increased risk of causing bronchospasm in susceptible patients with asthma, we also analyzed the use of NSAID use among adults with asthma.

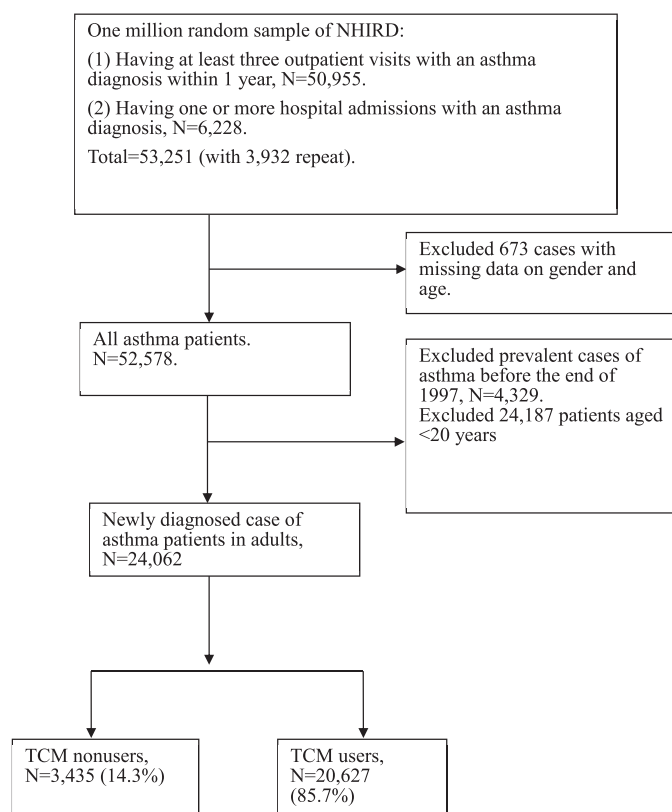
### Statistical Analysis

Data analysis consisted of descriptive statistics, including the prescription rates of the CHP users stratified by patient demographic characteristics, indications for the prescription of the CHP, and the most frequently prescribed herbal formula for treating asthma. Primary indications were classified according to their *ICD-9-CM* code. The diagnoses were coded according to the *ICD-9-CM* and grouped into a series of distinct broad disease categories. The potential antiasthmatic effects of Chinese herbs contained in 10 most commonly prescribed CHPs were grouped according to previous *in vivo* and *in vitro* studies, and these are summarized in Table 3.<sup>10–17</sup> Multiple logistic regression was conducted to evaluate the factors that correlated with CHP use. A significance level of  $\alpha = .05$  was selected. The statistical software package SAS, version 9.13 (SAS Institute Inc, Cary, North Carolina), was used for data management and analysis.

### Results

The database of outpatient claims from 1997 to 2008 contained information on 24,062 adults with asthma. Among them, 20,627 asthma patients (85.7%) used TCM services at least once. Most TCM users (86.0%) also received conventional asthma treatment. Details on the demographic distribution of TCM users and nonusers are provided in Table 1. The mean age of the non-TCM users was higher than that of the TCM users.

The adjusted odds ratios (aORs) and 95% confidence intervals (CIs) obtained by multiple logistic regression are given in Table 1. Compared with the other age groups and insured regions, those aged 20 to 29 years and who were residing in Northern and Central Taiwan were more likely to be TCM users. There was also a significant difference between TCM users and nonusers, with there being more of the former in the income group of NT\$20,000 to NT\$39,999. After adjusting for other factors, patients with chronic obstructive asthma (aOR, 1.26; 95% CI, 1.11–1.43) were more likely to



**Figure 1.** Flowchart of recruitment of subjects from the 1-million random sample of the National Health Insurance Research Database (NHIRD) from 1997 to 2008 in Taiwan.

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