Trends and prescription patterns of traditional Chinese medicine use among subjects with allergic diseases: A nationwide population-based study

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ABSTRACT

Background: The alarming rising prevalence of allergic diseases has led to substantial healthcare and economic burdens worldwide. The integrated use of traditional Chinese medicines (TCM) and Western medicines has been common in treating subjects with allergic diseases in clinical practice in Taiwan. However, limited studies have been conducted to evaluate long-term trends and prescription patterns of TCM use among subjects with allergic diseases. Thus, we conducted a nationwide population-based study to characterize TCM use among subjects with allergic diseases.

Methods: A total of 241,858 subjects with diagnosed atopic dermatitis, asthma or allergic rhinitis in the period of 2003–2012 were identified from the National Health Insurance Research Database (NHIRD) in Taiwan and included in this study. We assessed trends and prescribed patterns related to TCM (both single herbs and herbal formulas) among the study subjects over the 10-year study period.

Results: The overall proportions of TCM use were 30.5%, 29.0% and 45.7% in subjects with atopic dermatitis, asthma and allergic rhinitis, respectively. We found increasing trends of TCM use among subjects having atopic dermatitis and asthma, with annual increase of 0.91% and 0.38%, respectively, over the 10-year study period while the proportion remained steadily high (from 46.6% in 2003 to 46.3% in 2012) among subjects having allergic rhinitis. Moreover, the number of hospitalization due to allergic diseases in TCM users was significantly smaller than that in non TCM users for all three allergic diseases.

Conclusion: A notable proportion (30%–50%) of subjects with allergic diseases in Taiwan has used TCM, with the highest proportion of TCM use found in subjects with allergic rhinitis, whereas increasing trends of TCM use are found among subjects with atopic dermatitis and asthma, respectively. Our results suggest that TCM use may help reduce the severe episodes of allergic diseases necessitating hospitalizations.

Introduction

Allergic diseases such as atopic dermatitis, asthma and allergic rhinitis have increased noticeably in recent decades and are emerging as a major clinical and public health issue not only in Taiwan, but also worldwide. It has been documented by the World Allergy Organization (WAO) White Book on Allergy 2013 update that approximately 30–40% of the worldwide population is affected by one or more allergic diseases, such as atopic dermatitis, asthma, allergic rhinitis and food allergy etc. The increasing prevalence of allergic diseases during the past...
decades has also led to considerable economic, medical and social burdens.\(^5\)

It is long known that Western medicines, e.g., antihistamines, corticosteroids, leukotriene modifiers, beta2-agonists, and anticholinergics etc., have been widely administered to treat subjects with allergic diseases.\(^7\) However, available Western-medicine treatment for allergic diseases may only offer symptomatic benefit, but is lack of curative efficacy. Thus, managing allergic diseases using conventional Western medicines has remained a major challenge.

On the other hand, there is a general impression among some people in Chinese society including Taiwan that traditional Chinese medicine (TCM) is better in curing the root of a disease and has milder adverse effects when compared to Western medicines.\(^1\) In addition, the lack of curative efficacy in Western medicines may explain, at least in part, why a considerable proportion of subjects with allergic diseases seek complementary and alternative treatment, specifically, TCM.\(^9\) TCM has been used for thousands of years in Asian countries, including China, Japan, Korea and Taiwan. However, trends and prescription patterns of TCM use in subjects with allergic diseases have been largely unexplored.

The National Health Insurance Program (NHIP) in Taiwan has launched since 1995, covering nearly 99.6% of the total population residing in Taiwan.\(^10\) Since 1996, TCM use has been reimbursed by the NHIP. In the present study, using data collected by the NHIP, we investigated 10-year trends and prescription patterns of TCM use in subjects with three allergic diseases, specifically, atopic dermatitis, asthma and allergic rhinitis, from 2003 to 2012 in Taiwan.

Methods

Data source

In this study, we used registry data derived from the Longitudinal Health Insurance Database 2005 (LHID2005) composed of medical claims data, which are part of the National Health Insurance Research Database (NHIRD) in Taiwan. In brief, the NHIP, a government-run, single-payer program, has provided mandatory medical care to residents in Taiwan since 1995. The NHIRD contains reimbursement claims data collected by the NHIP, including demographic characteristics, outpatient and inpatient claims data and prescription records (both Western medicines and TCM). Previous studies have reported that enrollees representing nearly 99% of the total population in Taiwan.\(^10\)

The LHID2005, a subset derived from the NHIRD, included 1,000,000 individuals (approximately 5% of the total population of Taiwan) and randomly sampled from the 2005 National Health Insurance Registry for Beneficiaries of the original NHIRD. As described in the following link (http://nhird.nhri.org.tw/en/Data_Subsets.html) - “There was no significant difference in the gender distribution ($\chi^2 = 0.008, df = 1$, $P$-value = 0.931) between the patients in the LHID2005 and the original NHIRD”, the information has provided supportive evidence that the LHID2005 was representative for the entire Taiwan population. The Institutional Review Board of the National Health Research Institutes, Taiwan approved this study protocol (the ethics approval reference number: EC1050302-E).

Study population

In the present study, subjects diagnosed with atopic dermatitis, asthma and allergic rhinitis in the period of 2003–2012 were included. In considering substantial degree of variation in seeking treatment among prevalent subjects, we excluded subjects who were diagnosed as atopic dermatitis, asthma and allergic rhinitis before 2003. We defined subjects with allergic disease(s) based on the International Classification of Diseases (ICD)-9-CM codes during the study period of 2003–2012. Diagnoses of three examined allergic diseases in this study were described as follows: i) atopic dermatitis defined as at least one inpatient or two outpatient medical claims records within a year (ICD-9 code = 691.8)\(^1\), \(12\); ii) asthma defined as at least one inpatient or two outpatient medical claims records within a year (ICD-9 code = 493)\(^13\), \(15\); and iii) allergic rhinitis defined as at least one inpatient or two outpatient medical claims records within a year (ICD-9 = 477).\(^12\) The date of the second outpatient medical claims record or the date of one inpatient medical claims record were used for defining time to diagnosis of the three examined allergic diseases.

Assessment of traditional Chinese medicine use

Currently, the NHIP has reimbursed two kinds of Chinese herbal remedies: Chinese single herbs and Chinese herbal formulas. Each Chinese herbal formula is combined with two or more fixed proportions of Chinese single herbs, strictly followed the TCM classics. TCM use for the three allergic diseases evaluated in this study was directly recorded in the LHID2005. Thus, we identified Chinese herbal remedies based on prescription records from the LHID2005, then grouped study subjects as TCM users or non TCM users.

Data analysis

We calculated mean and corresponding standard deviation (SD), or counts and corresponding percentages for the baseline demographic and
Table 1
Demographic characteristics of patients with diagnosed atopic dermatitis, asthma and allergic rhinitis in the period of 2003–2012, grouped by status of TCM use.

|                          | Atopic dermatitis (n = 28,771) | Asthma (n = 71,838) | Allergic rhinitis (n = 191,851) |
|--------------------------|---------------------------------|---------------------|-------------------------------|
|                          | TCM use (n = 8772)              | No TCM use (n = 19,999) | TCM use (n = 20,866)          | No TCM use (n = 50,972) | TCM use (n = 87,649) | No TCM use (n = 104,202) |
| Age, years               |                                 |                     |                               |                          |                      |                           |
| Age<10                   | 1584 (18.06)                    | 5637 (28.19)        | 5272 (25.27)                  | 17,877 (35.07)           | 943.7                | 15,223 (17.37)          |
| 10 ≤ age<30              | 2414 (27.52)                    | 4639 (23.20)        | 3155 (15.12)                  | 6775 (13.29)             |                      | 28,950 (33.03)          |
| 30 ≤ age<50              | 2408 (27.45)                    | 3877 (19.39)        | 4608 (22.32)                  | 7643 (14.99)             |                      | 26,610 (30.36)          |
| Age≥50                   | 2366 (26.97)                    | 5846 (29.21)        | 7781 (37.29)                  | 18,677 (36.64)           |                      | 16,866 (19.24)          |
| Sex                      |                                 |                     |                               |                          |                      |                           |
| Females                  | 5343 (60.91)                    | 10,061 (50.31)      | 11,649 (55.83)                | 24,163 (47.40)           | 420.2                | 49,162 (56.09)          |
| Males                    | 3429 (39.09)                    | 9938 (49.69)        | 9217 (44.17)                  | 26,809 (52.60)           |                      | 49,487 (43.91)          |
| Enrollee category        |                                 |                     |                               |                          |                      |                           |
| I                        | 647 (7.38)                      | 1214 (6.07)         | 1476 (7.07)                   | 2962 (5.81)              | 138.3                | 7367 (8.41)             |
| II                       | 2594 (29.57)                    | 5677 (28.39)        | 5723 (27.43)                  | 13,307 (26.11)           |                      | 7054 (6.77)             |
| Ill                      | 2324 (26.49)                    | 5331 (26.66)        | 6291 (30.15)                  | 14,454 (28.36)           |                      | 32,947 (31.62)          |
| IV                       | 1022 (11.65)                    | 2737 (13.69)        | 2676 (12.82)                  | 7299 (14.32)             |                      | 24,837 (23.84)          |
| Other                    | 2185 (24.91)                    | 5040 (25.20)        | 4700 (22.52)                  | 12,950 (25.41)           |                      | 12,925 (12.40)          |
| Geographical area        |                                 |                     |                               |                          |                      |                           |
| Urban                    | 2661 (30.34)                    | 6043 (30.22)        | 5902 (28.29)                  | 14,269 (27.99)           | 11.9                 | 26,216 (29.91)          |
| Suburban                 | 4954 (56.48)                    | 10,918 (54.59)      | 11,885 (56.96)                | 28,667 (56.24)           |                      | 32,364 (31.06)          |
| Rural                    | 775 (8.83)                      | 1937 (9.69)         | 1957 (9.38)                   | 5061 (9.93)              |                      | 51,184 (58.40)          |
| Other                    | 382 (4.35)                      | 1101 (5.51)         | 1122 (5.38)                   | 2975 (5.84)              |                      | 4151 (4.74)             |
| Health utilization       |                                 |                     |                               |                          |                      |                           |
| No. of inpatient visits  | 0.18 ± 0.75                     | 0.23 ± 0.80         | 0.16 ± 0.84                   | 0.23 ± 0.94              | 0.36 ± 1.14          | 0.11 ± 0.52             |
| No. of outpatient visits | 31.43 ± 19.75                   | 25.07 ± 18.34       | 19.57 ± 9.63                  | 26.12 ± 17.95            | 51.3                 | 26.85 ± 17.33           |

Abbreviation: TCM: traditional Chinese medicine; SD: standard deviation; SMD: standardized mean difference.

a Health utilization is calculated based on one year after the index date.
b Critical values were calculated by chi-squared test.
c Critical values were calculated by Student’s t-test.
d SMD more than or equal to 0.1 between two groups is marked in bold.
clinical characteristics of study subjects, including: age, sex, enrollee category as a proxy measure to represent the study subjects’ socioeconomic status, geographical area and healthcare utilization of outpatient and inpatient visits one year after the index date. Student’s t-test was used for continuous variables and chi-square test was used for categorical variables, respectively, to compare demographic and clinical characteristics between subjects with and without TCM use. In addition to the corresponding statistical tests, we compared demographic and clinical characteristics between subjects with and without TCM use using standardized mean differences (SMDs), which were computed as the absolute difference in means or proportions divided by a pooled standard deviation in two groups. Previous studies have reported that SMDs are not sensitive to sample size and more suitable in determining meaningful differences than traditional significance tests. SMDs less than 0.1 are considered as adequate balance for corresponding variables between groups.

To investigate time trends for TCM use in each examined allergic disease, we first transformed the calendar year by subtracting 2003 from the year and dividing the results by 9. Thus, the transformed values were 0 for 2003 and 1 for 2012. Next, we performed linear regression analyses for evaluating 10-year time trends of TCM use for three examined allergic diseases (atopic dermatitis, asthma and allergic rhinitis) in this study. All of the analyses were performed using SAS version 8.2 (SAS institute, Cary, NC). P values less than 0.05 were declared to be statistically significant.

Results

A total of 241,858 subjects diagnosed with one or more allergic diseases including atopic dermatitis, asthma and allergic rhinitis in the period of 2003–2012 were included in this study and examined in the subsequent analyses. Among those, there were 28,771 subjects with atopic dermatitis, 71,838 subjects with asthma, and 191,851 subjects with allergic rhinitis. Fig. 1 shows the detailed flow chart regarding identification for the study subjects. For the percentages of TCM use, we found that 30.5% subjects with atopic dermatitis were TCM users; 29.0% subjects with asthma were TCM users; and 45.7% subjects with allergic rhinitis were TCM users.

Table 1 presents the distributions of baseline and clinical characteristics included age, sex, enrollee category, geographical area and healthcare utilization of outpatient and inpatient visits one year after the index date. The distributions of age, sex and enrollee category (except for atopic dermatitis) are different between subjects with and without TCM use in three allergic diseases examined in this study (all SMDs more than or equal to 0.1). There was no difference in distributions of geographic area in three examined allergic diseases (all SMDs < 0.1). The mean age and corresponding standard deviation at diagnosis of allergic diseases in subjects with TCM use was 32.81 ± 25.48 years, while the group of subjects without TCM use was 32.33 ± 21.37 years. Females were predominant in TCM users for all three allergic diseases. In terms of healthcare utilization one year after the index date, subjects with TCM use had more outpatient visits in three examined allergic diseases (all SMDs > 0.1), and less inpatient visits, compared to the group of subjects without TCM use in asthma and allergic rhinitis, but not atopic dermatitis. In terms of healthcare utilization, the proportions of TCM use among subjects with atopic dermatitis were 26.6% in 2003 and 34.7% in 2012, with a β of 0.91, indicating that there was a 0.91% annual increase of TCM use. The proportion of TCM use among subjects with asthma increased from 29.4% in 2003 to 31.9% in 2012, with a β of 0.38, indicating that there was a 0.38% annual increase of TCM use. On the other hand, the proportions of TCM use for subjects with allergic rhinitis ranged from 46.6% in 2003 to 46.3% in 2012, without a significant trend change over the 10-year study period (Fig. 2).

The top 10 TCM single herbs and herbal formulas for treating atopic dermatitis, asthma and allergic rhinitis, respectively, were shown in Tables 2–4. Among subjects with atopic dermatitis, three most commonly prescribed single herbs were Huang-qin (1.81%), Gan-cao (1.63%), and Yan-hu-suo (1.63%); and three most commonly prescribed herbal formulas were Xiao-feng-san (2.83%), Jia-wei-xiao-yao-san (2.63%), and Xin-yi-qing-fei-tang (2.49%) (Table 2). Among subjects with asthma, three most commonly prescribed single herbs were Bei-mu (2.49%), Jie-geng (2.32%), and Ku-xing-ren (2.3%); and three most commonly prescribed herbal formulas were Xiao-ching-lung-tang (3.37%), Ma-xing-gan-shi-tang (3.31%), and Xin-yi-qing-fei-tang (2.93%) (Table 3). Among subjects with allergic rhinitis, three most commonly prescribed single herbs were Jie-geng (2.07%), Bai-zhi (1.99%), and Huang-qin (1.94%); and three most commonly prescribed herbal formulas were Xin-yi-qing-fei-tang (4.13%), Xiao-ching-lung-tang (3.50%), and Xin-yi-san (3.15%) (Table 4).

Discussion

This study identified 10-year trends and prescription patterns of TCM use among subjects with allergic diseases over the study period of 2003–2012 in Taiwan. To the best of our knowledge, this is the first study simultaneously evaluating 10-year trends and prescription patterns of TCM use in subjects with three common allergic diseases, specifically, atopic dermatitis, asthma and allergic rhinitis. Our study demonstrated that considerable proportions of patients with allergic diseases (30.5% for atopic dermatitis, 29% for asthma, and 45.7% for allergic rhinitis, respectively) in Taiwan had used TCM. The results showed increasing trends of TCM use over the 10-year study period among subjects with atopic dermatitis and asthma, respectively. When we assessed the proportions of TCM use among three examined allergic diseases, the highest proportion of TCM use was observed in subjects with allergic rhinitis, but the trend remained steady over the 10-year study period. Taken together, a notable proportion (30–50%) of subjects with allergic diseases in Taiwan had used TCM. Moreover, our results indicated that the number of inpatient visits in subjects with TCM use was significantly smaller than that in subjects without TCM use for all three examined allergic diseases.

To date, the trends and prescription patterns of TCM use in subjects with allergic diseases remain largely unclear. Our study demonstrated...
Table 2
The top 10 commonly prescribed single herbs and herbal formulas for treating patients with atopic dermatitis in 2003–2012.

| Single herbs | Herbal formulas | Pin-yin name | Latin name | Botanical plant name | Therapeutic indication | N   | %   |
|--------------|-----------------|--------------|------------|----------------------|------------------------|-----|-----|
| Huang-qin    |                  | Radix Scutellariae | Scutellaria baicalensis Georgi | Clear heat and dry dampness, purge fire, relieve toxicity, cool blood and stop bleeding. | 1204 | 1.81 |
| Gan-cao      |                  | Radix Glycyrrhizeae | Glycyrrhiza uralensis Fisch. | Tonify qi of heart and spleen, dispel phlegm, relieve cough and dyspnea, relieve spasms and pain, clear heat, relieve toxicity, and harmonize property of medicine. | 1085 | 1.63 |
| Yan-hu-suo   |                  | Rhizoma Corydalis | Corydalis yanhusuo W. T. Wang (Platycodon grandiflorum (Jacq.) A. DC.) | Activate blood, promote flow of qi, and alleviate pain. | 1084 | 1.63 |
| Jie-geng     |                  | Radix Ployodonos | Cryptotympana pustulata Fabricius | Disperse wind-heat, relieve sore throat and produce sound, relieve itching, promote eruption, improve vision and remove nebula, extinguish wind and relieve spasms. | 1004 | 1.51 |
| Chan-tui     |                  | Periostracum Cicadae | Fritillaria chihouensis D. Don or Fritillaria thunbergii Miq. | Clear and resolve heat-phlegm, moisten and resolve dry phlegm, stop cough, dissipate nodulation and resolve swelling and cure abscesses | 1000 | 1.50 |
| Bei-mu       |                  | Bulbus Fritillariae Cirrhoseae or Bulbus Fritillariae Thunbergii | Fritillariae cirrhosa (Thunb.) Vahl. | Clear heat and remove toxicity, dispense wind-heat, and clear heart-heat. | 974 | 1.47 |
| Lian-qiao    |                  | Forsythia Fructus | Forsythia suspensa (Thunb.) Vahl. | Expel wind and release exterior, alleviate pain, relieve stuffy nose, dry dampness and stop leucorrhrea. | 968 | 1.46 |
| Bai-zhi      |                  | Radix Angelicae Dahuricae | Angelica dahurica (Hoffm.) Benth. & Hook.f. ex Franch. & Sav. | Clear heat and cool blood, activate blood and resolve stasis, and reduce deficiency heat. | 862 | 1.30 |
| Mu-dan-pi    |                  | Cortex Moutan | Paeonia suffrutcosa Andr. | Relieve cough and dyspnea, moisten intestines for relaxing bowels. | 855 | 1.29 |

| Herbal formulas | Pin-yin name | English name | Ingredients of herbal formula | Therapeutic indication | N   | %   |
|----------------|-------------|--------------|-------------------------------|------------------------|-----|-----|
| Xiao-feng-san  |             | Wind Dispersing Powder | Dans-gui (Radix Angelicae Sinensis), Sheng-di (Radix Rehmanniae), Fang-feng (Radix Ledeboeritae), Chan-tui (Periostracum Cicadae), Zhi-mu (Rhizoma Anemarrhenae), Ku-shen (Radix Sophorae Flavescentis), Hu-ma-ren (Semen Sesamum), Jing-jie (Herba Schizonepetae), Cang-zhu (Rhizoma Atractylodis), Niu-bang-zi (Fructus Arctii), Shi-gao (Gypsum Fibrosum), Gan-cao (Radix Glycyrrhizae), Mu-tong (Caulis Atractylodis), Niu-bang-zi (Fructus Arctii), Shi-gao (Gypsum Fibrosum), | Dispel wind pathogen, nourish blood, and remove dampness and heat. | 1583 | 2.83 |
| Jia-wei-xiao-yao-san | | Supplemented Free Wanderer Powder | Dans-gui (Radix Angelicae Sinensis), Fu-ling (Poria), Zhi-zhi (Fructus Gardeniae), Bo-he (Herba Menthae), Bai-shao-yao (Radix Paeoniae Alba), Xia-xin (Herba Menthae), Wu-wei-zi (Fructus Schisandrae), Bai-yao (Rhizoma Zingiberis), Wu-wei-zi (Fructus Schisandrae), Bai-yao (Rhizoma Zingiberis) | Tonify blood, clear liver fire and strengthen the spleen. | 1473 | 2.63 |
| Xin-yi-qing-fei-tang | | Magnolia and Gypsum Combination | Shi-gao (Gypsum Fibrosum), Huang-qin (Radix Scutellariae), Zhi-zhi (Fructus Gardeniae), Mai-men-dong (Radix Ophiopogonis), Bai-he (Herba Bulbii), Zhi-mu (Rhizoma Anemarrhenae), Pi-po-yu (Folium Eriobotryae), Xin-yi (Flos Magnoliae), Gan-cao (Radix Glycyrrhizae), Sheng-ma (Rhizoma Cimicificae) | Dispel the heat of lung, disseminate-heat-qing, and unblock the orifices, especially the nose. | 1395 | 2.49 |
| Ge-gen-tang   |             | Puerariae Decotion | Ge-gen (Radix Puerariae), Ma-huang (Herba Ephedrae), Gui-zhi (Ramulus Cinnamomi), Bai-shao (Radix Paeoniae), Zhi-gan-cao (Radix Glycyrrhizae), Sheng-jiang (Zingiberis Rhizoma Recens), Da-zao (Zizyphi Fructus) | Relieve exterior syndrome by means of diaphoresis, remove toxicity, relax the tendons, and temper the stomach and spleen. | 1203 | 2.15 |
| Ma-xing-gan-shi-tang | | Mahuang and Apricot Seed Combination | Ma-huang (Herba Ephedrae), Xing-ren (Semen Armeniacae), Zhi-gan-cao (Radix Glycyrrhizae), Shi-gao (Gypsum Fibrosum), Jiu-yin-hua (Flos Lonicerae), Lian-qiao (Forsythiae Fructus), Jie-geng (Radix Platycodi), Niu-bang-zi (Fructus Arctii), Bo-he (Herbas Menthae), Dan-dou-chi (Semen Sojae Praeparata), Jing-jie (Herba Schizonepetae), Dan-zhu-ye (Herba Lophatheri), Xian-lu-gen (Rhizoma Phragmitis), Gan-cao (Radix Glycyrrhizae), | Disperse superficial pathogens, and remove heat from the lung to relieve asthma. | 1159 | 2.07 |
| Yin-qiao-san  |             | Honeysuckle and Forsythia Powder | Jiu-yin-hua (Flos Lonicerae), Lian-qiao (Forsythiae Fructus), Jie-geng (Radix Platycodi), Niu-bang-zi (Fructus Arctii), Bo-he (Herbas Menthae), Dan-dou-chi (Semen Sojae Praeparata), Jing-jie (Herba Schizonepetae), Dan-zhu-ye (Herba Lophatheri), Xian-lu-gen (Rhizoma Phragmitis), Gan-cao (Radix Glycyrrhizae), | Dispel pathogenic factors in the superfluities, and clear away heat and toxic material. | 1115 | 1.99 |
| Xiao-ching-jung-tang | | Minor Blue Dragon Combination | Ma-huang (Herba Ephedrae), Shao-yao (Radix Paeoniae Alba), Gan-jiang (Rhizoma Zingiberis), Wu-wei-zhi (Fructus Schisandrae), Gui-zhi (Ramulus Cinnamomi), Ban-xia (Rhizoma Pinelliae), Xi-xin (Herba Asari), Zhi-gan-cao (Radix Glycyrrhizae), | Induce diaphoresis to reduce watery phlegm, and relieve cough and asthma. | 1040 | 1.86 |
| Jiu-fang-bai-du-san | | Schizonepetae and Siler Formula | Jing-jie (Herba Schizonepetae), Fang-feng (Radix Saponinoviae), Qiang-huo (Rhizoma et Radix Notopterygii), Du-huo (Radix Angelicae Pubescentis), Shi-ke (Herba Schizonepetae), Dans-gui (Radix Angelicae Sinensis), Shao-yao (Radix Paeoniae Alba), Sheng-di (Radix Rehmanniae), Cang-zhu (Rhizoma Atractylodis), Huo-niu-xi (Radix Achyranthis Bidentatae), | Dispel wind-cold, relieve exterior syndrome, and eliminate dampness. | 1006 | 1.80 |
| Shu-jing-huo-xue-tang | | Channel-Coursing Blood-Quenching Decotion | Dans-gui (Radix Angelicae Sinensis), Shao-yao (Radix Paeoniae Alba), Sheng-di (Radix Rehmanniae), Cang-zhu (Rhizoma Atractylodis), Huo-niu-xi (Radix Achyranthis Bidentatae), | Unblock and relax the channels, invigorate the blood, break up blood stasis, dispel wind-dampness, and strengthen the tendons. | 932 | 1.67 |

(continued on next page)
that considerable proportions of subjects with allergic diseases (30.5% for atopic dermatitis, 29% for asthma, and 45.7% for allergic rhinitis, respectively) had used TCM. Of note, we found increasing trends of TCM use among subjects with atopic dermatitis and asthma, respectively. Particularly, we observed a 0.91% annual increase for subjects with atopic dermatitis and a 0.38% annual increase for subjects with asthma, respectively. On the other hand, the proportions of TCM use for subjects with allergic rhinitis remained steadily high (from 46.6% in 2003 to 46.3% in 2012) over the 10-year study period. The reasons for the observed increasing trends of TCM use in three examined allergic diseases in Taiwan remain unclear but it may reflect common beliefs that TCM use may potentially “cure the root of allergic diseases” or “cut the tail of allergic diseases”. Besides, there is a general impression among some people in Chinese society including Taiwan that TCM use tends to have milder adverse effects, though with slower clinical effects than Western medicines.8

Previous studies have reported the therapeutic effects of TCM on allergic diseases.17,18 For example, Chen et al examined whether TCM use affected combined use of corticosteroid among children with atopic dermatitis and found that TCM use reduced the number of corticosteroid prescriptions (both topical and systemic) among children with atopic dermatitis within one-year follow-up.17 The results from the Hung et al study have suggested that asthmatic children receiving adjuvant treatment with integrated TCM decreased frequency of emergency room visits and hospital admissions.18 However, the concern related to low certainty of efficacy for TCM use has been reported by previous studies.19-21 Thus, further investigation in making conclusive evidence for efficacy of TCM on allergic diseases would be warranted.

In parallel, pharmacological effects of single herbs and herbal formulas on three examined allergic diseases have been reported by several studies. First, three major pharmacological effects for TCM in treating subjects with atopic dermatitis have been documented, including anti-inflammatory, reduction of histamine release, and anti-oxidation, respectively.17,22 For example, Cheng et al investigated treatment effect of Xiao-feng-san, the top one prescribed herbal formula for treating subjects with atopic dermatitis in this study. Their results suggested that Xiao-feng-san might be an alternative therapeutic choice for subjects with severe and extensive atopic dermatitis.22 Second, both observational and animal studies have indicated that anti-asthmatic activity of TCM was through inhibiting bronchoconstriction and the migration of TCM, all these three allergic diseases are related to the same visceral, lung. It is known that “lung” is a pair of organs locating in the thoracic cavity above the diaphragm. It controls respiration, dominates “qi” (the circulating life force whose existence and properties are the basis of traditional Chinese medicine and philosophy), governs diffusion and deputative down-bearing and regulates the waterways, therefore, is closely related to the function of the nose and skin surface.22 It is different from the view of Western medicines that both allergic rhinitis and asthma are related to respiratory system whereas atopic dermatitis is related to dermatological field. In addition, epidemiological data documents that coexistence of atopic dermatitis, asthma and allergic rhinitis is commonly occurred in the same subject, suggesting these allergic diseases share common causal mechanisms.23 Furthermore, previous studies have reported that Scutellariae radix (Latin name of Huang-qin) attenuates immunological responses in a mouse model of atopic dermatitis, mainly through decreasing IL-5 levels; modulates ovalbumin (OVA)-induced airway inflammation through suppressing IL-4/Stat6 signaling in a murine model of asthma; and baicalin, another component extracted from Scutellariae radix, effectively reduce allergic response in an OVA-induced allergic rhinitis animal model.24,25 Findings from previous studies have lent further support for the observed overlapping prescriptions of TCM in three allergic diseases investigated in this study.

Some caveats in this study should be noted. First, detailed information on clinical symptoms and laboratory reports are not available in the NHRID. But this issue should be undifferentiated between subjects with and without TCM use. Second, the NHIP in Taiwan only reimburses granular or powder forms of TCM herbs and formulas recording in the

| Pin-yin name | English name | Ingredients of herbal formula | Therapeutic indication | N | % |
|-------------|-------------|------------------------------|----------------------|---|---|
| Chen-pi | Pericarpium Citri Reticulatae | Tao-ren (Semen Persicae), Wei-ling-xian (Radix Cnidii), Qiang-huo (Rhizoma et Radix Notopertygi), Fang-feng (Radix Saposhnikoviae), Long-dan-cao (Radix Gentianae), Chuan-xiong (Rhizoma Chuanxiong), Bai-hzi (Radix Angelicae Dahuricae), Fu-ling (Poria), Gan-cao (Radix Glycyrrhizae) | Purge excessive pathogenic fire in the liver and gallbladder, and clear away damp-heat in the lower-jiao. | 929 | 1.66 |
| Long-dan-xie-gan-tang | Gentian Liver-Purging Decoction | Long-dan-cao (Radix Gentianae), Chai-hai (Radix Bupleuri), Huang-qin (Radix Scutellariae), Zhi-zi (Fructus Gardeniae), Ze-xie (Rhizoma Alismatis), Che-qian-zhi (Semen Plantaginis), Mu-tong (Caulis Akebiae), Dang-gui (Radix Angelicae Sinensis), Sheng-di (Radix Rehmanniae), Gan-cao (Radix Glycyrrhizae) | | | |

Table 2 (continued)
not included in this study. Therefore, it is likely that the prevalence of herbal folk medicine are not reimbursed by the NHIP and are "Taiwan Herbal Pharmacopeia" that is published by Taiwan's Ministry of Health and Welfare (https://www.mohw.gov.tw/dl-10568-0efff195-8aff-4f6a-b19f-c18fbb8d0b0.html). On the other hand, TCM in herbal form and herbal folk medicine are not reimbursed by the NHP and are not included in this study. Therefore, it is likely that the prevalence of TCM use in three examined allergic diseases may be underestimated. Third, our results may or may not be generalizable, as the common prescription knowledge base among licensed TCM physicians might vary across countries. As such, caution should be taken when interpreting the results in this study. Fourth, the big standard deviations of age at diagnosis of allergic diseases in subjects with or without TCM use were noticed. Since we did not exclude study subjects based on their age, both Form and herbal folk medicine are not reimbursed by the NHIP and are not included in this study. Therefore, it is likely that the prevalence of TCM use in three examined allergic diseases may be underestimated.

### Table 3

The top 10 commonly prescribed single herbs and herbal formulas for treating patients with asthma in 2003–2012.

| Pin-yin name | Latin name | Botanical plant name | Therapeutic indication | N  | % |
|--------------|------------|----------------------|------------------------|----|---|
| Bei-mu       | Bulbus Frullariarum Cirrhosae or Bulbus Frullariarum Thunbergii | Fritillaria chrysantha D. Don or Fritillaria thunbergii Miq. | Clear and resolve heat-phlegm, moisten and resolve dry-phlegm, stop cough, dissipate nodulation and resolve swelling, and cure abscess | 3974 | 2.49 |
| Jie-geng     | Radix Platycodonis | Platycodon grandiflorum (Jacq.) A. DC. | Ventilate lung, dispel phlegm, relieve sore throat, and expel pus. | 3704 | 2.32 |
| Ku-xing-ren  | Semen Armeniacae Amarum | Prunus armeniaca L. | Relieve cough and dyspnea, and moisten intestines for relaxinng bowels. | 3675 | 2.30 |
| Huang-qin    | Radix Scutellariae | Scutellaria baicalensis Georgii | Clear heat and dry dampness, purge fire, relieve toxicity, cool blood and stop bleeding. | 2940 | 1.84 |
| Gan-cao      | Radix Glycyrrhiza | Glycyrrhiza uralensis Fisch. | Tonify qi of heart and spleen, dispel cough and phlegm, relieve cough and dyspnea, relieve spam and pain, clear heat, relieve toxicity, and harmonize property of medicine. | 2655 | 1.66 |
| Yu-xing-cao  | Houttuyniae Herba | Houttuynia cordata Thunb. | Clear heat and remove toxicity, cure abscess and discharge pus, clear lung heat, clear heat and remove dampness. | 2324 | 1.45 |
| Yan-hu-xue   | Rhizoma Corydalis | Corydalis yanhusuo W. T. Wang | Activate blood, promote flow of qi, and alleviate pain. | 2317 | 1.45 |
| Bai-zhi      | Radix Angelicae Dahuricae | Angelica dahurica (Hoffm.) | Expel wind and release exterior, alleviate pain, relieve stuffy nose, dry dampness and stop leukorrhea. | 2255 | 1.41 |
| Mai-men-dong | Radix Ophiopogonis | Ophiopogon japonicus (L.f.) Ker-Gawl. | Nourish yin of stomach, lung and heart, clear heat of stomach, lung and heart, calm heart and induce tranquilization. | 2121 | 1.33 |
| Hou-po       | Magnoliae Officinalis Cortex | Magnolia officinalis Rehder et Wils. | Dry dampness, move qi, and relieve dyspnea. | 2004 | 1.25 |

### Table 3

| Pin-yin name | English name | Ingredients of herbal formula | Therapeutic indication | N  | % |
|--------------|--------------|-------------------------------|------------------------|----|---|
| Xiao-chung-tang | Minor Blue Dragon Combination | Ma-huang (Herba Ephedrae), Shao-yao (Radix Paoniae Alba), Gan-jiang (Rhizoma Zingiberis), Wu-weizi (Fructus Schisandrae), Gui-zhi (Ramulus Cinnamomun), Ban-xia (Rhizoma Pinelliae), Xi-xin (Herba Asari), Zhi-gan-cao (Radix Glycyrrhizae) | Induce diaphoresis to reduce watery phlegm, and relieve cough and asthma. | 4640 | 3.37 |
| Ma-xing-gan-shi-tang | Mahuang and Apricot Seed Combination | Ma-huang (Herba Ephedrae), Xing-ren (Semen Armeniacae), Zhi-gan-cao (Radix Glycyrrhizae), Shi-gao (Gypsum Fibrosum) | Disperse superficial pathogens, and remove heat from the lung to relieve asthma. | 4555 | 3.31 |
| Xin-yi-Qing-fei-tang | Magnolia and Gypsum Combination | Shi-gao (Gypsum Fibrosum), Huang-qin (Radix Scutellariae), Zhi-zi (Fructus Gardeniae), Mai-men-dong (Radix Ophiopogonis), Bai-he (Bulbus Lili), Zhi-mu (Rhizoma Anemarrhenaee), Pi-ya-ye (Folium Erizotyriei), Xin-yi (Flos Magnoliae), Gan-cao (Radix Glycyrrhizae), Sheng-ma (Rhizoma Cimicifugae) | Dispel the heat of lung, and disseminate lung-heat, and unblock the orifices, especially the nose. | 4029 | 2.93 |
| Ding-chuan-tang | Attack Wheezing Decoction | Bai-guo (Semen Ginkgo), Ma-huang (Herba Ephedrae), Su-zi (Fructus Perillae), Gan-cao (Radix Glycyrrhizae), Xuan-dong-hua (Flos Farfarae), Zhi-gan-cao (Radix Glycyrrhizae), Sheng-ma (Rhizoma Cimicifugae) | Facilitate the flow of the lung-qi to descend upward flow, eliminate phlegm and relieve asthma. | 3267 | 2.37 |
| Ge-gen-tang | Puerariae Decoction | Ge-gen (Radix Puerariae), Ma-huang (Herba Ephedrae), Gui-zhi (Ramulus Cinnamomun), Bai-shao (Radix Paronieae), Zhi-gan-cao (Radix Glycyrrhizae), Sheng-jiang (Zingiberis Rhizoma Recens), Da- dao (Zingyi Fructus) | Relieve exterior syndrome by means of diaphoresis, remove toxicity, relax the tendons and temper the stomach and spleen. | 3037 | 2.11 |
| Yin-qiao-san | Honeyuckle and Forsythia Powder | Jin-yin-hua (Flos Lonicieae), Lian-qiao (Forsythia Fructus), Jie-geng (Radix Platycodonis), Niu-bang-zi (Fructus Arctii), Bo-he (Herba Menthae), Dan-dou-chi (Semen Sojae Praeparata), Jing-jie (Herba Schizonepetae), Dan-zhu-ye (Herba Lophatheri), Xian-lu-gen (Rhizoma Phragmitis), Gan-cao (Radix Glycyrrhizae) | Dispel pathogenic factors in the superficies, and clear away heat and toxic material. | 2270 | 1.98 |
| Xin-yi-san | Magnolia Flower Powder | Xin-yi (Flos Magnoliae), Chuan-xiong (Rhizoma Chuanxiong), Mu-er (Fructus Magnoliae), Bai-cai (Flos Magnoliae), Bai-cai (Radix Angelicae Dahuricae), Zhi-gan-cao (Radix Glycyrrhizae) | Expel wind-cold, and unblock the nasal passages. | 2688 | 1.95 |
| Cang-er-san | Xanthium Powder | Cang-er-zhi (Fructus Xanthii), Xian-yi (Flos Magnoliae), Bai-cai (Radix Angelicae Dahuricae), Bo-he (Herba Menthae) | Disperse wind, alleviates pain, and unblock the nose. | 2678 | 1.94 |
| Zhi-sou-san | Stop Coughing Powder | Zi-wan (Radix Astris), Bai-bu (Radix Stemoneae), Bai-qian (Rhizoma Cynanchi Stauntonii), Jing-jie (Herba Schizonepetae), Jie-geng (Radix Platycodonis), Chen-pi (Pericarpium Citri Reticulatae), Gan-cao (Radix Glycyrrhizae) | Stop coughing, transform phlegm, release the exterior, and ventilate the lungs. | 2588 | 1.88 |
| Jia-wei-xiao- yao-san | Supplenented Free Wanderer Powder | Dang-gui (Radix Angelicae Sinensis), Fu-ling (Poria), Zhi-zi (Fructus Gardeniae), Bo-he (Herba Menthae), Bai-shao-yao (Radix Paoniae), Xi-xin (Radix Bupleuri), Gan-cao (Radix Glycyrrhizae), Bai-zhu (Rhizoma Macrocephalae), Mu-dan-pi (Cortex Moutan), Gan-jiang (Rhizoma Zingiberis) | Tonify blood, clear liver fire, and strengthen the spleen. | 2316 | 1.68 |
Table 4

The top 10 commonly prescribed single herbs and herbal formulas for treating patients with allergic rhinitis in 2003–2012.

| Single herbs | Botanical plant name                          | Therapeutic indication                                                                 | N     | %   |
|--------------|-----------------------------------------------|----------------------------------------------------------------------------------------|-------|-----|
| Jie-geng     | Radix Platycodonis                            | Ventilate lung, dispel phlegm, relieve sore throat, and expel pus.                      | 16,279| 2.07|
| Bai-zhi      | Radix Angelicae Dahuricae                     | Expel wind and release exterior, alleviate pain, relieve stuffy nose, dryness and stop leucorrhea. | 15,642| 1.99|
| Huang-qin    | Radix Scutellariae                            | Clear heat and dry dampness, purge fire and relieve toxicity, cool blood and stop bleeding. | 15,263| 1.94|
| Bei-mu       | Bulbus Fritillariae Cirrhosae or Bulbus Fritillariae Thunbergii | Clear and resolve heat-phlegm, moisten and resolve dry-phlegm, stop cough, dissipate nodulation and resolve swelling and cure abscesses | 14,443| 1.84|
| Cang-er-zi   | Fructus Xanthii                               | Relieve cough and dyspnea, and moisten intestines for relaxing bowels.                 | 13,146| 1.67|
| Ku-xing-ren  | Semen Armeniacae Amarae                      | Relieve cough and dyspnea, and moisten intestines for relaxing bowels.                 | 12,857| 1.64|
| Gan-cao      | Radix Glycyrrhizae                            | Tonify qi of heart and spleen, dispel phlegm, relieve cough and dyspnea, relieve spasm and pain, clear heat and relieve toxicity, and harmonize property of medicine. | 12,413| 1.58|
| Yu-xing-cao  | Houttuyniae Herba                            | Clear heat and remove toxicity, cure abscess and discharge pus, clear lung heat, clear heat and remove dampness. | 11,725| 1.49|
| Chan-tui     | Periostracum Cicae                            | Disperse wind-heat, relieve sore throat and produce sound, relieve itching and promote eruption, improve vision and remove nebula, and extinguish wind and relieve spasms. | 11,543| 1.47|
| Yan-bu-suo   | Rhizoma Corydalis                            | Activate blood, promote flow of qi, and alleviate pain.                                | 10,987| 1.40|

| Herbal formulas | Ingredients of herbal formula Pin-yin name (Latin name) Therapeutic indication | N     | %   |
|-----------------|---------------------------------------------------------------------------------|-------|-----|
| Xin-yi-qing-fei-tang | Magnolia and Gypsum Combination Shi-gao (Gypsum Fibrosum), Huang-qin (Radix Scutellariae), Zhi-zi (Fructus Gardeniae), Mai-men-dong (Radix Ophispogonosis), Bai-he (Bulbus Lili), Zhi-mu (Rhizoma Anemarrhenae), Pi-pa-ye (Folium Erbishiotaevae), Xin-yi (Flo Magnolidae), Gan-cao (Radix Glycyrrhynarea), Sheng-ma (Rhizoma Cimicifugae) | 27,222| 4.13|
| Xiao-ching-lung-tang | Minor Blue Dragon Combination Ma-huang (Herba Ephedrae), Shao-yao (Radix Paoniae Alba), Gan-jiang (Herba Zingiberis), Wu-we (Fructus Schinadiare), Gui-zhi (Ramulus Cinnamomei), Ban-xia (Rhizoma Pinelliae), Xi-xin (Herba Asari), Zhi-gan-cao (Radix Glycyrrhynarea) | 23,080| 3.50|
| Xin-yi-san     | Magnolia Flower Powder              | Expel wind-cold, and unblock the nasal passages.                          | 20,780| 3.15|
| Cang-er-san    | Xanthium Powder                     | Disperse wind, alleviates pain, and unblock the nose.                       | 19,686| 2.98|
| Ge-gen-tang    | Pueraiae Decoction                 | Relieve exterior syndrome by means of diaphoresis, remove toxicity, relax the tendons, and temper the stomach and spleen. | 18,857| 2.86|
| Ma-xing-gan-shi-tang | Mahuang and Apricot Seed Combination Ma-huang (Herba Ephedrae), Xing-ren (Semen Armeniacae), Zhi-gan-cao (Radix Glycyrrhynarea), Shi-gao (Gypsum Fibrosum) | 15,382| 2.33|
| Jia-wei-xiao-yao-san | Supplemented Free Wanderer Powder | Tonify blood, clear liver fire, and strengthen the spleen.                   | 14,737| 2.23|
| Yin-qiao-san   | Honeyuckle and Forsythia Powder      | Dispel pathogenic factors in the superificies, and clear away heat and toxic material. | 14,264| 2.16|
| Chuan-xiong-chao-tiao-san | Ligusticum Chuanxiong Powder to Be Taken with Green Tea Bo-he (Herba Menthae), Chuan-xiong (Rhizoma Chuanxiong), Qiang-bu (Rhizoma et Radix Notopterygi), Gao-ben (Radicae Ligustici Sinensis), Sheng-ma (Rhizoma Cimicifugae), Bai-zhi (Radix Angelicae Dahuricae), Zhi-gan-cao (Radix Glycyrrhynarea) | 12,212| 1.85|
| Bu-zhong-yi-qing-tang | Tonify the Middle and Augment the Qi Decoction Huang-qi (Radix Astragali), Gan-cao (Radix Glycyrrhynarea), Ren-shen (Radix Ginseng), Dang-gui (Rhizoma Angelicae Sinensis), Chi-chi (Pericarpium Citri Reticulatae), Sheng-ma (Rhizoma Cimicifugae), Chai-hu (Radix Bupleuri), Bai-zhu (Rhizoma Atractylodis Macrocephalae) | 11,027| 1.67|
children and adults were included in this study. It was likely a result of the observed big standard deviations.

Conclusion

In conclusion, a notable proportion (30–50%) of subjects with allergic diseases in Taiwan has used TCM, with the highest proportion of TCM use in subjects with allergic rhinitis, whereas increasing trends of TCM use are found among subjects with atopic dermatitis and asthma, respectively. Moreover, our results suggest that TCM use may help reduce severe episodes of these three allergic diseases that necessitate hospitalizations. Further investigation would be merited to better understand the efficacy and safety of TCM, particularly, potential interactions with Western medicines.

Declarations

Ethics approval and consent to participate

The Institutional Review Board of the National Health Research Institutes, Taiwan, approved this study protocol.

Consent for publication

Not applicable.

Availability of data and material

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

Authors’ contributions

Tsung-Chieh Yao and Hui-Ju Tsai conceptualized, designed and supervised the study; raised funding for the study and staff working on the project, assisted in data analysis, interpreted the results and drafted the manuscript. Ya-Wen Huang performed data analysis, assisted in data collection, interpreted the results, and drafted the manuscript. Pei-Ying Lin, Chun-Hui Chu and Fang-Yu Chang provided intellectual inputs and assisted in data analysis and results interpretation. All authors contributed to the interpretation and discussion of the results; read and approved the final article.

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