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Original article

Traditional Chinese medicine treatments for upper respiratory tract infections/common colds in Taiwan

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Abstract

Introduction: Traditional Chinese medicine (TCM) has been used to treat upper respiratory tract infections/common colds (URTIs) in Asian countries for over 2000 years. However, Chinese medicine doctors (CMDs) follow the traditional treatment rules to select or administer these diverse Chinese medicine formulae. The main purpose of our study was to explore data on the frequency of medication and medication habits by CMDs for the treatment of URTIs with Chinese herbs and Chinese medicine formulae.

Methods: The TCM treatments for patients consulting with an URTIs were analyzed from the National Health Insurance Research Database using the appropriate codes from the International Classification of Diseases, Ninth Revision, Clinical Modification diagnoses for Taiwan in 2009. A data mining and association rules, were used to analyze co-prescriptions of TCM for patients with URTIs.

Results: For 472,005 patients who sought the treatment of URTIs, a total of 46,805 patients with URTIs received TCM treatments, of these 29,052 patients sought both TCM and Western medication treatments. Of the URTIs patients who had received a TCM treatment, 79% presented with an acute common cold, 9% had influenza, and 9% had acute upper respiratory infections. Furthermore, 53.89% of the sample were aged between 20 and 49 years, and 62.84% were women, 3.56% of the patients used Yin-Qiao-San and 2.76% used Jie-Geng. Yin-Qiao-San and Ma-Xing-Gan-Shi-Tang were the most commonly combinations of prescriptions for patients with URTIs.

Conclusions: The patients experiencing URTIs were more likely to request TCM treatment if their symptoms were mild and they were women. The Chinese medicine doctors treating URTIs generally followed TCM theory. A coding system for TCM diagnostic classifications could improve evaluations of TCM treatments.

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Keywords: Traditional Chinese medicine, Upper respiratory tract infections/common colds; National Health Insurance Research Database in Taiwan, Prescribing

Introduction

Traditional Chinese medicine (TCM) has been used to treat upper respiratory tract infections/common colds (URTIs) in Asian countries for over 2000 years. URTIs-related symptoms, complications, treatment methods, and principles were thoroughly recorded in *ShanghanZabinglun*, which was written by Zhang Zhongjing during the Han Dynasty in China (150–219 A.D.) [1]. As part of the long-term development of URTIs treatment theories, Wen Bing Theory advocated by Wu Jutong was published during the Qing Dynasty

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(1758–1836 A.D.) because febrile diseases, including infectious diseases such as encephalitis, were added to the texts [2]. To the best of our knowledge, the current principles of the TCM treatments used for diseases, such as URTIs remain diverse. Therefore, this study employed a database analysis to investigate the basis of Chinese medicine doctors' (CMD) treatments. Several reports have described how TCM treatments for URTIs and related diseases, including influenza, can alleviate symptoms with fewer side effects [3,4]. The efficacy of TCM possibly results from the antibacterial and antiviral effects of the Chinese herbs and formulae [5]. Many articles mention Chinese herbal medicines may shorten the symptomatic phase in patients with the common cold and treat or prevent seasonal influenza. However, these articles are weak owing to the lack of high quality TCM trials. Well-designed clinical trials are required [6–8]. In spite of this, many extracts of medical herbs have been found to have the potential to treat URTIs and prevent colds [9,10]. Some Chinese herbs have even been recommended as a treatment to prevent severe acute respiratory syndrome (SARS) [11]. The same Chinese herbs or formulae may be used to treat many diseases, and CMDs may use a single Chinese herb or a mixture of herbs, depending on their experience. Nevertheless, how CMDs follow the treatment rules to select or administer these drugs or Chinese medicine formulae remains diverse [12]. This required further investigation.

To the best of our knowledge, there are no population based pharmacoepidemiologic studies of TCM for the treatment of URTIs. The main purpose of our study was to explore the data on the frequency of medication and medication habits by CMDs for the treatment of URTIs with Chinese herbs and Chinese medicine formulae.

Materials and methods

Data sources

Taiwan's National Health Insurance system was established in 1995 and covers 99% of inpatient and outpatient medical benefit claims for Taiwan's 23 million residents. The detailed clinical information for each patient for each visit includes the date of diagnosis, diagnostic codes, payments for consultations and prescriptions, and is contained in this claims data [13,14]. Traditional Chinese medicine is also covered in Taiwan's National Health Insurance program. The prescriptions are written by CMDs for treating various disorders that are recorded by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes [15].

We used a cohort database from the NHIRD that comprises of a million randomly sampled individuals who were alive in 2000. The TCM claims database for 2009 was analyzed in this study. The 2009 ambulatory file (CD2009) and corresponding prescription file (OO2009) were included in the TCM claims data. Encrypted personal identifications were used to protect patient privacy for avoiding the possibility of the ethical violation. Ethical approval and exemption was obtained from the institutional review board of Chi Mei Medical Center (IRB No. 10202-E09).

Participants

URTIs patients were identified from the 2009 ambulatory file (CD2009) and corresponding prescription file (OO2009) based on the ICD-9CM codes 460 (acute nasopharyngitis [common cold]), 462 (acute pharyngitis), 463 (acute tonsillitis), 465 (acute upper respiratory infections of multiple or unspecified sites), and 487 (influenza). Patients received either both Western and TCM medication, or only TCM treatment or Western medication in this study.

Statistical analysis

The mean (standard deviation) and frequency (percentage) were presented as continuous variables and discrete variables, respectively. The frequency of each variable category according to age group and TCM prescription patterns of a single herb or herbal formulae were shown as distributions among the URTIs patients.

For exploring the prescription patterns of the single TCM herbal drugs or formulae among the URTIs patients, a data mining method, association rule, was used to analyze individual patterns and combinations to determine the most common prescription patterns [16]. The method of association rule was often used in large databases for finding frequent item sets which are the lists of commonly displayed together or finding the strong relationships between two items [17,18]. This method has been used extensively in various published studies using the Taiwan NHIRD [19–22]. Each single herb or Chinese medicine formula was set as an independent fixed prescription to estimate the support probability of all of the prescriptions in the data set containing the fixed prescription in order to measure how frequently the association rule occurred in the data set. The minimum level of support was 0.4%. Statistical software R (version 2.13.2) and its package a rules were employed to perform all the statistical analyses.

Results

Clinical visit percentage of URTIs patients in Taiwan 2009

In our study, 472,005 patients sought the treatment of URTIs, including: 425,200 for the Western medication only, 29,052 for Western medication and TCM, and 17,753 for the TCM only. A total of 46,805 (9.92%) URTIs patients sought the TCM treatment, which accounted for 17.04% of the 274,662 patients underwent TCM treatment. Those 46,805 URTIs patients receiving TCM treatment as an outpatient, included; the common cold (79%), influenza (9%), acute upper respiratory infections of multiple or unspecified sites (9%), acute pharyngitis (2%), and acute tonsillitis (1%) (Fig. 1). The results showed that the most patients who suffered from URTIs mainly sought Western medicine treatment. The common cold was a most common condition for patients who sought treatment of TCM treatment.

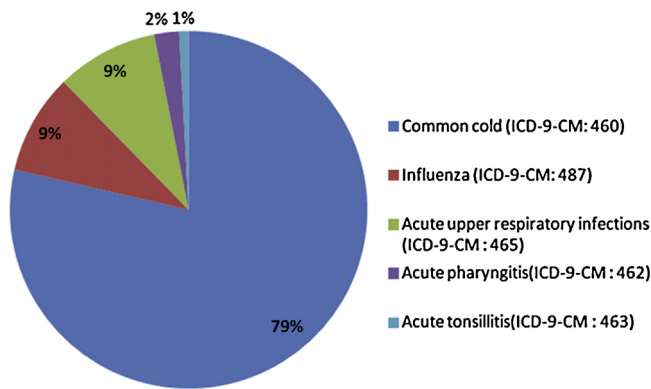


Fig. 1. The proportion of patients with URTIs/common colds treated with Traditional Chinese medicine in Taiwan in 2009.

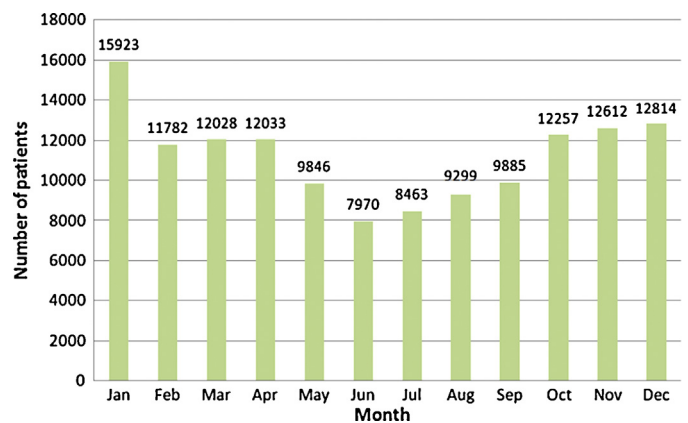


Fig. 2. Patients for URTIs/common colds treated with Traditional Chinese medicine by month in Taiwan in 2009.

Age distribution and gender among URTIs patients who sought the TCM treatment in Taiwan 2009

The age distribution of the 46,805 patients with URTIs showed that most of all (19.07%) were aged between 40 and 49 years, and 18.78% were between 30 and 39. The use of TCM to treat URTIs among women (62.84%) exceeded that for men (37.16%); the usage ratio for women to men was approximately 1.69:1 (Table 1). The main seasons of morbidity from URTIs were December and January (Fig. 2). The results indicated that the distribution was between 30 and 49, with females more likely than males consulting for TCM if they had a URTI.

Comorbidity in URTIs patients in Taiwan 2009

There were 6075 (12.98%) patients who also presented with comorbidity of gastroenteritis, 4054 (8.66%) with hypertension, 3097 (6.62%) with allergic rhinitis, 1586 (3.39%) with diabetes mellitus, and 1108 (2.37%) with urinary tract infections. Other comorbid conditions such as: mental disorders, cancer, chronic kidney disease, and cerebrovascular accidents for each accounted for less than 2% (Table 2). The results showed that the most common comorbidity was gastroenteritis in these URTIs patients.

Table 1 Age and gender distribution of patients with URTIs treated with TCM in Taiwan during 2009.

Age	Patient numbers (%)	Male (%)	Female (%)
<10	1482 (3.17)	749 (1.60)	733 (1.57)
10–19	7429 (15.87)	3588 (7.67)	3841 (8.21)
20–29	7507 (16.04)	2743 (5.86)	4764 (10.18)
30–39	8792 (18.78)	2861 (6.11)	5931 (12.67)
40–49	8928 (19.07)	2920 (6.24)	6008 (12.84)
50–59	7055 (15.07)	2342 (5.00)	4713 (10.07)
60–69	3399 (7.26)	1251 (2.67)	2148 (4.59)
70–79	1718 (3.67)	709 (1.51)	1009 (2.16)
≥80	4,95 (1.06)	230 (0.49)	265 (0.57)
Total	46,805 (100.00)	17,393 (37.16)	29,412 (62.84)

Male:female = 1:1.69.

Wind-heat pattern possibly was the most common TCM pattern of URTIs in Taiwan 2009

A total of 596,801 TCM prescriptions to treat URTIs were issued in Taiwan in 2009. There were 21,260 (3.56%) prescriptions for Yin-Qiao-San, the most popular TCM prescription, followed by 16,087 (2.70%) for Xin-Yi-Qing-Fei-Tang, 14,566 (2.44%) for Ma-Xing-Gan-Shi-Tang and 13,909 (2.33%) for Chuan-Xiong-Cha-Tiao-San (Table 3). Jie-Geng (*Radix Platycodi*) was the most popular Chinese herb and was included in 16,465 (2.76%) prescriptions of the total 596,801. This was followed by Yu-Xing-Cao (*Herbahouttuyniae*) with 11,852 (1.99%), and Bei-Mu (*Bulbus Fritillaria*) with 10,659 (1.79%) (Table 3). Overall, 3224 (0.54%) prescriptions contained combinations of Yin-Qiao-San and Ma-Xing-Gan-Shi-Tang, followed by 3191 (0.53%) with Yin-Qiao-San and Ban-Lan-Gen (*Radix Isatidis*) and 3085 (0.52%) with Yin-Qiao-San and Xin-Yi-Qing-Fei-Tang (Table 4). In summary, according to the TCM principle of clearing heat for the common cold, the TCM pattern of

Table 2 The 10 leading comorbidity diagnoses for patients with URTIs in Taiwan during 2009.

System disease	Major disease (ICD9)	Patients	%
Gastrointestinal disease	Unspecified functional disorder of the stomach (536.9)	6075	12.98
Hypertension	Unspecified essential hypertension (401.9)	4054	8.66
Allergic rhinitis	Allergic rhinitis, cause unspecified (477.9)	3097	6.62
Diabetes mellitus	Diabetes mellitus without complications (250.0)	1586	3.39
Urinary tract infection	Acute cystitis (595.0)	1108	2.37
Mental disorders	Anxiety, dissociative, and somatoform disorders (300.4)	678	1.45
Cancer	Malignant neoplasm in female breast (174.9)	568	1.21
Chronic kidney disease	Chronic kidney disease (585)	241	0.51
Cerebrovascular Accident	Unspecified late effects of cerebrovascular disease (438.9)	197	0.42

Total number of prescriptions = 596,801.

Table 3

The Chinese herbs and Chinese medicine formulae most commonly used for treating URTIs in Taiwan during 2009.

Chinese herb	Number of prescriptions	%	Chinese medicine formula	Number of prescriptions	(%)
Jie-Geng	16,465	2.76	Yin-Qiao-San	21,260	3.56
Yu-Xing-Cao	11,852	1.99	Xin-Yi-Qing-Fei-Tang	16,087	2.70
Bei-Mu	10,659	1.79	Ma-Xing-Gan-Shi-Tang	14,566	2.44
Huang-Qin	9811	1.64	Chuan-Xiong-Cha-Tiao-San	13,909	2.33
Xing-Ren	8583	1.4	Ge-Gen-Tang	13,600	2.28
Gan-Cao	8015	1.34	Xin-Yi-San	10,906	1.83
Ban-Lan-Gen	7866	1.32	Jing-Fang-Bai-Du-San	9932	1.66
Bai-Zhi	7347	1.23	Cang-Er-Sang	9653	1.62
She-Gan	7000	1.17	Sang-Ju-Yin	8687	1.46
Cang-Er-Zi	5936	0.99	Xiao-qing-long-tang	8031	1.35

Total number of prescriptions = 596,801.

Table 4

The combined TCM formulae most commonly used for treating URTIs in Taiwan in 2009.

Chinese medicine formula or herb	Number of prescriptions	Support
Yin-Qiao-San + Ma Xing Gan Shi Tang	3224	0.54
Yin-Qiao-San + Ban-Lan-Gen	3191	0.53
Yin-Qiao-San + Xin-Yi-Qing-Fei-Tang	3085	0.52
Yu-Xing-Cao + Xin-Yi-Qing-Fei-Tang	2903	0.49
Yu-Xing-Cao + Yin-Qiao-San	2895	0.49
Jie-Geng + Bei-Mu	2788	0.47
Jie-Geng + Ma-Xing-Gan-Shi-Tang	2756	0.46
Jie-Geng + Yin-Qiao-San	2562	0.43
Jie-Geng + Xin-Yi-Qing-Fei-Tang	2487	0.42
Jie-Geng + Yu-Xing-Cao	2484	0.42

Total number of prescriptions = 596,801.

wind-heat was a common trend for URTIs in Taiwan during 2009. The Yin-Qiao-San, Xin-Yi-Qing-Fei-Tang and Ma-Xing-Gan-Shi-Tang formula, and Ban-Lan-Gen belong to cold characteristics.

Discussion

This study was a database analysis of the Taiwanese population who used TCM to treat URTIs. A total of 46,805 patients with URTIs received TCM treatment in 2009. The primary reason for using TCM among people in Taiwan was the belief that Chinese herbs are natural products and, consequently, their associated side effects are less than those of Western drugs [23]. Of the URTIs patients, 79% presented with a common cold. The majority reported mild cold symptoms including nasopharyngeal inflammation [24], running and/or stuffy nose, oropharyngeal irritation or discomfort, cough, and fever [25]. TCM treatment of patients with influenza, acute pharyngitis, acute tonsillitis, or acute upper respiratory infections was relatively rare. Symptoms and signs of these diseases included a severe sore throat, tonsillar exudate, fever, and cervical lymphadenopathy [25,26].

Our results indicated that most patients with URTIs treated with TCM ranged between 30 and 49 years of age. People in this age group are generally healthy; thus, their URTIs symptoms were milder compared to those in older or younger age groups. Our results also indicated that the percentage of clinical visit for

URTIs female patients receiving TCM treatment was higher than for males (1.69:1). This result was very similar to the reports of Chen et al., who found the TCM utilization ratio was higher for females than males in Taiwan between 1996 and 2001 [15], but the real reasons still remain unclear and need further study.

In 2009, the period with the highest frequency of TCM treatment of URTIs was from October to April, and the main month of morbidity from URTIs was January. During the winter and spring, the weather is colder and the incidence of URTIs corresponds to the weather [27]. Although Lowen et al. concluded that both cold and dry weather favor transmission of the influenza virus [28], and the annual influenza epidemic season is the winter [20], the results of this study did not provide sufficient evidence to support their conclusion because the 9% influenza rate in 2009 was low.

The most likely connection between gastroenteritis and URTIs is the common mucosal immune system for the respiratory and gastrointestinal tracts. In this immune system, secretory IgA plays a critical role because it originates from the lymphoid tissue of the gastrointestinal and respiratory tracts, forming the first line of defense in these tracts [29].

Numerous patients had comorbid of hypertension. One study has reported that the Coxsackie virus is related to hypertension because it can cause cardiovascular disease and myocarditis [30]. We contend that this is unlikely because URTIs development resulting from Coxsackie viral infections is uncommon. A more probable suggestion is that hypertension is the underlying disease and a URTIs may cause rhinitis and sinusitis, resulting in obstructive sleep apnea and a lack of oxygen, which then leads to increased blood pressure [31].

Allergic rhinitis is another type of URTIs. One study reported that 42.55% of pre-school children had a history of allergic rhinitis and often experienced URTIs; they assumed that this association was because of an immunity deficiency [32]. A large environmental study suggested that a humid climate and airborne mold could easily induce multiple respiratory tract diseases including asthma, bronchitis, respiratory infections, common colds, and allergic rhinitis [33]. In other words, allergic rhinitis and URTIs can occur concurrently because of environmental factors. In addition, these two diseases may produce several similar symptoms, such as allergic rhinitis, a sore throat, coughing for longer durations, and a runny nose because of external environmental factors [34].

A number of Chinese herbs have been used to treat URTIs. TCM treatment of disease in Taiwan is generally in accordance with TCM theories and the personal experience of the CMDs. Our results showed that Yin-Qiao-San was the most popular TCM formula that was used to treat URTIs. Yin-Qiao-San first appeared in the record of *WenBingTiaoBian* (1798–1836 A.D.) and remains a common TCM prescription for treating seasonal influenza [35], as well as the common cold, fever, cough, and other respiratory tract diseases [36]. Yin-Qiao-San is comprised of the following 9 herbs: Jin-yin-hua (*Flos Lonicerae*), Lian-qiao (*Fructus Forsythiae*), Niu-bang-zi (*Fructus Arctii*), Jing-jie (*Herba Schizonepetae*), Bo-he (*Herba Menthae*), Dan-do-chi (*Semen Sojae Praeparatum*), Zhu-ye (*Herba Lophatheri*), Lu-gen (*Rhizoma Phragmitis*), and Gan-cao (*Radix Glycyrrhizae*). Based on the theory of TCM, Yin-Qiao-San can be used to treat a cough or sore throat resulting from warm-heat diseases (febrile disease). One study reported that Lian-qiao (*Fructus Forsythiae*) had antiviral, antibacterial, anti-inflammatory, and antioxidant effects, and that Jin-yin-hua (*Flos Lonicerae*) had anti-inflammatory, anticancer, and immune-boosting effects [37].

The second most popular Chinese medicine formula for treating URTIs was Xin-Yi-Qing-Fei-Tang. Xin-Yi-Qing-Fei-Tang is comprised of the following 10 Chinese herbs: Xin-yi (*Flos Magnoliae*), Bai-he (*Bulbus Lilii*), Zhi-mu (*Rhizoma Aemarrhenae*), Shi-gao (*Gypsum Fibrosum*), Pi-pa-ye (*Folium Eriobotryae*), Sheng-ma (*Cimicifuga Foetid*), Mai-dong (*Radix Ophiopogonis*), Zhi-zi (*Fructus Gardeniae*), Huang-qin (*Radix Scutellariae*), and Gan-cao. One study reported that Xin-Yi-Qing-Fei-Tang was the most commonly prescribed formula for treating allergic rhinitis [38]. Xin-yi is primarily used to treat allergic rhinitis, sinusitis, and headaches in TCM. Another study found that Xin-yi had anti-allergic and anti-inflammatory effects, and that these effects resulted from the inhibition of histamine, prostaglandin E2 (PGE2), platelet active factor (PAF), nitric oxide (NO), pro-inflammatory cytokine interleukin-1 α (IL-1 α), and tumor necrosis factor- α (TNF- α) [39].

In TCM, Ma-Xing-Gan-Shi-Tang is used mainly for the treatment of URTIs with a fever, cough, and yellow phlegm. The primary ingredients are the following 4 herbs: Ma-huang (*Herba Ephedrae*), Xing-ren (*Semen Armeniacae Amarum*), Gan-cao, and Shi-gao (*Gypsum Fibrosum*). An animal study found that Ma-Xing-Gan-Shi-Tang was an excellent antipyretic agent because of its antiviral and T-cell regulation effects. Therefore, Ma-Xing-Gan-Shi-Tang can inhibit the proliferation of influenza A [35].

Jie-Geng has long been employed in Asian countries for the treatment of URTIs, including the common cold, coughs, sputum, tonsillitis, and even asthma [40]. Furthermore, a number of studies have found that Jie-Geng has an immune regulatory effect and can inhibit the production of inflammatory substances, such as IL-6, PGD2, LTC4, and COX-2 protein, by mast cells; thus, it may reduce allergic reactions [40]. Jie-Geng is also an expectorant that can prevent secondary respiratory tract infections [41].

In TCM, Yu-Xing-Cao is considered to have heat-clearing and detoxifying actions, although this has seldom been

investigated [42]. Yu-Xing-Cao (*Herbahouttuyniae*) has also been suggested to have weak antibacterial efficacy [43]; however, it has been employed to treat severe acute respiratory syndrome (SARS) [44].

Bei-Mu (*Bulbus Fritillaria*) is commonly used to treat URTIs because it is an expectorant. In actuality, Bei-Mu is divided into Zhe-Beimu (*Bulbus Fritillariae Thunbergii*) and Chuan-Beimu (*Bulbus Fritillariae Cirrhosae*), and Chuan-Beimu is further divided into *Fritillaria Unibracteata*, *Fritillaria Przewalskii*, and *Fritillariadelavay* [45]. Chuan-Beimu is considered the best antitussive and expectorant in TCM. Zhe-Beimu contains a cholic acid-verticinoneester that may regulate central opioid receptors; thus, its excellent antitussive and expectorant effects are believed to be superior to those of codeine phosphate [46]. Extant studies had shown that Ban-Lan-Gen (*Radix Isatidis*) possesses anti-helicobacter [47], anti-*E. coli* [48], and anti-endotoxic effects [49]. Thus, we can conclude that the common Chinese herbs used to treat URTIs have antitussive and/or expectorant properties.

The CMD treating disease is accordance with the principles of TCM, treating cold with heat and treating heat with cold. The Yin-Qiao-San, Xin-Yi-Qing-Fei-Tang and Ma-Xing-Gan-Shi-Tang formula, and Ban-Lan-Gen are belong to cold in character. Therefore, we suggested the most common type of URTIs in Taiwan belonged to the TCM wind-heat pattern.

Although the results of this research investigated the prescription patterns of TCM for patients with URTIs, there are several limitations to this study: (1) some patients with URTIs may buy Chinese herbs from pharmacies by themselves, so the frequency of TCM treatment may be underestimated. However, the NHI program has the encyclopedic coverage of all population, so this selection biases may have been minimized by the large sample size; (2) the CMD prescribes a treatment according to the patient's clinical manifestations, which is, symptoms, the color and quality of the tongue, and the various pulse formations that comprise the so-called 4 examinations of TCM. These methods differ from the etiological diagnoses of Western medicine. Therefore, when selecting herbs for the treatment of disease, patient symptoms, such as appetite, thirst, and mood, play a crucial role [1]; (3) the study did not use condition probability to explore the relationship between herbs and diseases and further analysis the different patterns of herb or herb combination; (4) the study did not record the usage of Western medication, so therefore, information for common polypharmacy was unavailable; (5) the study is limited to the use TCM theory to explain the simple descriptive statistics. But the logistical regression analysis could not be carried out or that there was no statistical relationship. In the future research, developing a suitable coding system for TCM diagnostic classifications could improve evaluations of TCM and link the Western medicine for increasing the efficacy of TCM.

Conclusions

The results suggested that patients experiencing URTIs requested TCM treatment if the symptoms were mild and were more likely to be women. The Chinese medicine doctors treating

URTIs is accordance to TCM principles, such as treating cold with heat, to select the formula or herb.

Authors' contribution

All authors were involved in the design and writing of the study, and CHH conducted the statistical analysis. All authors approved the submitted version of the manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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