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Research paper

Prescription pattern of Chinese herbal products for hypertension in Taiwan: A population-based study

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ABSTRACT

Ethnopharmacological relevance: Traditional Chinese medicine (TCM) has been commonly used in Asia country. The aim of this study is to analyze the utilization of TCM among hypertensive patients in Taiwan. **Materials and methods:** The use of TCM for primary hypertensive patients was evaluated using a randomly sampled cohort of 1,000,0s recruited from the National Health Insurance Research Database in 5-year period from 2006 to 2010.

Results: Overall, 49.7% ($n=42,586$) of primary hypertension utilized TCM and 12.1% ($n=5132$) of them used TCM for the treatment of hypertension. Among the top 10 most frequently prescribed herbal formulae, *Tian-Ma-Gou-Teng-Yin*, *Gout-Teng-San*, *Liu-Wei-Di-Huang-Wang* and its derivatives were found to be the most common herbal formulae prescribed by TCM doctors for the treatment of hypertension in Taiwan.

Conclusion: This study showed the utilization pattern of Chinese herbal product in patients with hypertension. Further researches and clinical trials are needed to evaluate the efficacy of these Chinese formulae or its ingredients in treating hypertension.

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1. Introduction

Hypertension is a worldwide health problem and public health issue (Sliwa et al., 2011). It is a major risk factor for cerebrovascular disease, coronary heart disease and renal failure (Redwood, 2007). About 54% of stroke and 47% of ischemic heart disease worldwide were attributable to high blood pressure (Lawes et al., 2008). More than 20% of people in adult are hypertensive in Taiwan. Furthermore, the awareness rate of hypertension was less than two-thirds; the medication rate and control rate for hypertensive patients were 56% and 29.2%, respectively (Chiou et al., 2013). Effective treatment of hypertension is limited by availability, cost, and adverse effects of antihypertensive medications (Chobanian et al., 2003). Thus, due to the limitations of those, a certain proportion of the population, especially in Asia, has turned to complementary and alternative medicine (CAM) (Wood et al., 2003; Yen et al., 2006; Chen et al., 2012; Xu and Chen, 2012;

Wang and Xiong, 2013). CAM including Chinese herbal medicine (CHM) is becoming increasingly popular and frequently used among patients with chronic disease in searching for a treatment modality with potential efficacy and few adverse effects (Chen and Xu, 2003; Chen, 2008; Xu and Chen, 2008).

Previous studies of traditional Chinese medicines (TCM) have found that *tian ma* (Gastrodiae Rhizoma) (Wang et al., 2007), *gou teng* (Uncariae cum Uncis Ramulus) (Kim et al., 2008), *zhi zi* (Gardeniae Fructus) (Yang et al., 1999), *huang qin* (Scutellariae Radix) (Wang et al., 1974), *yin mu cao* (Leonuri Herba) (Chen and Kwan, 2001), *chuan niu xi* (Cyathulae Radix) (Li et al., 2012), *du zhong* (Eucommiae Cortex) (Luo et al., 2010), *sang ji shang* (Taxilli Herba) (Zhen, 2000), *ye jiao teng* (Polygoni Multiflori Caulis) (Wang et al., 2006), *fu lin* (Poria) (Zhao et al., 2012), *sheng jian* (Tabassum and Ahmad, 2011), *dang gui* (Angelicae Sinensis Radix) (Rhyu et al., 2005), *chuan xiong* (Chuanxiong Rhizoma) (Kim and Rhyu, 2010), *chi shao* (Paeoniae Rubra Radix) (Jin et al., 2012), *ze xie* (Alismatis Rhizoma) (Matsuda et al., 1987), *ru gui* (Cinnamomi Cortex) (Kang and Shin, 2012), *di long* (Pheretima) (Li et al., 2008) and *huang bai* (Phellodendri Cortex) (Hou et al., 2007) have been suggested to decrease blood pressure or vasodilatation.

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Unfortunately, evidence obtained in human studies is limited regarding patterns of use of classical TCM in relation to hypertension. Further research is essential in all areas of CAM to confirm the usefulness as an adjunct therapy (Lin et al., 2001).

TCM includes acupuncture, traumatology manipulative therapies and Chinese herbal products. These have been an important part of health care in Taiwan for hundreds of years and are fully reimbursed under the current National Health Insurance (NHI) system. NHI, the only national and official health insurance in Taiwan established since 1995, covers nearly all inhabitants (22,520,776 beneficiaries at the end of 2002) (Cheng, 2003). Thus the NHI research database is a platform for understanding the utilization of TCM therapies by TCM doctors. The aim of our study is to analyze a random sample from the comprehensive database and to determine the TCM utilization patterns of newly diagnosed primary hypertension in Taiwan. The results of this study should prove valuable information that will enable clinicians to respond to patient to use of TCM in an informed way, which will in turn strengthen further the patient–clinician relationship when treating hypertension related complications.

2. Materials and methods

2.1. Data resources

This study was designed as a retrospective population-based study analyzing a sample of 1,000,000 subjects selected at random from the 22 million beneficiaries of the NHI scheme of Taiwan. We aimed to determine the prevalence of using prescribed Chinese herbal products (CHP) among primary hypertensive patients between January 1, 2006 and December 31, 2010. All data were obtained from the NHI research database which includes all the reimbursement data of the NHI. All individual names are encrypted and transformed and the database is maintained by the National Health Research Institutes of Taiwan. The NHI research database contains gender, date of birth, date of clinical visits, three major diagnosed codes (ICD-9-CM) and name–dose–duration of prescribed drugs. This study was approved by the Joint Institutional Review Board of China Medical University.

2.2. Study subjects

The selection of study subjects from the random sample of one million individuals was performed as follows (Fig. 1). First, we included all patients that had at least three outpatient visits with a hypertension diagnosis within 1 year ($n=135,961$). Second, we excluded all patients with secondary hypertension or with missing information on gender and age ($n=412$). Third, cases of hypertension ($n=135,549$) that had been diagnosed before the end of 2005 were also excluded to ensure that all the subjects were newly diagnosed with primary hypertension in the time period 2006–2010. Fourth, subjects under 20 years of age ($n=48$) were also excluded to limit the study sample to adults. Finally, 85,622 study subjects were included in this study cohort. We further divided these subjects into TCM nonusers ($n=43,036$) and users ($n=42,586$) determined by the prescription of TCM at least one time or not.

2.3. Study variables

We selected a series of demographic factors based on previous studies. The subjects were categorized into four groups according to age: 20–39, 40–59, 60–79, determine the key independent variables for utilization of TCM among hypertensive patients (Gu et al., 2002; Cruickshank, 2004; Kearney et al., 2004; Tseng et al., 2012). and ≥ 80 years. Taiwan was divided into seven geographic regions: Taipei

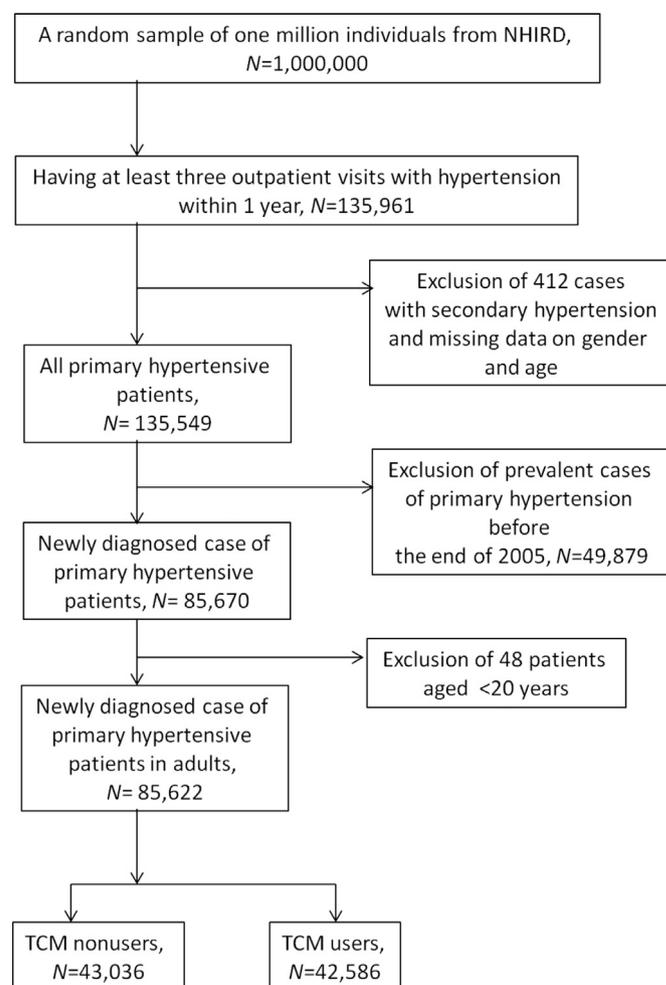


Fig. 1. Flow recruitment chart of subjects from the one million random samples obtained from the National Health Insurance Research Database (NHIRD), 2006–2010, in Taiwan.

city, Kaohsiung city, Northern region, Central region, Southern region, Eastern region and Outlying islands. We split the monthly wage of individuals into four levels: new Taiwan dollars (NT\$) 0, 1–19,999, 20,000–39,999 and $\geq 40,000$. We also searched the NHI research database for clinical potential complications and treatment records related to hypertension as independent variables. The complications associated with hypertension include heart (ICD 9 code 402, 404, 410–428.), brain (ICD 9 code 430), kidney (ICD 9 code 403–404, 581, 583, 585) and other atherosclerotic diseases (ICD 9 code 440–442) (Kannel et al., 1971; Collins et al., 1990; MacMahon et al., 1990; Wright et al., 2002; Girerd and Giral, 2004; Diamond and Phillips, 2005). The reimbursement database contains all details related to the prescription of conventional medicines for treating hypertension.

2.4. Statistical analysis

Data analysis consisted of descriptive statistics, including the prescription rates of TCM users stratified by patient's demographic characteristics, indications for the prescription of TCM (categories classified by ICD 9 code), and the most frequently prescribed herbal formulae used when treating hypertension. The diagnoses were coded according to the ICD-9 and grouped into a series of distinct broad disease categories. The potential effects of Chinese herbs contained in the 10 most commonly prescribed CHP were grouped according to previous studies and are summarized in

Table 4. Multiple logistic regression was conducted to evaluate the factors that correlated with TCM use. Software package SAS 9.20 was used for data management and analysis with a significant level of $\alpha=0.05$.

3. Results

The database of outpatient claims contained information on 85,622 patients with primary hypertension from 2006 to 2010. Among them, 42,586 (49.7%) patients used TCM outpatient services at least once. Among all TCM users, 12.1% ($n=5132$) used TCM for the treatment of primary hypertension. Details of the demographic distribution of TCM users and nonusers are presented in Table 1. The mean age of TCM users was slightly younger than that of TCM nonusers. There were more TCM users than nonusers with an income level of NT\$ 0 or residing in central region.

The adjusted odds ratios (aORs) and 95% confidence interval (95% CIs) obtained by multiple logistic regression are also presented in Table 1. Compared with the age group 40–59 years (aORs=1.00), those aged 20–39 years, 60–79 years and over 80 years were less likely to be TCM users. There was also a significant difference between users and nonusers with income groups of NT\$

0 and 1–19,999. Patients with more complications were more likely to seek TCM treatment than those with no complication (one complication aORs=1.16, CI: 1.13–1.20; two complication aORs=1.38, CI: 1.32–1.45; more than three complications aORs=1.61, CI: 1.45–1.38).

Among the primary hypertensive patients visiting TCM doctors, 372,835 (51%) visits involved the prescription of TCM, while the rest was prescribed acupuncture and traumatology manipulative therapies. Analysis of the major disease categories for all TCM visits made by 42,586 TCM users is summarized in Table 2. The findings show that “symptoms, signs, and ill-defined conditions” were the most common reasons for using CHP (32.7%, $n=121,737$), followed by “disease of musculoskeletal system and connective tissue” (15.7%, $n=58,451$), and “disease of respiratory system” (15.4%, $n=57,311$). Details of the most frequently prescribed CHP for treating primary hypertension by TCM doctors are provided in Table 3.

Tian-Ma-Gout-Teng-Yin (Gastrodia and Uncaria decoction) was the most frequently prescribed CHP, followed by *Gou-Teng-San* (Uncaria decoction), *Jia-Wei-Xiao-Yan-San* (Augmented Rambling powder), *Xue-Fu-Zhu-Yu-Tang* (Drive out stasis in the Mansion of blood decoction), *Zhi-Bai-Di-Huang-Wan* (Anemarrhena, Phellodendron and Rehmannia), *Qi-Ju-Di-Huang-Wan* (Lycium fruit, Chrysanthemum, and Rehmannia pills), *Zhi-Gan-Cao-Tang* (Prepared licorice decoction), *Ji-Sheng-Shen-Qi-Wan* (Kidney Qi pill), *Liu-Wei-Di-Huang-Wan*

Table 1
Demographic characteristics and results of multiple logistic regression showing the adjusted odds ratio (aOR) and 95% CI (confidence interval) for primary hypertension from 2006 to 2010 in Taiwan.

Characteristic	All patients	TCM ^a nonusers (%)	TCM users(%)	aOR ^b (95% CI ^c)
Number of cases	85,622	43,036	42,586	
Gender				
Male	45,923 (53.6)	25,627 (59.5)	20,296 (47.7%)	1
Female	39,699 (46.4)	17,409 (40.5)	22,290 (52.3%)	1.69 (1.64–1.73)
Age at diagnosis (years)				
Mean \pm SD	59.25 \pm 13.72	61.11 \pm 14.10	57.80 \pm 13.25	
20–39	5479 (6.40)	2244 (5.2)	3176 (7.5)	0.72 (0.68–0.76)
40–59	41,682 (48.7)	19,314 (44.9)	21,992 (51.6)	1
60–79	30,995 (36.2)	16,286 (37.8)	14,809 (34.8)	0.54 (0.51–0.57)
\geq 80	7466 (8.7)	5192 (12.1)	2609 (6.1)	0.30 (0.27–0.32)
Insured salaries (NT\$ ^d /month)				
0	4790 (5.6)	2334 (5.4)	2456 (5.8)	1
1–19,999	30,657 (35.8)	16,336 (38.0)	14,321 (33.6)	0.89 (0.83–0.95)
20,000–39,999	38,391 (44.8)	18,459 (42.9)	19,922 (46.8)	0.99 (0.93–1.06)
40,000	11,784 (13.8)	5907 (13.7)	5887 (13.8)	0.98 (0.92–1.05)
Insured region				
Taipei City	27,088 (31.6)	14,107 (32.8)	12,981 (30.5)	1
Kaohsiung City	13,693 (16.0)	6962 (16.2)	6731 (15.8)	1.08 (1.04–1.13)
Northern Taiwan	10,774 (12.6)	5635 (13.1)	5139 (12.1)	1.03 (0.98–1.08)
Central Taiwan	16,058 (18.8)	6827 (15.9)	9231 (21.7)	1.51 (1.45–1.57)
Southern Taiwan	14,225 (16.6)	7431 (17.3)	6794 (16.0)	1.01 (0.97–1.05)
Eastern Taiwan	2951 (3.4)	1573 (3.7)	1378 (3.2%)	0.97 (0.90–1.05)
Outlying islands	833 (1.0)	501 (1.2%)	332 (0.8%)	0.78 (0.60–0.90)
Number of potential complications				
0	35,822 (41.8)	18,387 (42.7)	17,435 (40.9)	1
1	38,174 (43.3)	18,986 (44.1)	19,188 (42.6)	1.16 (1.13–1.20)
Heart	33,094 (38.7)	16,395 (38.1)	16,699 (39.2)	
Brain	3473 (4.1)	1804 (4.2)	1669 (3.9)	
Kidney	262 (0.3)	123 (0.3)	139 (0.3)	
Other atherosclerosis disease	1345 (1.6)	664 (1.5)	681 (1.6)	
2	9986 (10.1)	4907 (11.4)	5079 (8.9)	1.38 (1.32–1.45)
Heart+brain	6720 (7.8)	3384 (7.9)	3336 (7.8)	
Heart+kidney	409 (0.5)	204 (0.5)	205 (0.5)	
Heart+others	2513 (2.9)	1167 (2.7)	1346(3.2)	
Brain+kidney	36 (0.0)	14 (0.0)	22 (0.1)	
Brain+others	294 (0.3)	132 (0.3)	162 (0.4)	
Kidney+others	14 (0.0)	6 (0.0)	8 (0.0)	
\geq 3	1640 (1.9)	756 (1.8)	884 (2.1)	1.61 (1.45–1.78)

^a TCM refers to traditional Chinese medicine.

^b OR refer to odds ratio.

^c CI refers to confidence interval.

^d NT\$ refers to new Taiwan dollars, of which US\$1=NT\$30 approximately.

Table 2

Frequency distribution of traditional medicine (TCM) visits by major disease categories (according to 9th ICD codes) among primary hypertension patients from 2006 to 2010 in Taiwan.

Major disease category	No. of visits (no. of patients)			
	ICD-9-CM codes	Chinese herbal remedies	Acupuncture or manipulative therapies	Total of TCM
Infectious and parasitic diseases	001-139	2001 (639)	144 (22)	2145 (645)
Neoplasms	140-239	3474 (380)	439 (36)	3913 (391)
Endocrines, nutritional, metabolic disease, and immunity disorders	240-279	14,797 (2496)	1166 (150)	15,963 (2526)
Hematologic disorders	280-289	1144 (255)	56 (5)	1200 (255)
Mental disorders	290-319	4228 (842)	882 (82)	5110 (868)
Disease of nervous system and sense organs	320-389	18,264 (4356)	10,625 (980)	28,899 (4747)
Diseases of circulatory system	390-459			
Hypertension	401-405	32,750 (5095)	2611 (259)	35,361 (5132)
Others		13,443 (2235)	16,255 (508)	29,698 (2430)
Diseases of respiratory system	460-519	57,311 (11,948)	2368 (427)	59,679 (11,961)
Diseases of digestive system	520-579	46,809 (9182)	2699 (417)	49,508 (9193)
Disease of genitourinary system	580-629	21,893 (4072)	1349 (177)	23,242 (4080)
Diseases of skin and subcutaneous tissue	680-709	9691 (2602)	377 (72)	10,068 (2604)
Disease of musculoskeletal system and connective tissue	710-739	58,451 (13,597)	160,124 (14,246)	218,575 (20,385)
Symptoms, sign, and ill-defined conditions	780-799	121,737 (18,979)	10,649 (1453)	132,386 (19,092)
Injury and poisoning	800-999	16,962 (7,244)	175,319 (16,632)	192,281 (17,495)
Supplementary classification ^a	V01-V82	21 (5)	16 (4)	37 (9)
	E800-E999	0 (0)	0 (0)	0 (0)
Others ^b		2240 (521)	1049 (79)	3289 (557)
Total		372,835 (35,159)	358,191 (24,895)	731,026 (42,586)

^a Supplementary classification of factors influencing health status and contact with health service, external causes of injury and poisoning.

^b Others include ICD-9-CM codes 280-289, 630-677, 740-759, 760-799 and missing/error data.

Table 3

Ten most common herbal formulae prescribed by TCM doctors for the treatment of primary hypertension among 42,586 patients from 2006 to 2010 in Taiwan.

Herbal formulae	English name	Number of Person-days N=841,942 (%)	Average daily dose (g)	Average duration for prescription (days)
<i>Tian-Ma-Gou-Teng-Yin</i>	Gastrodia and Uncaria decoction	95,523 (11.35)	11.35	10.36
<i>Gout-Teng-San</i>	Uncaria decoction	31,905 (3.79)	12.94	9.26
<i>Jia-Wei-Xiao-Yao-San</i>	Augmented Rambling powder	27,001 (3.21)	8.34	11.47
<i>Xue-Fu-Zhu-Yu-Tang</i>	Drive out stasis in the Mansion of blood decoction	25,324 (3.01)	8.96	10.05
<i>Zhi-Bai-Di-Huang-Wan</i>	Anemarrhena, Phellodendron and Rehmannia	22,630 (2.69)	8.48	11.22
<i>Qi-Ju-Di-Huang-Wan</i>	Lycium fruit, Chrysanthemum and Rehmannia pills	19,339 (2.3)	9.16	12.64
<i>Zhi-Gan-Cao-Tang</i>	Prepared licorice decoction	17,833 (2.12)	8.66	11.07
<i>Ji-Sheng-Shen-Qi-Wan</i>	Kidney Qi pill	17,660 (2.1)	9.8	12
<i>Liu-Wei-Di-Huang-Wan</i>	Six ingredient pills with Rehmannia	16,873 (2)	8.43	11.12
<i>Bu-Yang-Huan-Wu-Tang</i>	Tonify Yang to restore five-tenths decoction	15,268 (1.81)	8.99	11.35

(Six ingredient pills with Rehmannia) and *Bu-Yang-Huan-Wu-Tang* (Tonify Yang to restore five-tenths decoction).

Among the top 10 most frequently prescribed herbal formulae, *Zhi-Bo-Di-Huang-Wan*, *Qi-Ju-Di-Huang-Wan* and *Ji-Sheng-Shen-Qi-Wan*, which all contain *Rehmannia Radix Preparata*, *Corni Fruit*, *Dioscoreae Radix*, *Poria*, *Moutan Cortex*, *Alismatis Rizoma*, are three derivative formulae of *Liu-Wei-Di-Huang-Wan*. The potential effects of these Chinese herbs when used to treat primary hypertension are summarized in Table 4. These include increasing production of nitric oxide, blocking calcium channel, regulating renin-angiotensin system, increasing diuretic effect, acting on central vasomotor center.

4. Discussion

The prevalence of hypertension under treatment in Taiwan over 5 years in the study was 13.5% which is similar to the estimates given by previous surveys (Olives et al., 2013). The

5-year cumulative incidence of hypertension was high (8.6%) in our study as compared with the 2.4% in a previous survey with small sample size in 2007 in Taiwan. Not surprisingly, incidence rates of hypertension ranging between 3% and 18% have been reported, depending on the age, gender, ethnicity, and body size of the population studied (Hajjar et al., 2006).

In our study, the utilization of CAM (49.7%) in hypertensive patients was lower than that in the USA (69.5%) (Bell et al., 2006) or Japan (74.2%) (Hu et al., 2013) and higher than that in the UK (43.1%) (Gohar et al., 2008). Of the 42,586 CHP users, 12.1% reported using any CAM for treating hypertension, which is higher than the results of the USA study (7.8%) and lower than those of the Japan study (13.1%). However, the results of these studies are not directly comparable with this study because of differences in the definition of CAM use, study population, and study period. CAM usage in our study period among adults with primary hypertension in Taiwan may be underestimated on account of purchasing directly from TCM herbal pharmacies by patient himself. TCM is a unique traditional therapy which has been used

Table 4
Potential effects of herbs present in the 10 most common herbal formulae prescribed by TCM doctors for treating primary hypertension.

Herbal formulae	Number of herbs	Ingredient herbs
<i>Tian-Ma-Gou-Teng-Yin</i>	11	Gastrodiae Rz. ^a , Uncariae cum Uncis Ram. ^b , ConchaHaliotidis, Gardeniae Fr. ^e , Scutellariae Rx. ^{b,d,e} , Leonuri Hb. ^b , Cyathulae Rx. ^{a,b} , Eucommiae Cx. ^{a,b} , Taxilli Hb. ^{d,e} , Polygoni Multiflori Caul. ^a , Poriae Paradicis Scl.
<i>Gout-Teng-San</i>	12	Gastrodiae Rz. ^a , Citri Reticulatae Per., Pinelliae Preparatum Rx., Ophiopogonis Rx., Poriae Paradicis Scl. ^d , Ginseng Rx., Chrysanthemi Flos, Saposhnikoviae Rx., Glycyrrhizae Preparata Rx., Gypsum Fibrosum, Zingiberis Recens Rz. ^b
<i>Jia-Wei-Xiao-Yao-San</i>	10	Angelicac Sinensis Rx. ^{a,b} , Paeoniae Alba Rx., Poria ^d , Atractylodis Macrocephalae Rx., Bupleuri Rx., Moutan Cx., Gardeniae Fr. ^e , Glycyrrhizae Preparata Rx., Menthae Haplocalycis Hb., Zingiberis Recens Rz. ^b ,
<i>Xue-Fu-Zhu-Yu-Tang</i>	11	Persicae Sm., Carthami Flos, Angelicac Sinensis Rx. ^{a,b} , Chuanxiong Rx. ^b , Paeoniae Rubra Rx. ^b , Cyathulae Rx., Bupleuri Rx., Platycodi Rx., Aurantii Fr., Rehmanniae Rx., Glycyrrhizae Rx.
<i>Zhi-Bai-Di-Huang-Wan</i>	8	Anemarrhenae Rx., Phellodendri Cx. ^c , Rehmanniae Preparata Rx., Corni Fr., Dioscoreae Rx., Poria ^d , Moutan Cx., Alismatis Rz. ^{b,d}
<i>Qi-Ju-Di-Huang-Wan</i>	8	Lycii Fr., Chrysanthemi Flos, Rehmanniae Preparata Rx., Corni Fr., Dioscoreae Rx., Poria ^d , Moutan Cx., Alismatis Rz. ^{a,b}
<i>Zhi-Gan-Cao-Tang</i>	9	Glycyrrhizae Preparata Rx., Ginseng Rx., Cinnamomi Ram. ^b , Rehmanniae Rx., Ophiopogonis Rx., Colla Corii Asini, Cannabis Sm., Zingiberis Recens Rz. ^b , Zizyphi Jujube Fr.
<i>Ji-Sheng-Shen-Qi-Wan</i>	10	Cinnamomi Cx. ^b , Aconiti Lateralis Preparata Rx., Cyathulae Rx., Plantaginis Sm., Rehmanniae Preparata Rx., Corni Fr., Dioscoreae Rx., Poria ^d , Moutan Cx., Alismatis Rz. ^{a,b}
<i>Liu-Wei-Di-Huang-Wan</i>	6	Rehmanniae Preparata Rx., Corni Fr., Dioscoreae, Poria Rx. ^d , Moutan Cx., Alismatis Rz.
<i>Bu-Yang-Huan-Wu-Tang</i>	7	Astragali Rx., Angelicac Sinensis Rx. ^{a,b} , Chuanxiong Rx. ^b , Paeoniae Rubra Rx. ^b , Persicae Sm., Carthami, Pheretima Flos ^c

Rz. refers rhizoma; Ram. refers ramulus; Fr. refers fructus; Hb. Refers herba; Rx. refers radix; Cx. refers cortex; Caul. refers caulis; Scl. refers sclerotum; Sm. refers semen.

^a via increasing nitric oxide level.

^b via blocking calcium channel.

^c via inhibiting rennin-angiotensin system.

^d via dieresis.

^e via central mechanism.

in Taiwan for over hundreds of years, and this long period of use may contribute significantly to the high prevalence of TCM usage among primary hypertension. In addition, it should be noted that TCM treatment is covered by the NHI system. Therefore, unsurprisingly, the prevalence of CHP prescription among adults with primary hypertension is relatively higher in Taiwan than other countries. In our speculation, the reason for the prescription widely used in Taiwan is that Chinese people deeply believe that TCM has either fewer side effects than Western medicine or no side effects at all.

The present results showed that nearly 60% of newly diagnosed hypertensive patients receiving treatment in Taiwan have suffered from one or more complications of hypertension during the 5-year follow-up. Hypertensive cerebral disease and hypertensive cardiovascular disease were the two most common hypertensive complications. One possibility is that primary hypertension has a long asymptomatic preclinical phase that has resulted in a high incidence of vascular complications (Cerasola et al., 1996; Mosterd et al., 1999; Sever et al., 2003). The present study found that patients with newly diagnosed hypertension who developed more than one site of hypertensive complications were more likely to seek advice from a TCM doctor. However, regarding to the aim of utilizing CHM in hypertensive patients, it was used as an adjunct therapy rather than a replacement treatment.

The present findings showed that, among primary hypertension, female and those aged 20–39 years were more likely to be TCM users than males and other age group as shown in Table 1. The main aim of Table 2 is to find out the reason of visits categorized by 9th ICD code among patients with newly diagnosed hypertension using TCM from 2006 to 2010. Among them, only 5132 (12.1%) users called for the treatment of hypertension. “symptoms, sign and ill-defined conditions” were the most common reasons for using CHP, followed by “disease of musculoskeletal and connective tissue. Further analysis found that part of the reason of TCM doctors tend to use Chinese herbal remedies for treating musculoskeletal disease was to relieve the symptom of hypertension including neck soreness, headache or chest tightness. Although previous studies have demonstrated that

acupuncture might be an alternative therapy for treating hypertension (Flachskampf et al., 2007), the present study indicated that acupuncture in Taiwan is used mainly for disease of the musculoskeletal system and connective tissue in primary hypertensive patients.

Tian-Ma-Gou-Teng-Yin is widely used to treat hypertension related symptoms in clinical practice in East Asia and was the most frequently prescribed formulae in treating primary hypertension during the study period, as shown in Table 3. *Tian-Ma-Gou-Teng-Yin*, invented by doctor Hu, Guang Ci in 1956, is composed of nine Chinese herbs and the major function is to calm the liver and extinguish wind which might indicate it as a potential efficacious therapy for reducing blood pressure and related symptoms. Prescription of Chinese herbal formula is based on the principle of “Jun-Chen-Zuo-Shi” (Qiu, 2007). In the composition of *Tian-Ma-Gou-Teng-Yin*, *Rizoma Gastrodia* and *Uncariae cum Uncis Ramulus*, which play the role as “Jun” and is the major drug entity to target a disease, could calm the liver and extinguish wind; *Concha Haliotidis* and *Cyathulae Radix*, which play the role as “Chen” and either supports “Jun” or reduces the side effects of “Jun”, could sedate yang, clear liver heat and purge liver fire; the rest herbs of *Tian-Ma-Gou-Teng-Yin*, which play the role as “Zuo” and either reduces the adverse effects or eliminates the toxicity of “Jun” and “Chen”, could nourish the liver and kidneys, activate the blood and direct the blood flow downward, calm the spirit, and tranquilize the mind.

One meta-analysis review showed that *Tian-Ma-Gou-Teng-Yin* could use as an adjunctive formula to treat hypertension (Wang et al., 2013a). Another systematic review revealed that *Tian-Ma-Gou-Teng-Yin* could lower blood pressure effectively compared with classical medicine (Xun et al., 2010; Huang, 2013). Modern studies also showed that *Tian-Ma-Gou-Teng-Yin* could improve memory, regulate the secretions of vasoactive substances, increase the serum concentration of nitric oxide and nitric oxide synthase, decrease levels of endothelin and angiotensin II, reduce the left ventricular mass index and collagen content, and improve left ventricular remodeling (Xian et al., 2003; Wang et al., 2007; Ho et al., 2008). Nine of 11 ingredients of this formula have been proved the effect of vasodilatation or lowering blood pressure with

the possible mechanism (Table 4). Although previous studies have found that some Chinese herbs are able to reduce blood pressure, possibly by many mechanisms (Xiong et al., 2013b), there have not yet been any well-defined clinical trials that have demonstrated the efficacy and safety of *Tian-Ma-Gou-Teng-Yin* or its ingredients when treating hypertension (Zhang et al., 2012). Some active ingredients in the herbs related to *Tian-Ma-Gou-Teng-Yin* have been identified, such as gastrodin in *tian ma*, rhynchophylline in *gou teng*, leonurine in *yi mu cao*, baicalin in *huang qin*, geniposide in *zhizi*, quercetin in *sang ji sheng*, emodin in *ye jiao teng*, and chlorogenic acid in *du zhong*, which could lower blood pressure provided in previous researches (Pharmacopoeia Commission, 2005).

Among the top 10 most frequently prescribed formulae for treating primary hypertension, *Zhi-Bai-Di-Huang-Wan*, *Qi-Ju-Di-Huang-Wan* and *Ji-Sheng-Shen-Qi-Wan*, which are all derivatives of *Liu-Wei-Di-Huang-Wan*, are prescribed to alleviate various common symptoms of primary hypertension, namely, hot sensation, blurred vision, and oliguria, respectively. Other frequently prescribed formulae are associated with the syndrome of liver wind (*Gou-Teng-San*), liver qi stagnation (*Jia-Wei-Xiao-Yao-San*), heart blood stagnation (*Xue-Fu-Zhu-Yu-Tang*) heart qi deficiency (*Zhi-Gan-Cao-Tang*) and qi and yang deficiency (*Bu-Yang-Huang-Wu-Tang*). Systematic review showed that *Liu-Wei-Di-Huang-Wan* (Wang et al., 2012) combined with antihypertensive drugs appears to be effective in improving blood pressure and symptoms in patients with essential hypertension. *Qi-Hi-Di-Huang-Wan* (Wang et al., 2013b) also has the same effect.

In general TCM doctors treated hypertensive patients' complaints according to the syndrome differentiation theory other than by making a specific diagnosis; this is based on holistic consideration of health in hypertensive patients who are suffering from symptoms and complications at various sites. (Nahas, 2008; Wang and Xiong, 2012, 2013; Xiong et al., 2013a). According to previous studies, hypertension could be divided into three major types (stage) on the basis of the holistic diagnosis and treatment in traditional Chinese (Bian Zheng Lun Zhi) (Wang and Xiong, 2013; Xiong et al., 2013b). First type (stage) is liver fire syndrome of which classical formula is *Tian-Ma-Gou-Teng-Yin*; Second type (stage) is phlegm-fluid retention syndrome of which classical formula is *Wuling powder*; Third stage (type) is kidney deficiency syndrome of which classical formula is *Liu-Wei-Di-Huang-Wan* and its derivatives (Wang and Xiong, 2013; Xiong et al., 2013b). Apparently, we could not differentiate the different “Zheng” or syndromes of those patients with hypertension from the claim database of NHI. However, from the pattern of TCM use, we could distinguish what kinds of formulae were suitable for the different symptomatology classifications and typological presentations of patients with hypertension based on the discriminating theory of “Bian Zheng Lun Zhi”. By way of analyzing the 10 most frequent uses of Chinese herbal formulae in the study, we may postulate that liver fire syndrome and kidney deficiency syndrome are the most encountered “Zheng” in patients with primary hypertension. This is the reason why *Tian-Ma-Gou-Teng-Yin* and *Liu-Wei-Di-Huang-Wan* were the most prescription patterns of Chinese herbal products.

In this context and in line with previous results, the present study found that TCM doctors in Taiwan prescribed herbal medicine mainly to optimize the body's ability to function normally, rather than as a cure for hypertension. Moreover, lack of adequate data on the clinical safety and efficacy of CHP when treating hypertensive patients, a large number of double-blind, placebo-control studies should be performed to prove the efficacy of these CHP. Based on the present trend and medical care system of TCM utilization, herbal remedies for treating hypertension or related symptom will continue to be used. On account of respecting the patient's choice of medical care, either Chinese herb or Western medicine, we recommend that TCM doctor should

carefully monitor patients' blood pressure and the potential side effects of CHP when they are being used along. Further studies are warranted to assess the formulae generally used by TCM doctors in this study in order to determine whether they are really useful as add-on treatments for patients receiving anti-hypertension treatment.

The present study has three limitations. First, this study neither included Chinese herbal decoctions that were purchased directly from TCM herbal pharmacies, nor involved health food containing herbs. Thus, the frequency of CHP utilization might have been underestimated. However, the likelihood that subjects purchased a lot of other herbs outside the NHI system is not high on account of the cost that was cheaper in the NHI system. Secondly, we are unable to draw any conclusion about the value of blood pressure with respect to TCM utilization owing the lack of actual clinical data. Lastly, this was a retrospective study in this study and thus does not include a randomized placebo group. Thus, great caution is necessary when interpreting the results of the most commonly prescribed Chinese formulae obtained in the present study due to the possibility of a placebo effect.

In conclusion, this study provided the prescription patterns of Chinese herbal products in patients with hypertension. Among the top 10 most frequently prescribed herbal formulae, *Tian-Ma-Gou-Teng-Yin*, *Gou-Teng San*, *Liu-Wei-Di-Huang-Wan* and its derivatives were found to be the most common herbal formulae prescribed by TCM doctors for the treatment of hypertension. Although previous researches do support that the use of TCM was effective in lowering blood pressure, the mechanism and the therapeutic effect of the Chinese formulae as well as its ingredients in treating hypertension needs to be elucidated and explored more, especially with well designed researches or efficacy-based clinical trials.

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