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# Use of traditional Chinese medicine in patients with hyperlipidemia: A population-based study in Taiwan



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## ABSTRACT

**Ethno-pharmacological relevance:** Chinese herbal products (CHPs) are commonly used in patients with hyperlipidemia in traditional Chinese medicine (TCM). Because hyperlipidemia and related disease are common issues worldwide, this study analyzed the prescription patterns and frequencies of CHPs for treating patients with hyperlipidemia in Taiwan.

**Background:** Traditional Chinese medicine (TCM) has become popular as a therapy for controlling symptoms in patients with hyperlipidemia. This study aimed to analyze the prescription patterns of TCM for patients with hyperlipidemia in Taiwan.

**Methods:** The study population was recruited from a random-sampled cohort of 1,000,000 people from the National Health Insurance Research Database between 2003 and 2009. We identified 30,784 outpatient visits related with hyperlipidemia diagnosis and collected these medical records. Association rules of data mining were conducted to explore the co-prescription patterns for Chinese herbal products (CHPs).

**Results:** The most commonly prescribed herbal formula for hyperlipidemia treatment was Xue-Fu-Zhu-Yu-Tang (16.1%), and Shan Zha (*Crataegi fructus*; 25.0%) was the most commonly prescribed single herb. The most commonly prescribed combination of an herbal formula and a single herb was Xue-Fu-Zhu-Yu-Tang and Dan Shen (*Radix Salviae Miltiorrhizae*), and the most commonly prescribed combination of couplet herbs was Dan Shen and Shan Zha.

**Conclusion:** Xue-Fu-Zhu-Yu-Tang is the most frequently prescribed formula and is typically prescribed with Shan Zha, Dan Shen, and He Shou Wu for patients with hyperlipidemia. Clinical trials are warranted in future research to investigate the effects of the CHPs in terms of safety and efficacy and in particular to evaluate potential interactions with conventional treatments.

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## 1. Introduction

Hyperlipidemia involves abnormally elevated levels of one or more lipids and/or lipoproteins in the blood triglyceride (TG) or cholesterol and pathological lipid qualities, such as elevated levels of low-density lipoprotein (LDL), the most common form of dyslipidemia. Hyperlipidemia results from complex interactions between genetic and environmental factors and is a significant factor in the progress of atherosclerosis and coronary artery disease (Haffner, 1999). Hyperlipidemia can be treated with dietary alterations and

medications that regulate lipid metabolism through various mechanisms.

Statins are the first-line therapy for lowering LDL levels and act by inhibiting 3-hydroxy-3-methylglutaryl-coenzymeA (HMG-CoA) reductase. However, statins have adverse effects, including muscle myopathy and derangements in hepatic function (Maggo et al., 2011).

Although numerous drugs other than statins are also available, many of the conventional drugs (fibrates, ezetimibe, bile sequestrants and niacin) cause significant adverse effects, such as increased serum creatinine concentration, absorption of other drugs, flushing, nausea, vomiting, diarrhea, and anorexia (Al-Mohaisen et al., 2010; Filippatos and Mikhailidis, 2009; Jun et al., 2010). Thus, managing hyperlipidemia in patients intolerant to the adverse effects of such conventional drugs remains a major challenge.

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In addition to Western medical treatment, traditional Chinese medicine (TCM) is highly accessible and widely used in Taiwan. Even before TCM was incorporated into the National Health Insurance (NHI) program, more than one-third of Taiwanese people used TCM, and 79% of them regarded TCM as slower in action but more effective than Western medicine for treating diseases (Chiu et al., 1990; Pan et al., 2013).

The NHI program, implemented in Taiwan in 1995, provides unified, universal, and comprehensive health insurance to all residents of Taiwan. In 2010, 99% of the entire population, 23 million people, was enrolled in the NHI program, and the Bureau of NHI (BNHI) has established contracts with 92% of the medical institutions in Taiwan. The NHI Research Database (NHIRD) provides data of prescriptions with well-defined registration for research (Cheng et al., 2011). In this study, we used the NHIRD to analyze the frequency and prescription patterns of TCM among patients with hyperlipidemia; concomitant use of TCM/CHPs with conventional (synthetic) antihyperlipidemia drugs has not been evaluated.

## 2. Materials and methods

### 2.1. Data source

The NHIRD includes detailed medical records, including each clinic visit date, sex, date of birth, medical care facilities and specialties, prescribed drugs with the duration of medication, and/or management for treatment, transferred identification number, and three major diagnosis codes in the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) format.

Both TCM and Western medicine physicians follow the standard diagnosis protocol of using the ICD-9-CM coding system when claiming for reimbursement. Furthermore, the BNHI of Taiwan conducts crosschecks and validates the charts to ensure the accuracy of diagnosis coding.

The NHI system stores the longitudinal data of the beneficiaries of TCM and Western medicine. Thus, a random sample database of 1,000,000 patients (approximately 4.5% of the total population) was obtained for the current study.

In this study, we included patients with hyperlipidemia diagnosis (ICD-9-CM codes 272.0, 272.1, 272.2, 272.3, and 272.4) who made outpatient visits more than 2 times within one year and evaluated their medical records (Fig. 1).

### 2.2. List of TCM remedies

Based on the TCM philosophy, each prescription can contain one or more Chinese herbal drugs of various doses and/or a standard formula (remedy, Fu-Fang or Fang-Ji) composed of medicinal plants, animal products, and minerals in fixed doses, as mentioned in ancient TCM textbooks. In this study, all herbal materials with therapeutic effects were referred as Chinese herbal products (CHPs). CHPs are presented as concentrated powder prepared by extraction, fractionation and purification processes. Single herbs (SH) were CHPs with single medicinal substances only; these were often used together with other CHPs. Herbal formulas (HF) were CHPs composed of multiple SH with fixed proportion that were used alone or with other CHPs (World Health Organization, 2007.). The list of CHPs covered by the NHI program was downloaded from the BNHI website (National Health Insurance Administration, 2014). The corresponding drug information of the respective mixtures was then obtained from the Committee on Chinese Medicine and Pharmacy website, including the proportions of each ingredient, date and period of approval as a drug, code, and the name of the manufacturer (Committee on Chinese Medicine and Pharmacy, 2009).

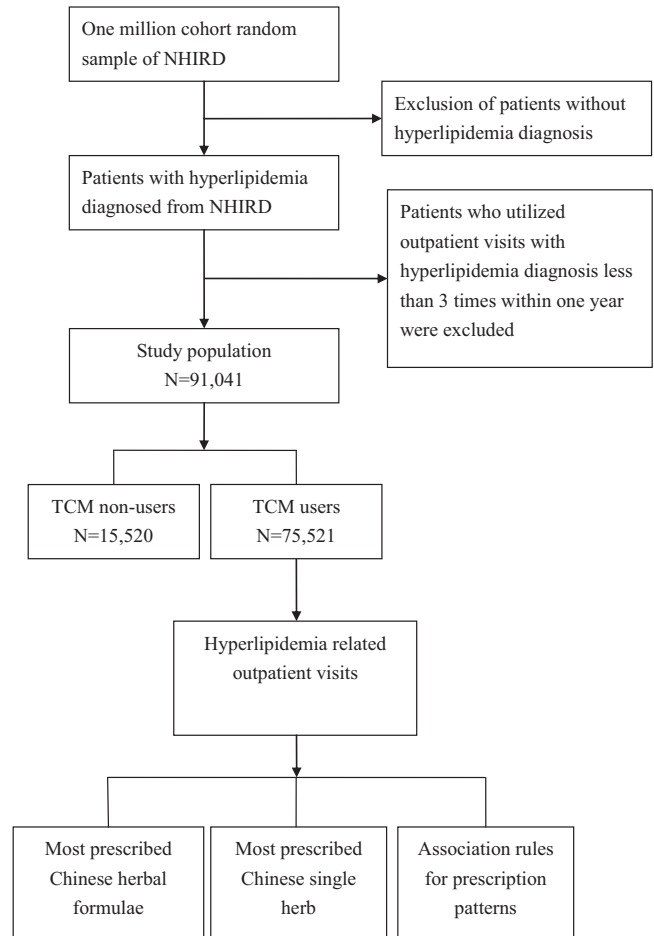


Fig. 1. Flow recruitment chart of subjects from the one million random samples obtained from the National Health Insurance Research Database (NHIRD), 2003–2009, in Taiwan.

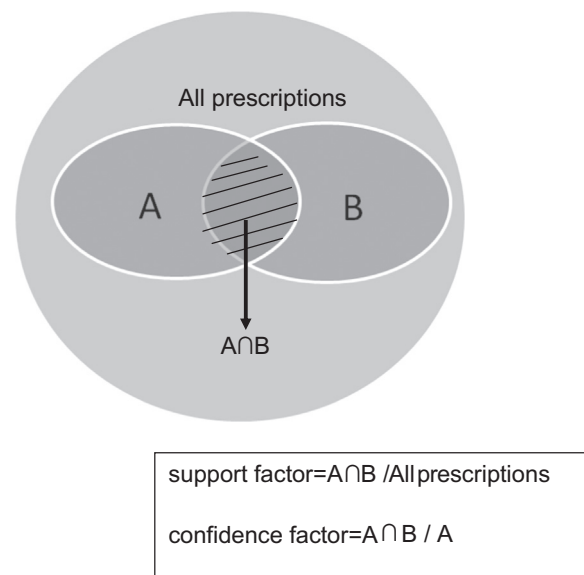


Fig. 2. Basic concepts and algorithms of association rules.

### 2.3. Statistical analysis

The prescribed frequencies and percentages, including the dosage and duration, of herbal formulae and/or single herbs were analyzed.

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