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# Prescription patterns of Chinese herbal products for patients with uterine fibroid in Taiwan: A nationwide population-based study



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## ARTICLE INFO

## Article history:

Received 18 February 2015

Received in revised form

27 April 2015

Accepted 25 May 2015

Available online 4 June 2015

## Keywords:

Complementary and alternative medicine

Gui-Zhi-Fu-Ling-Wan

National health insurance research database

Rhizoma Sparganii

Traditional Chinese medicine

Uterine fibroid

## ABSTRACT

**Ethnopharmacological relevance:** Uterine fibroid (myoma) is one of the most common diseases in women. Although there are several studies on the efficacy of Chinese herbs, there is a lack of large-scale survey on the use of traditional Chinese medicine (TCM) for the treatment of uterine fibroid. This study aimed to investigate the utilization of Chinese herbal products for patients with uterine fibroid, prescribed by licensed TCM doctors in Taiwan.

**Materials and methods:** A random sample comprised of one million individuals with newly diagnosed uterine fibroid between 2002 and 2010 from the Taiwanese National Health Insurance Research Database was analyzed. Demographic characteristics, TCM usage, the frequency as well as average daily dose of Chinese herbal formulas and the single herbs prescribed for patients with uterine fibroid, were analyzed. **Results:** Overall, 35,786 newly diagnosed subjects with uterine fibroid were included. Majority of these patients (87.1%;  $n = 31,161$ ) had visited TCM clinics. Among them, 61.8% of their visits used Chinese herbal remedies. Patients less than 45 years of age tended to use TCM more frequently than elder patients. Gui-Zhi-Fu-Ling-Wan (Cinnamon Twig and Poria Pill) was the most frequently prescribed Chinese herbal formula, while San-Leng (Rhizoma Sparganii) was the most commonly prescribed single herb.

**Conclusions:** Our study identified the characteristics and prescription patterns of TCM for patients with uterine fibroid in Taiwan. Further basic mechanistic studies and clinical trials are needed to confirm the therapeutic effects and mechanisms.

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## 1. Introduction

Uterine fibroids, also known as uterine leiomyomas, uterine myomas, uterine leiomyomata, are benign tumors that arise from the smooth muscle compartment of uterus (Stewart, 2001). These tumors are hormone responsive; usually appear after menarche and progress with age during reproductive years. Uterine fibroids are the most frequently occurring tumor in women. Although remaining benign, they may reach significant size and number and cause great discomfort. They are therefore the leading indication

for hysterectomy in women of reproductive age (Cramer and Patel, 1990; Okolo, 2008). The clinical symptoms are apparent in about 25% of women (Buttram and Reiter, 1981), but the true prevalence might prove to be even higher with advancement of imaging techniques such as ultrasound (Marsh et al., 2013). With careful surgical pathology examination, the prevalence may be as high as 77% (Cramer and Patel, 1990). By ultrasound examination, the estimated cumulative incidence of uterine fibroids was about 80% for African-American women and 70% for Caucasian women by the age of 50. (Baird et al., 2003).

Most uterine fibroids are not life threatening tumors but many women suffered from significant annoying symptoms. These symptoms may generally be classified into three categories: (1) Abnormal uterine bleeding, menorrhagia or hypermenorrhea (Yang et al., 2011); (2) Pelvic pressure and pain (Lippman et al., 2003); and (3) Reproductive disorders, infertility or pregnancy

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complications (Bajekal and Li, 2000; Somigliana et al., 2007). The treatment for uterine fibroids depends on the symptom severity, the age, the desire for a future pregnancy, and the types and locations of the fibroids (Stewart, 2001). The US Food and Drug Administration (FDA) have approved four therapies to treat uterine fibroids at present: (1) Lupron, (2) embolic agents for uterine artery embolization, (3) magnetic resonance imaging-guided focused ultrasound, and (4) robotic assisted surgery (Segars et al., 2014). As benign tumors, asymptomatic uterine fibroids could be managed conservatively (Khan et al., 2014). For symptomatic fibroids, surgical intervention has been the standard treatment. For women who have completed childbearing, hysterectomy is indicated to resolve the symptoms and eliminate chance of recurrence (Kjerulff et al., 2000). On the other hand, myomectomy is suggested for women who still have reproductive desires (Sankaran and Manyonda, 2008).

However, many women do not want to receive surgery due to possible complications. Alternative therapies for the relief of uterine fibroid symptoms have been sought and evaluated for years (Mehl-Madrona, 2002; Sabry and Al-Hendy, 2012). Traditional Chinese medicine (TCM), including Chinese herbal products and acupuncture, is a commonly used alternative therapy to treat uterine fibroids (Liu et al., 2013; Zhang et al., 2010). It has been reported that *Herba scutellariae barbatae* (Ban-Zhi-Lian), *Tripterygium wilfordii* (Lie-Gong-Teng) and Gui-Zhi-Fu-Ling-Wan (Cinnamon Twig and Poria Pill) may have the potential to treat uterine fibroids (Liu et al., 2013; Zhou and Qu, 2009). However, there is a lack of large-scale survey on the use of traditional Chinese medicine (TCM) to treat uterine fibroid.

TCM is a medical option often sought by patients in Taiwan, and has been reimbursed under the National Health Insurance (NHI) system since 1995 (Huang et al., 2014; Yen et al., 2013). While efficacy of current drugs is limited, and patients are often opted to surgery, TCM might offer an additional way to manage this condition. In order to explore the feasibility of TCM as a treatment option, and to address the lack of large-scale studies in this field, we analyzed a randomly sampled cohort of one million beneficiaries from the National Health Insurance Research Database (NHIRD) during 2002–2010. The results

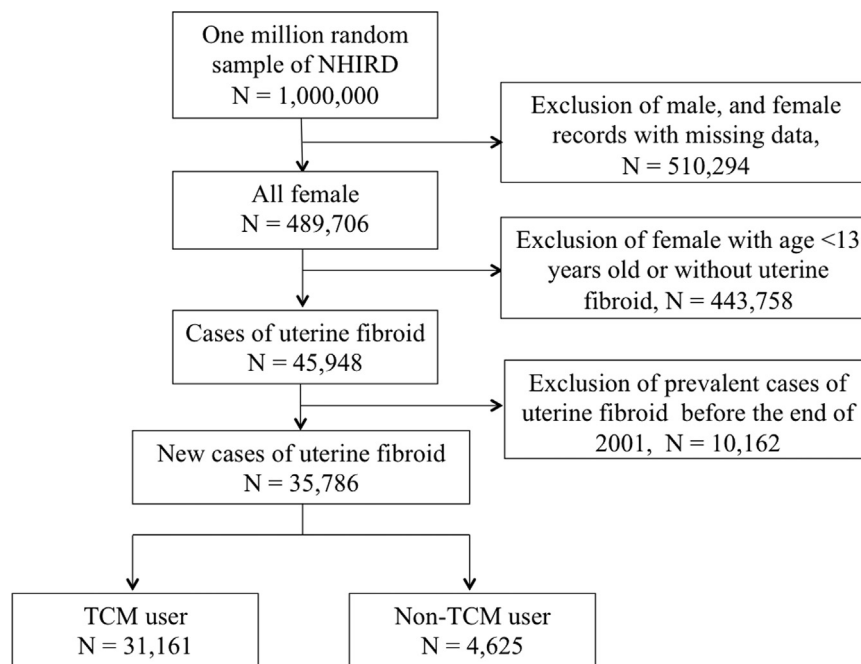
of this study should provide valuable information regarding the use of TCM for uterine fibroid patients.

## 2. Materials and methods

### 2.1. Data source

In Taiwan, approximately 23 million people, comprising 99.89% of the total population, were enrolled in the National Health Insurance Program in 2010 (BoNH, 2010). The program covers a highly representative sample of Taiwan's general population because the reimbursement policy is universal and mandatory. Claims data from the National Health Insurance program were sorted into registration files and original claim data for reimbursement. These data files are de-identified by scrambling the identification codes and sent to the National Health Research Institutes to form the original files of NHIRD. The NHI reimbursement program makes TCM and Western medicine equally accessible to patients from all income levels, so the data in this study should not be influenced by any economic factor.

This population-based study analyzed a sample of one million individuals randomly selected from the NHIRD (Longitudinal Health Insurance Database; LHID 2010), to survey the prevalence of prescribed Chinese herbal preparation taking among women with uterine fibroids from 2002 to 2010. The datasets used in this study contains all the original claim data of 1,000,000 beneficiaries randomly sampled from the year 2010 Registry for Beneficiaries of the NHIRD, where registration data of everyone who was a beneficiary of the National Health Insurance program during the period of January 1st 2010 to December 31 2010 were drawn for random sampling. There was no significant difference in the gender distribution ( $\chi^2=0.067$ ,  $df=1$ ,  $p$ -Value=0.796) between the patients in the LHID2010 and the original NHIRD ([http://nhird.nhri.org.tw/en/Data\\_Subsets.html](http://nhird.nhri.org.tw/en/Data_Subsets.html)). All beneficiary information are acquired from the NHIRD, including gender, date of birth, clinical outpatient and inpatient visits, prescribed herbs and dosage, and up to three diagnostic codes in the format of International



**Fig. 1.** Flow recruitment chart of subjects from the one million samples randomly selected from the National Health Insurance Research Database (NHIRD) from 2002 to 2010 in Taiwan.

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