



## Decreased risk of stroke in patients receiving traditional Chinese medicine for vertigo: A population-based cohort study



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### ABSTRACT

**Ethnopharmacological relevance:** Patients with vertigo are reported to exhibit a higher risk of subsequent stroke. However, it remains unclear if Traditional Chinese Medicine (TCM), the most common form of complementary and alternative medicine, can help lower the risk of stroke for these patients. So the aim of the study was to investigate the effects of TCM on stroke risk among patients with vertigo.

**Materials and methods:** This longitudinal cohort study used the Taiwanese National Health Insurance Research Database to identify 112,458 newly diagnosed vertigo patients aged  $\geq 20$  years who received treatment between 1998 and 2007. Among these patients, 53,203 (47.31%) received TCM after vertigo onset (TCM users), and the remaining 59,201 patients were designated as a control group (non-TCM users). All enrollees received follow-up until the end of 2012 to measure stroke incidence. Cox proportional hazards regression was used to compute the hazard ratio (HR) of stroke in recipients of TCM services.

**Results:** During 15-year follow-up, 5532 TCM users and 12,295 non-TCM users developed stroke, representing an incidence rate of 13.10% and 25.71% per 1000 person-years. TCM users had a significantly reduced risk of stroke compared to non-TCM users (adjusted HR=0.64; 95% confidence interval CI=0.59–0.74). The predominant effect was observed for those receiving TCM for more than 180 days (adjusted HR=0.52; 95% CI=0.49–0.56). Commonly used TCM formulae, including Ban-Xia-Bai-Zhu-Tian-Ma-Tang, Ling-Gui-Zhu-Gan-Tang, Bai Zhi (*Angelica dahurica* (Hoffm.) Benth. & Hook.f. ex Franch. & Sav., root), Ge Gen (*Pueraria lobata* (Willd.) Ohwi, root) and Hai Piao Xiao (*Endoconcha Sepiae*, Cuttlefish Bone) were significantly associated with lower risk of stroke.

**Conclusions:** Results of this population-based study support the effects of TCM on reducing stroke risk, and may provide a reference for stroke prevention strategies. The study results may also help to integrate TCM into clinical intervention programs that provide a favorable prognosis for vertigo patients.

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### 1. Introduction

Vertigo is a subtype of dizziness that is defined as an illusion of

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movement, and usually a sense of rotation. As such, vertigo is a common symptom of vertebrobasilar ischemia (VBI) and posterior inferior cerebellar artery (PICA) infarction (Lee et al., 2014a). Medications for treating vertigo have typically consisted of anti-vertiginous and antiemetic drugs, which were used mainly used to relieve symptoms of dizziness (Baloh, 1998). However, to date, no medication in daily practical use has been well established for its curative or prophylactic value or has been considered suitable for

long-term palliative use (Ozdemir et al., 2013; Yardley et al., 2004). Therefore, the related health threat of vertigo has attracted more attention. Results of a recent study showed that dizziness or vertigo was a major risk factor for subsequent vascular events (Lee et al., 2012).

Traditional Chinese Medicine (TCM) has been an important part of health care in Taiwan for centuries and continues to have growing popularity in Taiwan and many other Asian countries. In fact, TCM is fully reimbursed under the current Taiwanese National Health Insurance (NHI) system (Pan et al., 2014; Tsai et al., 2014). TCM physicians are specialized practitioners who use meticulous approaches to gather patients' clinical symptoms and signs, which are then used to make diagnoses and determine treatment strategies (Hsu et al., 2014). As explained above, dizziness and vertigo occur frequently in vertebrobasilar ischemia (Lee et al., 2014a). In such cases, physicians may consider prescribing traditional Chinese herbal medicine (Han et al., 2015; Liu et al., 2015; Xie et al., 2014). Results of a previous study indicated that acupuncture can improve cerebral blood flow in patients with vertigo induced by posterior circulation ischemia (Deng et al., 2015). However, to date, no study has been conducted to address whether TCM can affect the risk of developing stroke in patients with vertigo. Therefore, to address this concern, this study aimed was to assess the risk of stroke incidence among vertigo patients who either received or did not receive TCM services.

## 2. Material and methods

### 2.1. Data source

This retrospective cohort study used claims data from the Longitudinal Health Insurance Database (LHID) of the Taiwan National Health Insurance Administration, whose information is made available to Taiwanese researchers. Taiwan launched the single-payer NHI program in 1995 to remove financial barriers to medical care for all legal residents. As of 2010, over 99% of Taiwan's

population was enrolled in this program (National Health Research Institute, 2011). The LHID is a sub-dataset of the NHI program made up of 1,000,000 randomly sampled people who were alive in 2000. For this study, all medical records of these individuals were collected from 1997 to 2012. Because a multistage stratified systematic sampling method was used, no statistically significant differences regarding sex or age existed between the one million insured individuals and the general population (National Health Research Institute, 2011). This database contains all NHI enrolment files, claims data, and the registry for prescription drugs, providing comprehensive utilization information for the subjects covered by the insurance program. To date, more than 300 published papers have used this de-identified secondary database for their studies. The present study was conducted in accordance with the Helsinki Declaration and was also evaluated and approved by the local institutional review board and ethics committee of Buddhist Dalin Tzu Chi Hospital, Taiwan (No. B10004021-1). Since the LHID files contained only de-identified secondary data, the review board waived the requirement for obtaining informed consent from the patients.

### 2.2. Study population

Selection of study subjects is shown in Fig. 1. All diagnoses in the insurance claims data were coded with the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM). Inclusion criteria for the study cohort were: patients aged 20 years or older with newly diagnosed vertigo within the 1998–2007 time period (ICD-9-CM codes: 078.81, 386.XX, or 780.4). The index date was defined as the day of vertigo diagnosis. To reduce concerns of disease misclassification, only those patients with at least three diagnoses in outpatient visits or those being admitted to a hospital with a primary diagnosis of vertigo within the observational period ( $n=125,640$ ) were selected. A total of 9664 vertigo patients were then excluded because they had a prior diagnosis of stroke (ICD-9-CM: 430–437) as indicated by linking the vertigo patients to the catastrophic illness registry. In Taiwan,

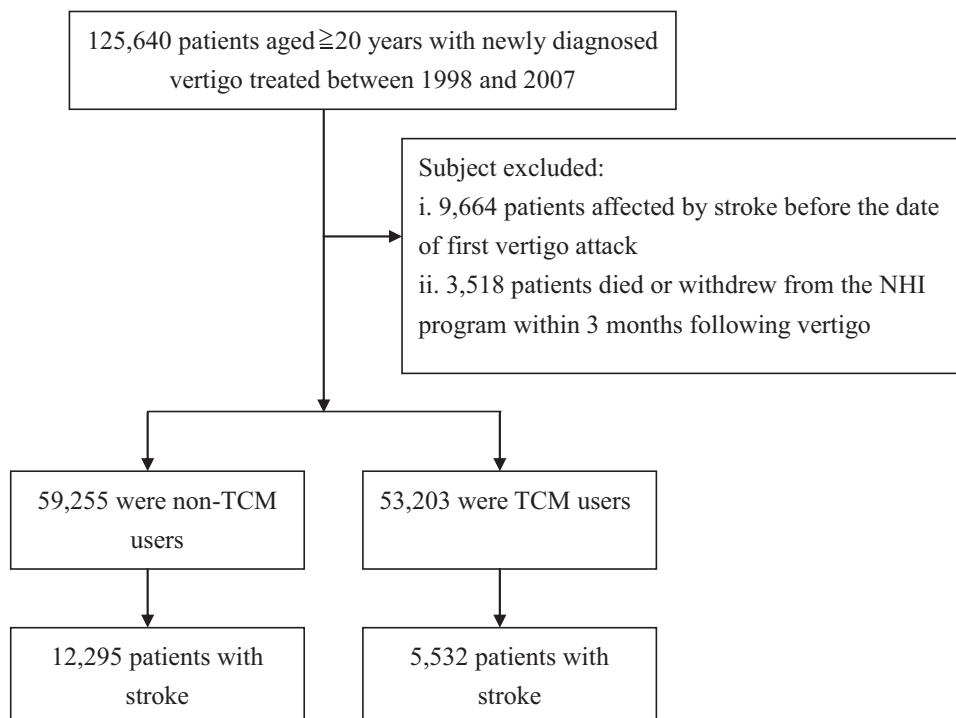


Fig. 1. Flowchart of selection and follow-up of study subjects.

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