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#### Research article

## Efficacy of acupuncture in reducing accidental injury risk in stroke patients: A national-scale cohort study

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#### ABSTRACT

Background: Falls among stroke patients pose a significant health concern, leading to injuries, reduced mobility, and functional limitations. Recent research has suggested the potential benefits of acupuncture in enhancing balance and motor function in stroke patients. However, large-scale, long-term studies on acupuncture's role in reducing the risk of accidental injuries are scarce. This study aimed to evaluate acupuncture's effectiveness in decreasing the risk of accidental injuries in stroke patients.

Materials and methods: This study employed a large-scale cohort design, utilizing data from the 2000 Longitudinal Generation Tracking Database (LGTD 2000) in Taiwan, covering two million individuals. The cohort comprised stroke patients hospitalized between 2001 and 2012, with follow-up periods of at least six years to estimate accidental injury incidence and risk. Acupuncture treatments during both inpatient and outpatient phases after stroke diagnosis were included. Accidental injury data, including vehicular accidents and falls, were extracted from specialized hospitalization records. Hazard ratios were calculated, adjusting for variables like comorbidities, hypnotic medication usage, and demographic factors.

Result: A total of 108,196 newly diagnosed stroke patients were included in the final cohort, with 42,083 receiving acupuncture treatment and 66,113 not receiving acupuncture. The acupuncture group exhibited a significantly lower incidence rate of accidental injuries (10.2 per 1,000 person-years) compared to the non-acupuncture group (15.8 per 1,000 person-years). After adjusting for various covariates, the acupuncture group had a reduced risk of accidental injuries with an

Abbreviations: LGTD 2000, 2000 Longitudinal Generation Tracking Database; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10, International Classification of Diseases, Tenth Revision; NHI, National Health Insurance; CKD, chronic kidney; RA, rheumatoid arthritis; OA, Osteoarthritis; DM, Diabetes mellitus; CHD, coronary heart disease; HTN, hypertension; HL, Hyperlipidemia; CCI, Charlson Comorbidity Index; HR, hazard ratio; 95 % CI, 95 % confidence interval; aHR, adjusted hazard ratios; OP, Osteoporosis; PD, Parkinsonism; PAC, Post-Acute Care Integrated Services; PT, Physical Therapy.

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adjusted hazard ratio (aHR) of 0.74 (95 % CI: 0.51–0.92). Subgroup analyses revealed consistent protective effects of acupuncture across different patient profiles and treatment characteristics, including age, sex, comorbidities, and hypnotic medication usage.

Conclusion: This study provides evidence supporting the potential of acupuncture as an adjunctive therapy to reduce the risk of accidental injuries among stroke patients. Regardless of stroke subtype, age, or comorbidity burden, acupuncture was associated with a lower risk of accidental injuries.

#### 1. Introduction

#### 1.1. Background

Stroke patients represent a high-risk group for accidental injuries, particularly falls. Batchelor et al. (2012). highlighted that fall occur frequently throughout all stages post-stroke, with serious consequences such as injuries, functional limitations, and reduced mobility. These falls are attributed to a mix of pre-stroke risk factors and stroke-related impairments like weakened strength and balance, hemineglect, and visual issues [1]. Divani et al. (2009). focused on elderly stroke survivors, finding a high prevalence of falls and related injuries. Key risk factors for falls included living arrangements, poor general health, psychiatric problems, urinary incontinence, and motor impairments. Injuries from falls were more likely in females, those in poor health, with a history of falls or multiple strokes. These studies underscore the need for targeted interventions to prevent falls in stroke survivors, thereby improving their quality of life and reducing caregiver burdens [2].

Recent research has increasingly highlighted the benefits of acupuncture in enhancing balance and motor function in stroke patients. Liu et al. (2009) demonstrated significant improvements in balance function with acupuncture treatment, as evidenced by reduced displacement from the center of gravity and increased muscle strength in the lower extremities [3]. Xie et al. (2022) explored the synergistic effects of combining acupuncture with modern rehabilitation training for ischemic stroke-induced limb motor dysfunction. Their findings showed marked improvements in motor function scores across both body and head acupuncture groups, with head acupuncture yielding better outcomes [4]. Additionally, Sánchez-Mila et al. (2018) found that incorporating deep dry needling into Bobath concept-based treatment sessions effectively reduced spasticity and improved balance, range of motion, and stability in post-stroke patients [5]. These studies collectively underscore the role of acupuncture as a valuable adjunct to conventional stroke rehabilitation, enhancing balance and motor functions critical to the recovery process.

Although numerous randomized controlled clinical trials have validated the effectiveness of acupuncture in improving balance and motor functions post-stroke, large-scale and long-term follow-up studies assessing the efficacy of acupuncture as an adjunct therapy in reducing the risk of accidental injuries in stroke patients are still lacking.

Recent research utilizing large health databases has increasingly validated the feasibility and effectiveness of acupuncture in long-term stroke care. Wu et al.'s (2022) systematic review and meta-analysis, focused on data from the Taiwan National Health Insurance Research Database, scrutinized nationalized cohort studies comparing acupuncture with non-acupuncture control groups among stroke patients. This comprehensive review, which included eight studies, revealed that acupuncture significantly reduced the risk of various poststroke comorbidities, such as stroke recurrence, acute myocardial infarction, pneumonia, dementia, epilepsy, urinary tract infection, and depression. The meta-analysis demonstrated a marked reduction in the risk of these comorbidities among the acupuncture group, highlighting the clinical benefits of acupuncture in reducing poststroke comorbidities. This evidence from large-scale cohort studies substantiates the therapeutic potential of acupuncture in post-stroke care and the prevention of comorbidities [6].

The fundamental hypothesis of this study posits that acupuncture treatment can effectively reduce the risk of accidental injuries in patients who have experienced a stroke. This assumption is grounded in previous research that has demonstrated the benefits of acupuncture in ameliorating various post-stroke comorbidities, suggesting a potential positive impact on preventing accidental injuries as well.

#### 1.2. Objectives

The main objective was to assess the effectiveness of acupuncture in decreasing the risk of accidental injuries in stroke patients.

#### 2. Material and methods

#### 2.1. Study design

This study aims to investigate the efficacy of acupuncture in reducing the risk of accidental injury among stroke patients using a large-scale cohort study design. We employed a propensity score design to match patients who received acupuncture with the control group, thereby enhancing the comparability between the two cohorts. The Taipei City Hospital Research Ethics Committee has approved this research study in April 13, 2024, with the case number: TCHIRB-11103028-E.

#### 2.2. Setting

This study utilizes data from the 2000 Longitudinal Generation Tracking Database (LGTD 2000), a comprehensive dataset containing the healthcare records of two million individuals sampled from the entire population of Taiwan in the year 2000. The LGTD 2000 database was created through a stratified random sampling approach, ensuring representation from various demographic groups and geographic regions, including Taiwan and its affiliated islands. Prior to analysis, the database underwent rigorous data cleaning procedures to remove duplicate records, individuals with unspecified gender, those with missing birthdate information, cases with illogical age values, and individuals with unclear geographical information.

#### 2.3. Participants

The primary criterion for participants inclusion was hospitalization due to cerebrovascular disease within the timeframe of 2001–2012. To identify eligible participants, the research team utilized healthcare records from the LGTD 2000 database, specifically the "Inpatient Expenditures by Admissions" file (H\_NHI\_IPDTE). Diagnosis codes in the (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) 430–435 and (International Classification of Diseases, Tenth Revision (ICD-10) I60-I65 code systems were used.

The study incorporated three distinct exclusion criteria to maintain the cohort's integrity and ensure accurate follow-up calculations, given the intricate relationship between stroke progression, activity levels, and the risk of accidental injuries. The first criterion involved the exclusion of patients who had experienced cerebrovascular disease, specifically stroke, within the defined screening period of January 1, 2000, to December 31, 2000. This screening period was established to accurately assess follow-up time for the stroke cohort and ensure that all participants were initial stroke incidents. The second criterion mandated the exclusion of participants with incomplete demographic data, including missing information on insurance coverage amounts and residential areas, to ensure the availability of comprehensive demographic information for analysis. Thirdly, Individuals with a history of trauma-related cerebrovascular events or those with unclear etiology for their cerebrovascular disease diagnosis were excluded. Lastly, the study excluded participants who had been previously hospitalized for accidental injuries before the onset of stroke or during the screening period. This exclusion aimed to maintain the study's focus on evaluating the impact of acupuncture treatment on reducing the risk of subsequent accidental injuries among stroke patients and to exclude participants who were no longer at risk due to prior accidental injuries.

All participants in the study were followed from the time of their hospitalization due to cerebrovascular disease onwards, until the study's termination on December 31, 2018, or until the occurrence of specific endpoints, including patient mortality or discontinuation of insurance coverage due to emigration. To ensure comprehensive data collection, all hospitalizations and outpatient medical records of the participants were meticulously documented, including both traditional Chinese medicine and modern medical diagnoses and treatment information. This comprehensive approach allowed for a holistic assessment of the participants' healthcare utilization patterns, which is crucial for evaluating the efficacy of acupuncture treatment in reducing accidental injury risk among stroke patients.

#### 2.4. Main outcome

The primary outcome of this study is the occurrence of accidental injuries among stroke patients. Within the LGTD 2000 database, records of accidental injuries are specifically identified through the registration codes EXT\_CODE1 and EXT\_CODE2. Physicians are mandated to document information on every patient hospitalized due to accidental injuries according to the ICD-9-CM Supplementary Classification of External Causes Of Injury And Poisoning (E000-E999) and ICD-10-CM External causes of morbidity (V00-Y99). Accidental injuries encompass a wide range of incidents, including falls, slips, trips, traffic accidents, and other external causes of harm. These events are carefully recorded in the database, allowing for the systematic tracking and analysis of injury-related information. We utilized the hospitalization date for accidental injuries as the endpoint for the follow-up period.

#### 2.5. Variables

In Taiwan, the National Health Insurance (NHI) system provides acupuncture services to both inpatient and outpatient stroke patients. Information regarding acupuncture treatment was collected from two distinct sources within the LGTD 2000 database: the "Details of Inpatient Orders" (H\_NHI\_IPDTO) and the "Details of Ambulatory Care Orders" (H\_NHI\_OPDTO). These sources provided comprehensive data on the type, frequency, and date of acupuncture treatments administered. It is important to note that the NHI system in Taiwan reimburses only licensed healthcare professionals, such as qualified physicians, for the provision of therapeutic acupuncture treatments. Consequently, this study exclusively included data pertaining to therapeutic acupuncture treatments carried out by licensed medical practitioners. Acupuncture treatments administered for cosmetic purposes, weight management, or those performed by non-physicians were not included in the dataset.

Comorbidities in patients can affect their risk of accidental injury [1,7]. Comorbid conditions such as chronic kidney disease (CKD) are known to diminish physical strength and disrupt balance, while autoimmune disorders including rheumatoid arthritis (RA) and gout can lead to joint pain and limit mobility, complicating movement. Osteoarthritis (OA), characterized by joint stiffness and pain, particularly impairs weight-bearing joints, subsequently raising the risk of falls. Diabetes mellitus (DM) often presents complications such as peripheral neuropathy and vision impairment, which can further affect coordination and balance. Additionally, cardiovascular diseases like coronary heart disease (CHD) and hypertension (HTN) negatively impact endurance and exercise capacity. Hyperlipidemia (HL), commonly associated with cardiovascular health issues, may also indirectly increase the risk of injuries. Thus, these

comorbidities, whether through direct physical debilitation or as part of a broader spectrum of health challenges, markedly increase the probability of falls and other accidental injuries among stroke survivors. Consequently, we have included these comorbidities as variables in our study.

The International Classification of Diseases codes for several common comorbidities are as follows: Chronic Kidney Disease is coded as 585 in ICD-9-CM and as N18 in ICD-10-CM. Rheumatoid Arthritis is listed under 714 in ICD-9-CM and M06 in ICD-10-CM. Gout is identified by 274 in ICD-9-CM and M10 in ICD-10-CM. Osteoarthritis has codes 715.0, 715.16, and 715.15 in ICD-9-CM for generalized, knee, and hip osteoarthritis, respectively, and M15, M17, and M16 in ICD-10-CM. Diabetes Mellitus is categorized as 250 in ICD-9-CM and E08-E13 in ICD-10-CM. Coronary Heart Disease falls under 410-414 in ICD-9-CM and I20-I25 in ICD-10-CM. Hypertension is coded as 401-405 in ICD-9-CM and I10-I15 in ICD-10-CM. Hyperlipidemia is coded as 272 in ICD-9-CM and E77, E78 in ICD-10-CM. Cancer is coded as 140-239 in ICD-9-CM and as C00-D49 in ICD-10-CM. Fracture is listed under 800-829 in ICD-9-CM and as S02-S92 in ICD-10-CM. Anemia is identified by 280-285 in ICD-9-CM and as D50-D64 in ICD-10-CM. Osteoporosis (OP) is categorized as 733.0 in ICD-9-CM and as M80-M81 in ICD-10-CM. Epilepsy falls under 345 in ICD-9-CM and G40 in ICD-10-CM. Dementia is coded as 290 in ICD-9-CM and as F01-F03 in ICD-10-CM. Lastly, Parkinsonism (PD) is classified under 332 in ICD-9-CM and as G20 in ICD-10-CM.

In addition to specific comorbidities, the number of concurrent comorbidities in patients is a crucial factor influencing the risk of accidental injuries [8]. For this study, we utilized the Charlson Comorbidity Index (CCI) as a variable to estimate the burden of multiple comorbidities for each patient. The CCI is widely used in large-scale medical and health data research in public health and is strongly associated with the occurrence and prognosis of accidental injuries such as falls [9].

Hypnotic medications significantly affect the risk of falls in stroke patients. Consequently, we have incorporated the usage of the three most common types of hypnotic medications - Benzodiazepines, Barbiturates, and Z-drugs - into our study variables [7,9,10].

#### 2.6. Bias

The key methodological considerations of potential biases common in medical database analyses was immortal time bias and indication bias [11,12]. Immortal time bias arises from mismatched follow-up periods between treatment and control groups, leading to an underestimation of the injury risk in the treatment group and an overestimation of the therapeutic effects of acupuncture. To mitigate this, we adjusted the follow-up initiation for the acupuncture treatment group. The period between stroke diagnosis and the commencement of acupuncture treatment, known as the immortal time, was excluded from the follow-up duration to reduce the impact of this bias.

Indication bias stems from the inherent non-comparability between patients selecting acupuncture treatment and those in the control group, often mistakenly attributing the reduced risk in patients to the effect of acupuncture. Due to the unique nature of acupuncture therapy, locating an appropriate active comparator posed significant challenges. Therefore, to minimize the effects of indication bias on our research, we employed propensity score matching with demographic and medical characteristics. This method allowed for the pairing of factors likely influencing the choice of acupuncture, thereby ensuring a more balanced comparison between the treated and control cohorts.

#### 2.7. Statistical methods

In the descriptive statistics component of our study, we computed counts and percentages for each variable in both the acupuncture and control groups. The differences between these groups were estimated using the standardized mean difference. As part of our cohort study, survival curves were plotted using the Kaplan-Meier method, and the impact of acupuncture treatment on the rate of accidental injuries was estimated by calculating the p-value for the log-rank test.

We calculated the incidence rate of accidental injuries among stroke patients per 1,000 person-years, along with the crude hazard ratio (HR) and its 95 % confidence interval (95 % CI). Additionally, adjusted hazard ratios (aHR) were computed after controlling for variables such as age, sex, insurance amount, urbanization level, comorbidities, and the use of sedative hypnotic drugs.

The adjusted hazard ratios and their confidence intervals were presented separately for all participants and for the groups matched by Propensity Score Matching. In order to verify the stability of acupuncture's effect in reducing accidental injuries among stroke patients, adjusted hazard ratios were calculated for different patient subgroups based on age, sex, insurance amount, urbanization level, and comorbidities. Additionally, we estimated the potential impact of the number of acupuncture sessions, follow-up duration, types of accidents, and the Charlson Comorbidity Index on the efficacy of acupuncture treatment. These subgroup analyses were conducted to explore the consistency and potential variability of acupuncture's protective effects across different patient profiles and treatment characteristics. This approach enables a more nuanced understanding of how acupuncture's effectiveness might vary in specific patient groups or under different clinical scenarios.

In our study, the predetermined level of statistical significance was set at  $\alpha = 0.05$ . We defined a standardized mean difference exceeding 0.2 as indicative of a significant difference between the acupuncture and control groups. All statistical analyses and computations were performed using SAS software, Version 9.4.

#### 3. Results

#### 3.1. Descriptive data

Of the two million random samples from the LGTD 2000 cohort, we excluded 1,879,812 due to the absence of stroke diagnosis. From the remaining participants, 120,188 met our eligibility criteria, which consisted of stroke patients diagnosed by specialists and undergoing inpatient treatment. Further refinement based on specific criteria led us to exclude individuals with a stroke diagnosis made within the screening period (10,252), those with incomplete demographic data (171), and those who experienced an accidental injury during the screening period (1,569). This process resulted in a final cohort of 108,196 newly diagnosed stroke patients at risk of accidental injury. We then classified this cohort into two distinct groups based on their treatment: 42,083 (38.9 %) had undergone acupuncture treatment, whereas 66,113 (61.1 %) had not. During our follow-up, we observed that 4,264 (10.1 %) of the acupuncture-treated group experienced accidental injuries, in contrast to 8,802 (13.3 %) in the non-acupuncture group, as shown in Fig. 1.

Table 1 presents the demographic and comorbidity profiles of 42,083 stroke patients who received acupuncture and 66,113 who did not. Among the stroke patients who underwent acupuncture, the predominant age group was those aged 70 and above. Females were more represented than males. The majority hailed from areas with high urbanization. When considering insured amounts, the largest portion fell into the "1–19999" bracket. Hypertension emerged as the most common comorbidity among these patients.

In terms of age, 13.0% of the acupuncture group were below 50 years, compared to 9.2% in the non-acupuncture group. Those aged 70 and above constituted 49.2% of the acupuncture group and 63.6% of the non-acupuncture group. Regarding sex, males represented 46.7% of the acupuncture group and 54.7% of the non-acupuncture group, while females accounted for 53.3% and 45.3% respectively. Urbanization showed that 31.1% of the acupuncture patients lived in very high urbanized areas, versus 23.6% of the non-acupuncture group. For insured amounts, 11.3% of the acupuncture group and 7.4% of the non-acupuncture group were in the highest category ( $\geq 40000$ ). Among comorbidities, diabetes mellitus was observed in 46.2% of acupuncture patients and 44.9% of non-acupuncture patients. Hyperlipidemia and rheumatoid arthritis were more prevalent in the acupuncture group at 59.1% and 9.4%, compared to 46.0% and 5.8% in the non-acupuncture group. The standardized mean difference highlighted distribution disparities between the groups. In our study, we employed a propensity score matching technique to pair patients 1:1% between the acupuncture group and the non-acupuncture group, considering a variety of factors including demographic characteristics and comorbid diseases. A total of 31,249% patient pairs were successfully matched. The standardized mean difference indicated no significant statistical differences in the distribution of the variables post-matching, suggesting that the matching process effectively created comparable groups for the subsequent analysis.

#### 3.2. Outcome data

In Fig. 2, we employed the Kaplan-Meier method to depict the survival curves for stroke patients, contrasting those who received acupuncture with those who did not. A significant divergence between the two curves was observed, substantiated by a *p*-value of less than 0.001 in the log-rank test. In the acupuncture group, the average follow-up duration was 16.5 years, with a 95 % confidence interval for the mean ranging from 16.52 to 16.64 years. In the control group, the average follow-up period was 15.8 years, with the 95 % CI for the mean extending from 15.81 to 15.94 years.

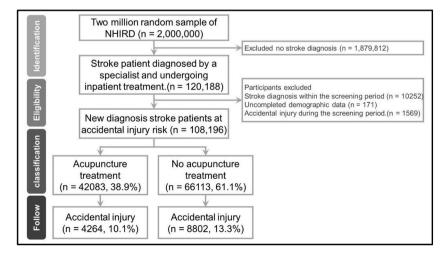


Fig. 1. Flowchart of participant selection and accidental injury assessment in a stroke patient study.

Table 1
Demographic characteristics and comorbidity disease of the stroke cohort.

Variables	Original cohort			Propensity matching cohort		
	Acupuncture	Non- Acupuncture	Standardized mean difference	Acupuncture No. (%)	Non- Acupuncture	Standardized mean difference
	No. (%)	No. (%)			No. (%)	
Total	42083 (100.00 %)	66113 (100.00 %)	-	31249 (100.0 %)	31249 (100.0 %)	
Age at diagnosis			-0.290*			<0.001
<50	5453 (13.0 %)	6104 (9.2 %)		4022 (12.9 %)	4144 (13.3 %)	
50-60	6619 (15.7 %)	6752 (10.2 %)		4906 (15.7 %)	4906 (15.7 %)	
60-70	9305 (22.1 %)	11208 (17.0 %)		6837 (21.9 %)	6975 (22.3 %)	
≥ 70	20706 (49.2 %)	42049 (63.6 %)		15484 (49.6 %)	15224 (48.7 %)	
Sex			-0.159			< 0.001
Male	19670 (46.7 %)	36155 (54.7 %)		14593 (46.7 %)	14593 (46.7 %)	
Female	22413 (53.3 %)	29958 (45.3 %)		16656 (53.3 %)	16656 (53.3 %)	
Urbanization			-0.154			< 0.001
Very high	13068 (31.1 %)	15610 (23.6 %)		9815 (31.4 %)	9816 (31.4 %)	
High	23761 (56.5 %)	40676 (61.5 %)		17656 (56.5 %)	17656 (56.5 %)	
Moderate	3777 (9.0 %)	6605 (10.0 %)		2869 (9.2 %)	2812 (9.0 %)	
Low	1478 (3.5 %)	3222 (4.9 %)		909 (2.9 %)	965 (3.1 %)	
Insured amount			0.113			< 0.001
Dependent	12244 (29.1 %)	20069 (30.4 %)		9275 (29.7 %)	9093 (29.1 %)	
1-19999	12298 (29.2 %)	22308 (33.7 %)		9216 (29.5 %)	9034 (28.9 %)	
20000-39999	12796 (30.4 %)	18854 (28.5 %)		9690 (31.0 %)	9405 (30.1 %)	
$\ge 40000$	4745 (11.3 %)	4882 (7.4 %)		3068 (9.8 %)	3717 (11.9 %)	
Comorbidity						
Diabetes mellitus	19443 (46.2 %)	29709 (44.9 %)	0.025	14293 (45.7 %)	14581 (46.7 %)	-0.038
Chronic kidney	6899 (16.4 %)	11579 (17.5 %)	-0.030	5074 (16.2 %)	5176 (16.6 %)	-0.013
disease						
Coronary heart disease	7340 (17.4 %)	10797 (16.3 %)	0.067	5546 (17.7 %)	5492 (17.6 %)	0.007
Hypertension	32222 (76.6 %)	52654 (79.6 %)	-0.074	24415 (78.1 %)	24176 (77.4 %)	0.031
Rheumatoid arthritis	3969 (9.4 %)	3825 (5.8 %)	0.138	2996 (9.6 %)	2908 (9.3 %)	0.012
Hyperlipidemia	24868 (59.1 %)	30422 (46.0 %)	0.264*	18283 (58.5 %)	18468 (59.1 %)	-0.024
Gout	2640 (6.3 %)	3510 (5.3 %)	0.106	1988 (6.4 %)	1988 (6.4 %)	< 0.001
Osteoarthritis	12255 (29.1 %)	14532 (22.0 %)	0.164	9003 (28.8 %)	9093 (29.1 %)	-0.012

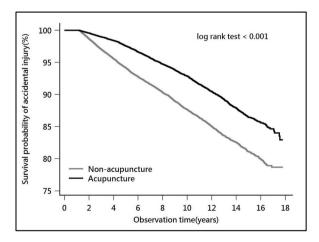


Fig. 2. Kaplan-Meier analysis of stroke patients based on acupuncture treatment.

#### 3.3. Main result

Table 2 illustrates the risk of accidental injury in relation to acupuncture treatment and various covariates among stroke patients. Patients who received acupuncture exhibited a notably reduced incidence rate of 10.2 per 1,000 person-years, compared to those who did not undergo acupuncture, with an incidence rate of 15.8. The adjusted hazard ratio for the acupuncture group was 0.71 (95 % CI: 0.67–0.75), emphasizing the potential protective effect of acupuncture against accidental injury. Females registered an incidence rate

**Table 2**Risk of accidental injury in terms of acupuncture treatment and covariates among patients with stroke in original cohort.

Variables	N	Person- year	Incidence rate per 1,000 person- year	Crude hazard ratio (95 % confidence interval)	Adjusted hazard ratio (95 % confidence interval)
Acupuncture					
Yes	8802	557243.1	10.2	0.66 (0.62-0.70)*	0.71 (0.67-0.75)
No	4264	417741.8	15.8	Reference	Reference
Sex					
Female	6761	481430.6	14.0	1.43 (1.24-1.65)*	1.14 (1.07-1.22)*
Male	6305	493553.9	12.8	Reference	Reference
Age					
< 50	878	113758.4	7.7	Reference	Reference
50-60	1274	126347.2	10.1	1.72 (1.48–2.00)*	1.43 (1.24–1.65)*
60-70	2435	190750.0	12.8	2.29 (1.99-2.64)*	1.75 (1.54–2.00)*
$\geq 70$	8479	544128.9	15.6	2.40 (2.10-2.75)*	1.85 (1.65–2.08)*
Insurance amount					
Dependent	3881	287098.5	13.5	Reference	Reference
1-19999	4566	289739.3	15.8	1.17 (1.08–1.26)*	1.16 (1.08–1.25)*
20000-39999	3995	301020.1	13.3	0.94 (0.87-1.02)	0.96 (0.89-1.03)
$\ge 40000$	623	97127.3	6.4	0.54 (0.46-0.62)*	0.56 (0.48-0.65)*
Urbanization					
Very high	2905	276789.6	10.5	Reference	Reference
High	8029	564945.2	14.2	1.29 (1.19-1.38)*	1.27 (1.18–1.37)*
Moderate	1464	92515.0	15.8	1.42 (1.28–1.58)*	1.39 (1.25–1.55)*
Low	668	40735.1	16.4	1.39 (1.20–1.60)*	1.33 (1.15–1.54)*
Comorbidity					
Diabetes mellitus	5877	456856.3	12.9	0.91 (0.85-0.97)	0.96 (0.91–1.03)
Chronic kidney disease	1871	110815.0	16.9	1.20 (1.10–1.31)*	1.26 (1.16–1.37)*
Coronary heart disease	2191	150029.7	14.6	1.01 (0.95–1.08)	1.09 (1.02–1.16)*
Hypertension	10486	767193.4	13.7	0.89 (0.78-1.03)	1.02 (0.94–1.11)*
Rheumatoid arthritis	926	65192.9	14.2	1.09 (0.97-1.22)*	1.06 (0.95–1.19)*
Hyperlipidemia	5588	252736.3	22.1	1.78 (1.67–1.89)*	1.65 (1.54–1.75)*
Gout	691	51041.82	13.5	0.90 (0.84-0.96)	1.01 (0.94–1.08)*
Osteoarthritis	3641	213940.6	17.1	1.18 (1.09–1.36)*	1.15 (1.04–1.26)*
Sedative Hypnotic Drug	gs				
Benzodiazepines	9991	423863.7	23.6	1.81 (1.66–1.81)	1.75 (1.64–1.80)
Barbiturates	2038	65656.2	31.0	2.39 (2.21-2.34)	2.16 (2.03-2.14)
Z-drug	8267	427570.6	19.3	1.49 (1.38-1.51)	1.37 (1.3-1.38)

of 14.0, while their male counterparts exhibited a rate of 12.8. Post-adjustment, females presented an augmented hazard ratio of 1.14, with a 95 % confidence interval demarcated between 1.07 and 1.22. Age was a significant determinant. The incidence rate increased with age, with those aged 70 and above showing the highest rate at 15.6. The adjusted hazard ratios also increased progressively with age, with the oldest age bracket having a ratio of 1.85 (95 % CI: 1.65–2.08), underscoring age as a potent risk factor for accidental injury. Regarding insurance amounts, those insured for amounts \$\geq 40000\$ had the lowest incidence rate of 6.4. The adjusted hazard ratio for this group was a protective 0.56 (95 % CI: 0.48–0.65).

Urbanization seemed to influence the risk as well. Patients from low urbanized areas had a higher incidence rate (16.4) with an adjusted hazard ratio of 1.33 (95 % CI: 1.15-1.54). Similarly, those from moderate urbanized areas had an adjusted hazard ratio of 1.39 (95 % CI: 1.25-1.55). Comorbidity analysis revealed that hyperlipidemia patients had the highest incidence rate of 22.1 with an adjusted hazard ratio of 1.65 (95 % CI: 1.54-1.75). Other comorbidities, such as chronic kidney disease with a hazard ratio of 1.26 (95 % CI: 1.16-1.37) and coronary heart disease with a hazard ratio of 1.09 (95 % CI: 1.02-1.16), also exhibited elevated adjusted hazard ratios, indicating the intricate relationship between these conditions and accidental injury risk.

For Benzodiazepines, among 9,991 individuals followed over 423,863.7 person-years, the incidence rate was 23.6 per 1,000 person-years. The crude hazard ratio for this group was 1.81 (95 % CI: 1.66–1.81), and the adjusted hazard ratio was slightly lower at 1.75 (95 % CI: 1.64–1.80), indicating a considerable increase in risk after adjustment for potential confounders. In the case of Barbiturates, 2,038 individuals were followed for 65,656.2 person-years, with an incidence rate of 31.0 per 1,000 person-years. This group exhibited a higher risk compared to Benzodiazepines, with a crude HR of 2.39 (95 % CI: 2.21–2.34) and an aHR of 2.16 (95 % CI: 2.03–2.14), suggesting a substantial risk associated with Barbiturate use. Lastly, for those using Z-drugs, over 8,267 individuals and 427,570.6 person-years, the incidence rate was 19.3 per 1,000 person-years. The crude HR for this group was 1.49 (95 % CI: 1.38–1.51), with an aHR of 1.37 (95 % CI: 1.3–1.38). Although the risk increase with Z-drug use is apparent, it is comparatively lower than that associated with Benzodiazepines and Barbiturates.

Following propensity score matching to equate the acupuncture and non-acupuncture cohorts, we recalculated the adjusted hazard ratios for accidental injuries among stroke patients, as depicted in Fig. 3. The analysis revealed that those receiving acupuncture had an aHR of 0.74 (95 % CI: 0.51-0.92). When stratified by age, the groups of 0-60, 60-70, and  $\geq$ 70 years displayed progressively increased risks, with aHRs of 1.66 (95 % CI: 1.15-1.99), 2.04 (95 % CI: 1.43-2.44), and 2.2 (95 % CI: 1.58-2.58), respectively, compared to the

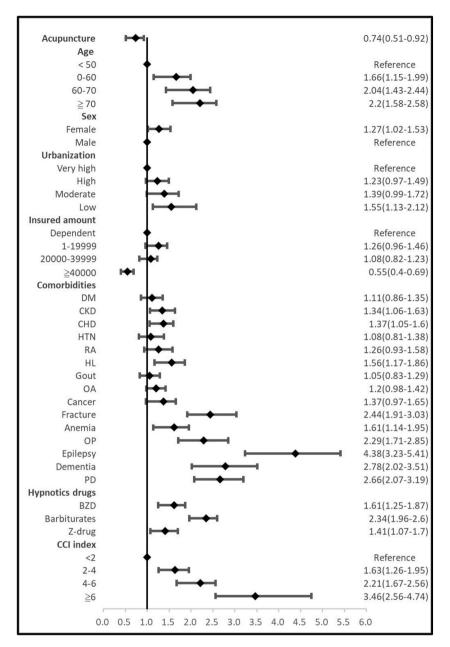


Fig. 3. Adjusted hazard ratios for accidental injuries post-stroke following propensity score matching; DM, Diabetes mellitus; CKD, Chronic kidney disease; CHD, Coronary heart disease; HTN, Hypertension; RA, Rheumatoid arthritis; HL, Hyperlipidemia; OS, Osteoarthritis; BZD, Benzodiazepines; OP, Osteoporosis; PD, Parkinsonism.

reference group of <50 years. In terms of sex, females demonstrated a heightened risk with an aHR of 1.27 (95 % CI: 1.02–1.53). For urbanization levels, compared to the very high urbanization reference category, the high, moderate, and low urbanization groups reported aHRs of 1.23 (95 % CI: 0.97–1.49), 1.39 (95 % CI: 0.99–1.72), and 1.55 (95 % CI: 1.13–2.12), respectively. Within the insurance amount categories, the 1–19999 bracket exhibited an increased risk with an aHR of 1.26 (95 % CI: 0.96–1.46), while the  $\geq$ 40000 category showed a notably reduced risk with an aHR of 0.55 (95 % CI: 0.4–0.69).

Patients with chronic kidney disease exhibited an aHR of 1.34 (95 % CI: 1.06-1.63), indicating a moderately increased risk. Similarly, those with coronary heart disease had an aHR of 1.37 (95 % CI: 1.05-1.6), also suggesting an elevated risk. Hypertension, with an aHR of 1.08 (95 % CI: 0.81-1.38), showed a marginal, albeit not statistically significant, increase in risk. Rheumatoid arthritis patients had an aHR of 1.26 (95 % CI: 0.93-1.58), indicating a potential increase in risk, though the confidence interval suggests some uncertainty. Hyperlipidemia was associated with a more pronounced risk increase, with an aHR of 1.56 (95 % CI: 1.17-1.86).

Additional comorbidities also presented varying levels of risk: cancer patients had an aHR of 1.37 (95 % CI: 0.97-1.65), indicating a

potential risk increase. Fracture patients showed a significantly higher risk with an aHR of 2.44 (95 % CI: 1.91-3.03). Anemia was associated with an elevated risk, with an aHR of 1.61 (95 % CI: 1.14-1.95), while osteoporosis (OP) patients had an aHR of 2.29 (95 % CI: 1.71-2.85). Epilepsy presented the highest risk with an aHR of 4.38 (95 % CI: 3.23-5.41). Dementia patients had an aHR of 2.78 (95 % CI: 2.02-3.51), and those with Parkinson's disease (PD) had an aHR of 2.66 (95 % CI: 2.07-3.19).

These findings underscore the varying degrees of risk for accidental injury associated with different comorbid conditions, highlighting the need for tailored risk management strategies in these patient populations.

#### 3.4. Other analyses

In Fig. 4, we conducted an analysis evaluating the effectiveness of acupuncture in reducing accidental injury risk across various parameters, encompassing demographic variables, comorbidities, medication usage, and stroke classifications. For individuals under 50 years, the adjusted hazard ratio was a compelling aHR of 0.61 (95 % CI: 0.44–0.79), and this beneficial trend varied across older

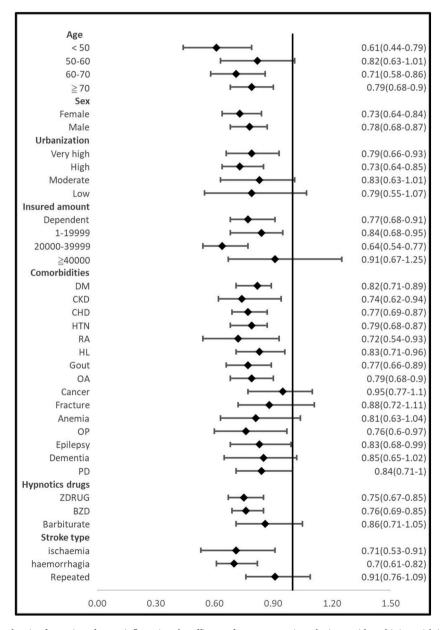


Fig. 4. Adjusted hazard ratios for various factors influencing the efficacy of acupuncture in reducing accidental injury risk in stroke patients; DM, Diabetes mellitus; CKD, Chronic kidney disease; CHD, Coronary heart disease; HTN, Hypertension; RA, Rheumatoid arthritis; HL, Hyperlipidemia; OA, Osteoarthritis; BZD, Benzodiazepines; OP, Osteoporosis; PD, Parkinsonism.

demographics, with aHRs of 0.82 (95 % CI: 0.63–1.01) for 50–60 years, 0.71 (95 % CI: 0.58–0.86) for 60–70 years, and 0.79 (95 % CI: 0.68–0.9) for those aged  $\geq 70$  years. Both sexes witnessed advantages, with males and females manifesting aHRs of 0.78 (95 % CI: 0.68–0.87) and 0.73 (95 % CI: 0.64–0.84), respectively. The protective efficacy of acupuncture echoed across varying degrees of urbanization, with aHRs of 0.79 (95 % CI: 0.66–0.93) for very high urbanization, 0.73 (95 % CI: 0.64–0.85) for high urbanization, 0.83 (95 % CI: 0.63–1.01) for moderate urbanization, and 0.79 (95 % CI: 0.55–1.07) for low urbanization. Insurance amount categories showed similar patterns, with dependent patients having an aHR of 0.77 (95 % CI: 0.68–0.91), the 1–19999 bracket at an aHR of 0.84 (95 % CI: 0.68–0.95), 20000–39999 at an aHR of 0.64 (95 % CI: 0.54–0.77), and >40000 at an aHR of 0.91 (95 % CI: 0.67–1.25).

Regarding comorbidities, diabetes mellitus exhibited an aHR of 0.82 (95 % CI: 0.71–0.89), chronic kidney disease had an aHR of 0.74 (95 % CI: 0.62–0.94), and coronary heart disease showed an aHR of 0.77 (95 % CI: 0.69–0.87). Hypertension was associated with an aHR of 0.79 (95 % CI: 0.68–0.87), while rheumatoid arthritis patients had an aHR of 0.72 (95 % CI: 0.54–0.93). Hyperlipidemia presented an aHR of 0.83 (95 % CI: 0.71–0.96), and gout showed an aHR of 0.77 (95 % CI: 0.66–0.89). Osteoarthritis patients had an aHR of 0.79 (95 % CI: 0.68–0.9), and other conditions such as cancer, fractures, anemia, osteoporosis, epilepsy, dementia, and Parkinson's disease displayed varying levels of risk with aHRs of 0.95 (95 % CI: 0.77–1.1), 0.88 (95 % CI: 0.72–1.11), 0.81 (95 % CI: 0.63–1.04), 0.76 (95 % CI: 0.6–0.97), 0.83 (95 % CI: 0.68–0.99), 0.85 (95 % CI: 0.65–1.02), and 0.84 (95 % CI: 0.71–1.00), respectively. Within the hypnotic drug categories, ZDRUG users demonstrated an aHR of 0.75 (95 % CI: 0.67–0.85), and BZD users an aHR of 0.76 (95 % CI: 0.69–0.85). Barbiturate users had an aHR of 0.86 (95 % CI: 0.71–1.05). Both ischemic and hemorrhagic stroke patients reaped the benefits of acupuncture, displaying aHRs of 0.71 (95 % CI: 0.53–0.91) and 0.7 (95 % CI: 0.61–0.82), respectively. However, the benefits of acupuncture were less pronounced in patients with repeated strokes, who had an aHR of 0.91 (95 % CI:

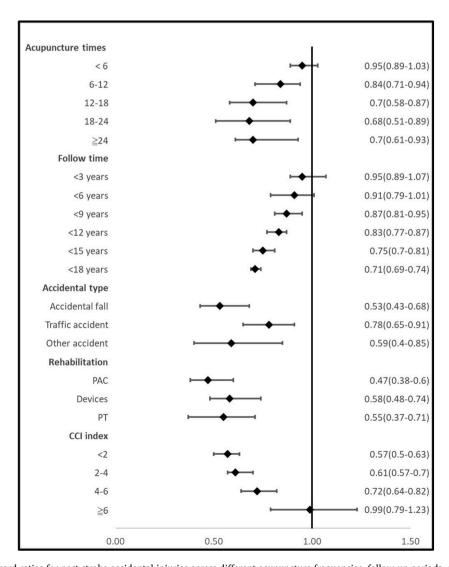


Fig. 5. Adjusted hazard ratios for post-stroke accidental injuries across different acupuncture frequencies, follow-up periods, and injury types; CCI index, Charlson Comorbidity Index; PAC, Post-Acute Care Integrated Services; PT, Physical Therapy.

0.76–1.09), indicating a reduced effectiveness of acupuncture in this specific cohort. This pervasive protective attribute of acupuncture underscores its potential value in fortifying safety outcomes for stroke patients, although it suggests that repeated stroke patients might not derive substantial benefits from acupuncture in terms of reducing their risk of accidental injuries.

In our sensitivity analysis (Fig. 5) examining the efficacy of acupuncture in mitigating the risk of accidental injuries among post-stroke patients, we observed distinct patterns based on various conditions and patient characteristics. We did not identify a clear dose-response effect. Although the lowest adjusted hazard ratio for accidental injuries was observed at 12–18 acupuncture sessions, with an aHR of 0.70 (95 % CI: 0.58–0.87), this benefit did not progressively enhance with increased sessions. In fact, the aHRs modestly rose to 0.68 (95 % CI: 0.51–0.89) for 18–24 sessions and to 0.70 (95 % CI: 0.61–0.93) for those undergoing 24 or more sessions. Across all frequency categories, the aHRs clustered between 0.68 and 0.95, underscoring a consistent but limited effect of acupuncture without a significant incremental benefit beyond a certain number of treatments.

Regarding follow-up duration, longer periods showed a progressively enhanced benefit of acupuncture. For follow-ups less than 3 years, the aHR was relatively higher at 0.95 (95 % CI: 0.89–1.07), which gradually reduced to 0.71 (95 % CI: 0.69–0.74) for follow-ups under 18 years. This suggests a long-term protective effect of acupuncture against accidental injuries in post-stroke patients.

When analyzing the impact of acupuncture on different types of accidental injuries, a significant reduction in risk was observed for accidental falls, with an aHR of 0.53 (95 % CI: 0.43–0.68). This contrasted with the more moderate benefits for traffic accidents (aHR of 0.78, 95 % CI: 0.65–0.91) and other accidents (aHR of 0.59, 95 % CI: 0.4–0.85).

Furthermore, the Charlson Comorbidity Index (CCI) was a critical modifier of acupuncture's effectiveness. Patients with a CCI score of less than 2 showed a markedly lower risk (aHR of 0.57, 95 % CI: 0.5–0.63), and this advantage gradually decreased as the CCI score increased, culminating in an aHR of 0.99 (95 % CI: 0.79–1.23) for those with a score of 6 or above.

Additionally, the type of rehabilitation was an important factor influencing acupuncture's efficacy. Patients who received post-acute care integrated services (PAC) had an aHR of 0.47 (95 % CI: 0.38–0.6), suggesting a significant benefit. In comparison, those using assistive devices had an aHR of 0.58 (95 % CI: 0.48–0.74), and those undergoing physical therapy (PT) showed an aHR of 0.55 (95 % CI: 0.37–0.71).

#### 4. Discussion

#### 4.1. Key results

In this long-term cohort study encompassing a cohort of one hundred thousand stroke patients over an 18-year period, we sought to validate the impact of acupuncture therapy as an adjunctive medical intervention on the risk of accidental injuries. The primary findings of this study indicate a significant association between acupuncture therapy and a reduced risk of accidental injuries, with an adjusted hazard ratio of 0.75 (95 % CI: 0.62–0.88) observed within the propensity score matching cohort. Notably, acupuncture demonstrated efficacy in lowering the risk of accidental injuries among both hemorrhagic and ischemic stroke patients. Additionally, our analysis revealed that acupuncture was associated with a decreased risk of accidental falls and traffic accidents. However, it is important to note that we did not observe a significant dose-response relationship between the frequency of acupuncture sessions and the reduction of accidental injury risk. Furthermore, the effectiveness of acupuncture in reducing accidental injury risk did not show statistical significance in subgroups of patients with high comorbidity burdens (CCI index greater than or equal to six), those receiving barbiturate drug therapy, and individuals insured in less urbanized areas.

#### 4.2. Interpretation

This study has demonstrated that the inclusion of acupuncture as part of the standard treatment regimen for stroke patients can reduce the incidence of accidental injuries by 32 %. The beneficial effects of acupuncture remain consistent across various subgroups, including age, gender, comorbidities, stroke types, and injury categories. With a study cohort comprising over one hundred thousand stroke patients, followed for a minimum of six years, the substantial sample size and extended follow-up duration enhance the credibility of our research findings.

Acupuncture's positive impact on motor function, balance, and daily activities in stroke patients has been previously validated in clinical trials [3,5,6]. Our study corroborates these findings and, through long-term generational research, further underscores the role that acupuncture can play in population-based healthcare.

However, some unexpected results have emerged from our analysis. Firstly, we found no significant dose-response relationship between the frequency of acupuncture sessions and the risk of post-stroke accidental falls. While acupuncture as part of routine care is beneficial, there should be caution against indiscriminately increasing the frequency of acupuncture treatment.

Secondly, we observed that the relative risk reduction of accidental injuries associated with acupuncture becomes more pronounced after a follow-up period exceeding nine years. This suggests that acupuncture therapy requires a sustained duration to maximize its benefits. While previous studies have indicated that the therapeutic effects of acupuncture may manifest within weeks, mitigating the risk of accidental injuries, which demands improvements in balance, coordination, and environmental awareness, necessitates a longer treatment duration.

Furthermore, we noted that acupuncture treatment did not significantly reduce the risk of accidental falls in patients with multiple comorbidities and those taking barbiturate medications. This outcome may be attributed to the severity of their underlying conditions and medication usage, which place them at a higher risk of falls beyond the scope of acupuncture's therapeutic reach. Consequently, the development of tailored acupuncture strategies for these patient populations warrants future research.

Lastly, we observed that in low-urbanization areas and among high-income patients, the correlation between acupuncture and a reduction in accidental injuries was not statistically significant. This polarized outcome may be explained by the limited availability of acupuncture resources in low-urbanization areas and the challenges in maintaining a consistent treatment frequency. Conversely, high-income patients already benefit from superior healthcare access, resulting in lower baseline risks of accidental falls, which may diminish the discernible benefits of adding acupuncture treatment.

#### 4.3. Generalizability

The generalizability of this study is primarily limited by its confinement to a single country, namely Taiwan and its affiliated islands. Traditional Chinese medicine, including acupuncture, is highly prevalent in Taiwan. In this study, 38.9 % of the patients received acupuncture treatment, a proportion significantly higher than in most non-East Asian countries. The high level of acceptance of acupuncture among study participants could potentially lead to an overestimation of its effects, and observational cohort studies cannot mitigate this limitation through randomization and blinding procedures. To partially address the issue of generalizability resulting from indication bias, we employed propensity score matching to match individuals based on known factors affecting acupuncture usage. However, we still anticipate that future randomized double-blind controlled trials will be necessary to validate the conclusions drawn from this study.

The LGTD 2000 database utilized in this study was obtained through stratified random sampling from the general population, ensuring representativeness in terms of age and gender. Additionally, the study encompassed various stroke subtypes and demographic variables, which can enhance the external validity of the study's findings to a broad spectrum of stroke patients.

In this study, we included only patients who were hospitalized for a stroke for the first time during the research period. Some patients, due to the less severe nature of their stroke, received only emergency medical care or were found to have a history of prior stroke during outpatient visits. Such patients were excluded from this study. However, these stroke patients still belong to a high-risk group for accidental injuries. Therefore, we conducted a sensitivity analysis including these patients and found that acupuncture reduced the risk of accidental events to 0.64 (95 % CI: 0.51–0.79). The results of the sensitivity analysis suggest that the observed reduction in accidental events attributed to acupuncture may potentially be extrapolated to patients with milder forms of stroke.

#### 4.4. Limitations

This study has several limitations that warrant consideration. First and foremost, the retrospective nature of the study design introduces inherent limitations related to data accuracy and completeness. While utilizing a comprehensive medical database, the reliance on medical records may result in underreporting or misclassification of certain variables, potentially affecting the precision of our findings.

Second, despite employing propensity score matching to mitigate indication bias, the observational nature of this research inherently carries the risk of residual confounding due to unmeasured or inadequately controlled factors. While we have endeavored to account for various covariates, including comorbidities and medication usage, the potential for unobserved variables influencing the results cannot be entirely eliminated.

Third, the long-term effects of acupuncture were assessed over a minimum follow-up period of six years. Although this duration provided valuable insights into the sustained benefits of acupuncture, it may not capture the full spectrum of effects that could emerge with even longer-term follow-up. Future studies with extended observation periods could provide additional insights into the durability of acupuncture's impact on accidental injury risk.

Fourth, the dosage and specific protocols of acupuncture treatment were not standardized across all patients, as this study was based on real-world clinical practice. Variability in acupuncture approaches may introduce heterogeneity into the treatment group, potentially impacting the consistency of treatment effects.

Furthermore, the definition of stroke was based solely on ICD-9 and ICD-10 codes, without accounting for individual variations in stroke severity, such as consciousness level, muscle strength, or dependency in daily activities, which are important factors influencing accidental injury risk. The "2000 Longitudinal Generation Tracking Database" used in this study does not provide these clinical details. Future research should use databases with more comprehensive clinical data to better understand the impact of stroke severity on the effectiveness of acupuncture in reducing accidental injury risk.

We acknowledge that the supportive system of the surrounding environment is an important factor that can influence mobility and the risk of accidental injury in stroke patients. However, the "2000 Longitudinal Generation Tracking Database (LGTD 2000)" used in this study does not include data on environmental support systems, which is a limitation of our analysis.

#### 5. Conclusion

These key results underscore the potential benefits of acupuncture therapy as an adjunctive approach in the prevention of accidental injuries among stroke patients, irrespective of the stroke subtype. Nevertheless, further investigation is warranted to explore the nuances of acupuncture dosage and its interaction with specific patient characteristics, comorbidities, and medication regimens. Such insights will contribute to a more tailored and effective integration of acupuncture into the holistic care of stroke patients, enhancing their overall quality of life and safety during the recovery process.

#### CRediT authorship contribution statement

Ming-Jen Wang: Writing – original draft, Conceptualization. Hui-Jer Chou: Writing – original draft, Formal analysis, Data curation. Shun-Ku Lin: Formal analysis, Data curation, Conceptualization.

#### Ethics statement

This study was reviewed and approved by The Taipei City Hospital Research Ethics Committee with the approval number: TCHIRB-11103028-E, dated 2022/04/13. The Taipei City Hospital Research Ethics Committee waived the requirement for patient informed consent because this study utilized the 2000 Longitudinal Generation Tracking Database (LGTD 2000), which is collected by Taiwan's Ministry of Health and Welfare. The data were de-identified at the time of collection, and researchers cannot identify or contact individual participants.

#### Data availability statement

This study utilizes data from the 2000 Longitudinal Generation Tracking Database (LGTD 2000), which is managed directly by the Ministry of Health and Welfare in Taiwan. Access to the dataset is restricted, and researchers may apply for usage permissions directly through the Ministry. Due to the Ministry's data sharing policies, this dataset cannot be shared with other researchers.

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#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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