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Clinical effects of acupuncture treatment for prevention of insomnia-induced stroke: A large-scale cohort study

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ABSTRACT

Background: Recent research has established an association between insomnia and an elevated risk of stroke. Given the severe global impact of stroke on public health, exploring nonpharmacological interventions, such as acupuncture, that can mitigate stroke risk among individuals with insomnia is crucial.

Methods: In this retrospective cohort study, we used data from the Taiwan National Health Insurance Database (NHIRD) to examine the relationship between acupuncture and the risk of stroke among individuals who received a diagnosis of insomnia between 2000 and 2017. The study participants were divided into two cohorts: the acupuncture group that received acupuncture and a matched control group that did not. The primary outcome was the occurrence of stroke.

Results: Of the 217,356 patients included in the study, 3668 individuals in the acupuncture group and 4913 in the control group experienced stroke. The incidence rate of stroke was lower in the acupuncture group (4.51 per 1000 person-years) than in the control group (6.86 per 1000 person-years). After adjustment for various potential confounders, patients who received acupuncture exhibited a notably reduced risk of stroke, with an adjusted hazard ratio of 0.66 (95 % confidence interval [CI]: 0.63, 0.69). Furthermore, a dose–response relationship was evident, in that individuals who received 6–11 acupuncture sessions experienced a 24 % reduction in stroke risk, whereas those who received 12–17 sessions, 18–29 sessions, and ≥30 sessions exhibited reductions of 31 %, 34 %, and 42 %, respectively.

Conclusion: Acupuncture treatment was significantly associated with a reduced risk of stroke among patients with insomnia.

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1. Introduction

1.1. Background

Insomnia and stroke exhibit a robust and complex relationship, as evidenced by recent studies in the past decade. Sawadogo et al. (2023) conducted a comprehensive investigation by using data from the Health and Retirement Study, with a focus on individuals aged ≥50 years in the United States. Their findings revealed a dose–response relationship between insomnia symptoms and the risk of stroke. Notably, this risk was more pronounced in individuals aged <50 years. This association was partly mediated by comorbidities such as diabetes, hypertension, heart disease, and depression, indicating that insomnia is a risk factor for stroke.[1] Furthermore, Chen et al. (2023) conducted a large-scale prospective study involving more than 400,000 Chinese adults who had no history of coronary heart disease, stroke, or insomnia symptoms. Their findings revealed a U-shaped relationship between sleep duration and cardiovascular disease (CVD), including stroke. Individuals with very short sleep duration (≤5 h) and those with very long sleep duration (≥10 h) exhibited significantly elevated risks of total stroke, ischemic stroke, intracerebral hemorrhage, and major coronary events. These results highlight the pivotal role of sleep patterns in determining the risk of stroke and the potential impact of insomnia on CVD outcomes.[2]

The efficacy of acupuncture has been demonstrated for enhancing objective sleep indices among patients with primary insomnia. A systematic review and meta-analysis of 11 studies revealed that acupuncture led to an increase in the total sleep time, improvement in sleep efficiency, and reductions in wake after sleep onset and the number of awakening times compared with sham or placebo acupuncture.[3] Additionally, Zhang et al. (2020) compared active acupuncture with placebo acupuncture and revealed that active acupuncture significantly improved insomnia and mood disorders in patients. After just 2 weeks of treatment, the total score on the Pittsburgh Sleep Quality Index (PSQI) was markedly lower in the active acupuncture group than in the placebo acupuncture group, and this improvement persisted throughout the 1-month follow-up period.[4] Furthermore, Yin et al. (2017) conducted a randomized controlled trial, where patients with primary insomnia received either real acupuncture or sham acupuncture treatment for 4 weeks. The acupuncture group exhibited significant improvements in insomnia severity, sleep efficiency, and total sleep time and reductions in depression scores compared with those at baseline.[5] These studies have collectively highlighted the potential of acupuncture as an effective intervention for improving sleep in individuals with insomnia.

The rationale for this investigation is strengthened by the need for novel preventive strategies against stroke, given its substantial burden on public health and health-care systems worldwide. Should acupuncture prove effective in reducing the risk of stroke among individuals with insomnia, it holds potential as a nonpharmacological and potentially cost-effective strategy for stroke prevention.

Abbreviations

BZDs	benzodiazepines
CAD	coronary artery disease
CHF	congestive heart failure
CI	confidence interval
CVD	cardiovascular disease
DM	diabetes mellitus
ICD-9-CM	*International Classification of Diseases, Ninth Revision, Clinical Modification*
ICD-10-CM	*International Classification of Diseases, Tenth Revision, Clinical Modification*
MAOIs	monoamine oxidase inhibitors
NHI	National Health Insurance
NHIRD	National Health Insurance Research Database
Non-BZD	nonbenzodiazepines
NSAIDs	nonsteroidal anti-inflammatory drugs
PSQI	Pittsburgh Sleep Quality Index
SMD	standardized mean difference
SSRIs	selective serotonin reuptake inhibitors
TCM	traditional Chinese medicine.

1.2. Objectives

The objective of this retrospective cohort study is to explore the relationship between acupuncture treatment and the reduced risk of stroke among patients with insomnia.

2. Materials and methods

2.1. Data source

The data source for this study was the Taiwan National Health Insurance Database (NHIRD), which comprises registration files and original claims data for nearly the entire population of Taiwan. The database was established from 1995, when the Taiwanese government launched the National Health Insurance (NHI) program with the aim to improve the country's health-care system and overall public health. The dataset encompasses the demographic characteristics of insurants, records of hospital admissions and discharges, disease diagnoses, prescribed medications, received treatments, and the associated expenses from all health-care settings. The diagnosis codes were based on the World Health Organization's International Classification of Diseases, Clinical Modification, Ninth Revision and Tenth Revision (ICD-9-CM and ICD-10-CM, respectively). This study protocol was approved by the Institutional Review Board of China Medical University Hospital (CMUH110-REC1-038(CR-2)).

2.2. Study population

The study population comprised individuals diagnosed as having insomnia (ICD-9-CM codes 307.41, 307.42, 780.50, 780.52 and ICD-10-CM codes F51.0, G47.0, G47.8, G47.9) and sleep apnea (ICD-9: 327.2, 780.51, 780.53, 780.57 and ICD-10-CM codes G47.3), who had at least two outpatient visits or one inpatient admission between 2000 and 2017. These patients with insomnia were categorized into two groups: the case cohort included individuals with insomnia who received acupuncture treatment (procedure codes B41, B42, B43, B44, B45, B46, B80–B94, P27041, P31103, P31206, P32103, P33031, P33032), whereas the control cohort comprised those with insomnia who did not receive acupuncture. Individuals in the control group were matched to those in the case cohort based by the year of insomnia diagnosis, the year of the index date, sex, age, insurance coverage amount, urbanization level, comorbidities, and related medications. For acupuncture users, the index date was defined as the first prescription date for acupuncture treatment, whereas for controls, it was set as a random date following insomnia diagnosis. Patients who were less than 20 or more than 100 years of age, had a stroke diagnosis before the index date, had a follow-up period of less than 1 year from the index date, or had received acupuncture treatment fewer than six times were excluded from the study. Each patient who received acupuncture was matched with a patient who did not receive acupuncture through propensity score matching. The variables used for matching included age, sex, insurance coverage amount, urbanization level, comorbidities, and related medications (Fig. 1).

Age stratification into four groups: 20–39, 40–59, 60–79, and ≥80 years, was chosen to reflect the distinct physiological and pathological characteristics prevalent across different life stages, which may

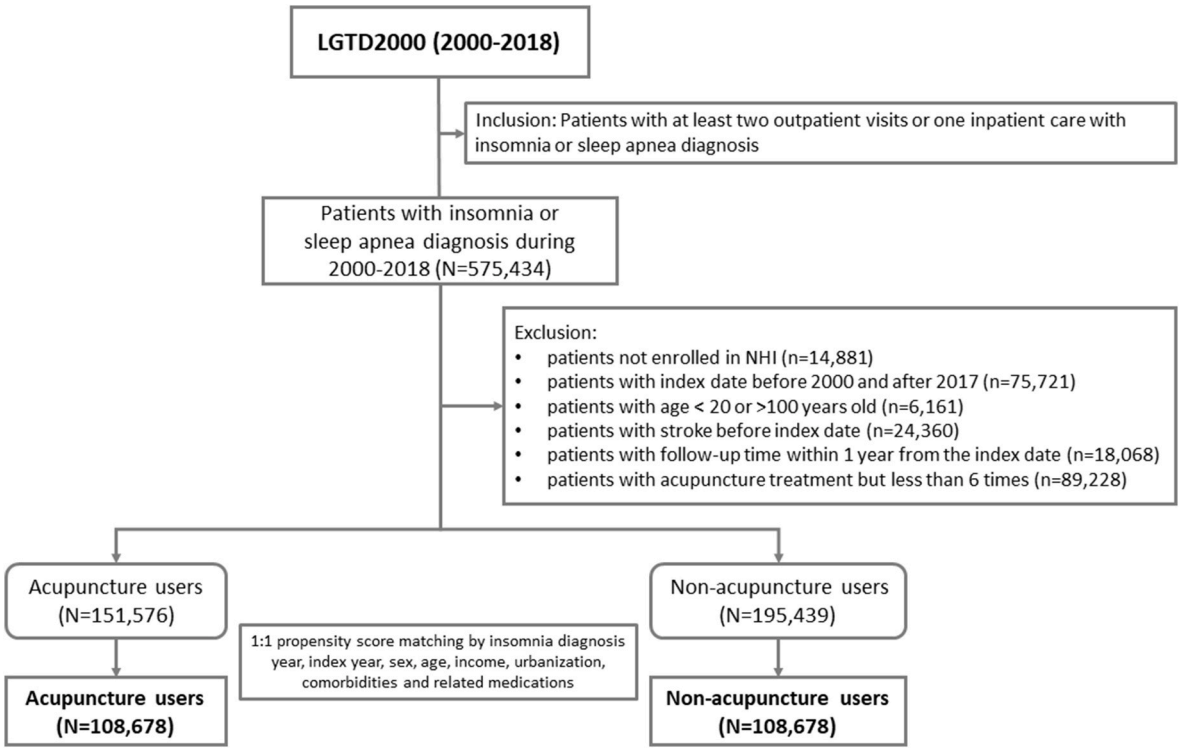

Fig. 1. Study population flowchart. A total of 575,434 patients with insomnia, newly diagnosed between 2000 and 2018, were initially identified. Propensity score matching was applied in a 1:1 propensity score to match the cohorts based on insomnia diagnosis year, index year, sex, age, income, urbanization, comorbidities and related medications. The groups of acupuncture users and nonacupuncture users each comprised 108,678 patients. LGTD 2000: Longitudinal Generation Tracking Database 2000.

influence both the incidence of insomnia and the risk of stroke.[6] This division enables a more precise analysis of the age-specific effects of acupuncture on stroke prevention. Such stratification ensures that the analysis is sensitive to age-related differences in response to acupuncture, which might vary significantly between younger adults and the elderly due to factors like skin elasticity, nerve sensitivity, and overall health condition.[7]

Furthermore, the choice of using six acupuncture sessions as a segmentation basis in the study is rooted in the administrative and practical framework of Taiwan's NHI system. Under the NHI, a package of six acupuncture sessions forms a standard unit of reimbursement, which not only reflects a common clinical practice pattern but also aligns with the insurance policy's requirements for medical treatment assessment and renewal. After every six sessions, there is a mandated evaluation by the attending physician to determine the necessity and plan for further treatment. This checkpoint is crucial for ensuring the ongoing appropriateness of care based on patient response and health economics considerations. Additionally, after this threshold, patients may incur higher medical expenses, making it a critical point for evaluating cost-effectiveness and patient commitment to continued acupuncture therapy.[8,9]

2.3. Primary outcomes and comorbidities

The primary outcomes examined in this study was the occurrence of stroke (*ICD*-9-CM codes 430–438 and *ICD*-10-CM codes I60–I69), which was defined based on one inpatient admission. Additionally, the study assessed the risk of different types of stroke, including ischemic stroke, hemorrhage stroke, and other stroke types between acupuncture users and nonusers. To account for potential confounders, we considered various variables including age, sex, insurance coverage amount, urbanization level, comorbidities, and related medications. Age was categorized into four groups: 20–39 years, 40–59 years, 60–79 years, and ≥80 years. Comorbidities examined in this study included diabetes mellitus (DM) (*ICD*-9-CM code 250, *ICD*-10-CM codes E08–E13), hypertension (*ICD*-9-CM codes 401–405, *ICD*-10-CM codes I10–I15), hyperlipidemia (*ICD*-9-CM code 272, *ICD*-10-CM codes E77, E78), coronary artery disease (CAD) (*ICD*-9-CM codes 410–414, *ICD*-10-CM codes I20–I25), congestive heart failure (CHF; *ICD*-9-CM code 428, *ICD*-10-CM code I50), anxiety (*ICD*-9-CM codes 300.0, 300.2, 300.3, 308.3, and 308.9, *ICD*-10-CM codes F40, F41, F42, F43.0 and R45.7), alcoholism (*ICD*-9-CM codes 291, 303, 305.00, 305.01, 305.02, 305.03, 571.0–571.3, 790.3, V11.3 and V79.1, *ICD*-10-CM code F10, K70, R78.0 and Z65.8), smoking (*ICD*-9-CM codes 305.1, V15,82, *ICD*-10-CM codes F17.2, Z87.891), obesity (*ICD*-9-CM code 278, *ICD*-10-CM code E66), and depression (*ICD*-9-CM codes 296.2, 296.3, 296.82, 300.4, 309.0, 309.1, 309.28 and 311, *ICD*-10-CM codes F32, F33, F34.1, F43.21, F43.23). The related drugs examined included nonsteroidal anti-inflammatory drugs (NSAIDs), oral steroids, statins, benzodiazepines (BZDs), non-BZD hypnotic drugs, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, and other antidepressant drugs.

2.4. Statistical analysis

To compare the differences in baseline characteristics between the two cohorts, categorical variables were evaluated using a chi-square test, whereas continuous variables were analyzed using Student's *t*-test. Additionally, to quantify the disparities in covariates between the two groups, standardized mean differences (SMDs) were calculated, with an SMD of <0.1 indicating a negligible difference. To compare the risk of stroke between acupuncture users and nonusers, Cox proportional-hazards models were employed. The cumulative incidence of stoke in both the acupuncture and control cohorts was estimated using the Kaplan–Meier method, and the log-rank test was used to determine significance. All statistical analyses were performed using

SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.1.0. The significance level for the study was set at a p value of <0.05.

3. Results

3.1. Descriptive data

A total of 217,356 patients were included in this study, with 108,678 participants in each group. In this retrospective cross-generational study, we investigated the characteristics of individuals with newly diagnosed insomnia who had either received acupuncture treatment or had not received such treatment; acupuncture users and controls were matched through propensity score matching. Table 1 presents a summary of key comparisons between these two groups. Minimal differences were observed in the distribution of sex, with 63.64 % of patients in the acupuncture group and 64.18 % of patients in the nonacupuncture group being women (SMD = 0.011). Similarly, no significant differences were observed in the age distribution, with the majority of patients in the acupuncture and nonacupuncture groups (43.90 % and 44.37 %; SMD = 0.007) being in the age group of 40–59 years. Furthermore, insurance coverage, urbanization level, and comorbidities demonstrated only slight variations, with SMD values consistently below 0.1. Medication usage patterns were similar in both groups, with SMD values consistently below 0.1 for various medications. In the acupuncture group, 87.78 % received manual acupuncture of the traditional Chinese medicine type, whereas 11.05 % received a combination of manual acupuncture and electroacupuncture. The mean follow-up time differed between the two groups, with 7.48 months in the acupuncture group and 6.59 months in the nonacupuncture group (SMD: 0.223). The mean number of acupuncture visits was 39 during the study period.

3.2. Outcome data

Fig. 2 illustrates the cumulative incidence of stroke in the acupuncture and nonacupuncture cohorts. During the follow-up period, a total of 4901 patients who did not receive acupuncture treatment experienced stroke relative to the 3727 patients who received acupuncture. The cumulative observation time, measured in person-years, was 722,201.88 in the nonacupuncture group and 816,405.90 in the acupuncture group. The incidence rate of stroke, calculated per 1000 person-years, was 6.79 in the nonacupuncture group and 4.57 in the acupuncture group. The log-rank test revealed a p value of <0.001 in the Kaplan–Meier estimator curves, indicating a statistically significant difference. These findings strongly suggest a potential association between acupuncture treatment and a reduced risk of stroke in patients with insomnia.

3.3. Stroke risk analysis results

The analysis presented in "Table 2" assessed the impact of various confounding factors on stroke risk among patients with insomnia or sleep apnea, incorporating covariates such as acupuncture treatment, demographic characteristics, socioeconomic status, and health conditions. The study found that acupuncture significantly reduced stroke risk, with those receiving treatment exhibiting an adjusted hazard ratio (aHR) of 0.66 (95 % CI: 0.63–0.69) compared to those who did not receive acupuncture, achieving statistical significance with a p-value of less than 0.001.

Sex and age were major determinants of stroke risk, with males showing a higher risk than females, indicated by an aHR of 1.47 (95 % CI: 1.41–1.53). The risk of stroke dramatically increased with age; for example, those aged 60–79 had an aHR of 11.40 (95 % CI: 10.1–13.07), and those 80 or older had an aHR of 22.40 (95 % CI: 19.49–25.85), with both groups showing highly significant differences.

Socioeconomic factors such as insurance amount and urbanization

Table 1
Characteristics of patients with newly diagnosed insomnia or sleep apnea who did or did not receive acupuncture.

Variables	Non-Acupuncture (N = 108,678)		Acupuncture (N = 108,678))		SMD[b]
	N	%	n	%	
Sex					0.011
Female	69,166	63.64	69,753	64.18	
Male	39,512	36.36	38,925	35.82	
Age					
20-39	28,074	25.83	28,900	26.59	0.017
40-59	47,706	43.90	48,215	44.37	0.009
60-79	28,744	26.45	28,301	26.04	0.009
≥80	4154	3.82	3262	3.00	0.045
mean, (SD)[a]	51.17	15.80	50.58	15.46	0.038
Insurance amount					
0–19999 (lowest)	71,610	65.89	71,351	65.65	0.005
20,000-39999	25,425	23.39	25,712	23.66	0.006
≥40,000 (highest)	11,643	10.71	11,615	10.69	0.001
Urbanization[c]					
1 (highest)	57,134	52.57	57,318	52.74	0.003
2	31,391	28.88	31,319	28.82	0.001
3	6515	5.99	6512	5.99	<0.001
4 (lowest)	13,638	12.55	13,529	12.45	0.003
Comorbidities					
Diabetes mellitus	19,201	17.67	18,766	17.27	0.011
Hypertension	38,541	35.46	37,650	34.64	0.017
Hyperlipidemia	33,672	30.98	33,188	30.54	0.010
Coronary artery disease	20,643	18.99	20,025	18.43	0.015
Congestive heart failure	2975	2.74	2743	2.52	0.013
Anxiety	38,039	35.00	37,962	34.93	0.001
Alcoholism	2856	2.63	2750	2.53	0.006
Smoking	2229	2.05	2341	2.15	0.007
Obesity	1767	1.63	1733	1.59	0.002
Depression	18,385	16.92	18,390	16.92	<0.001
Atrial fibrillation	13,703	12.61	13,446	12.37	0.007
Medications[d]					
NSIADs	89,897	82.44	90,439	82.94	0.013
Oral steroid	44,552	40.86	44,762	41.05	0.004
Statin	14,317	13.13	14,186	13.01	0.004
BZD	70,170	64.35	70,134	64.32	0.001
non-BZD	37,964	34.82	37,667	34.54	0.006
MAOI	886	0.81	881	0.81	0.001
SSRI	7637	7.00	7865	7.21	0.008
Tricyclic	11,666	10.70	11,467	10.52	0.006
Other anti-depressant drugs	12,437	11.41	12,531	11.49	0.003
Aspirin	21,727	19.99	20,952	19.28	0.018
Clopidogrel	1847	1.70	1724	1.59	0.009
Other anticoagulants	2416	2.22	2277	2.10	0.009
Types of acupuncture					
Manual acupuncture of TCM type	.	.	95,394	87.78	
Electroacupuncture	.	.	1273	1.17	
Combination of manual acupuncture and electroacupuncture	.	.	12,011	11.05	
Mean, (SD)					
Duration between insomnia date and index, days	1311.51	1173.51	1290.04	1281.60	0.017
Acupuncture visits, times	.	.	38.98	69.06	
Follow-up time	6.59	4.04	7.48	3.92	0.223

*Chi-square test.
[a] SD: standard deviation.
[b] SMD: standardized mean difference.
[c] Urbanization was categorized into four levels according to the population density of the residential areas, with level 1 representing the most urbanized and level 4 the least urbanized.
[d] Medications included the following: nonsteroidal anti-inflammatory drugs (NSAIDs), oral steroids, statins, benzodiazepines (BZDs), non-BZD hypnotic

drugs, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, and other antidepressants.

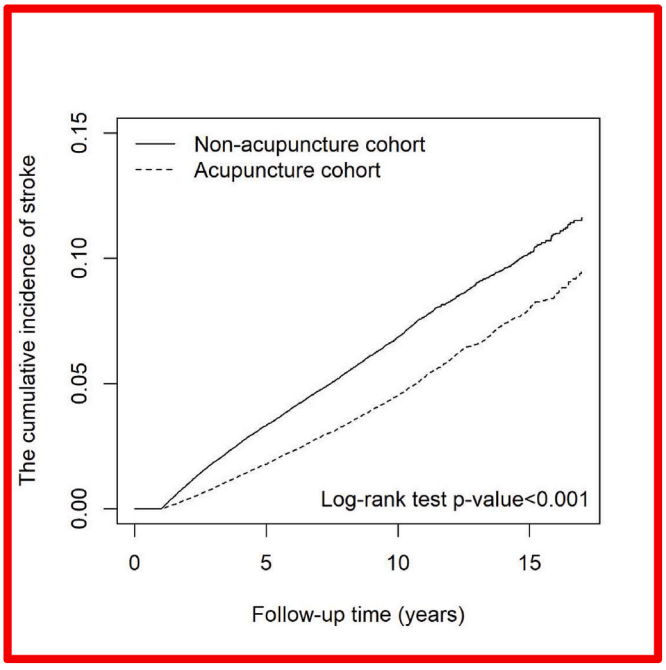

Fig. 2. Cumulative incidence of stroke in the acupuncture and nonacupuncture cohorts. The cumulative incidence of stroke in the acupuncture cohort was significantly lower than that in the nonacupuncture cohort (log-rank test, $p < 0.001$).

also influenced stroke risk. Patients with higher insurance coverage displayed lower risk, with the highest insurance bracket showing an aHR of 0.75 (95 % CI: 0.70–0.81). Urbanization appeared to have a moderate impact, with the lowest urbanization areas having an aHR of 1.14 (95 % CI: 1.06–1.21).

The study further considered comorbidities, where conditions such as diabetes mellitus and hypertension substantially increased stroke risk with aHRs of 1.51 (95 % CI: 1.44, 1.58) and 1.80 (95 % CI: 1.70, 1.91), respectively. Besides, congestive heart failure and alcoholism were associated with a higher risk, evidenced by aHRs of 1.37 (95 % CI: 1.26–1.48) and 2.02 (95 % CI: 1.80–2.27), respectively.

Medication use also played a role in modulating stroke risk. Notably, the use of Statin was linked to a decreased risk with an aHR of 0.91 (95 % CI: 0.86–0.97), while clopidogrel use was associated with a slight reduction in risk, evidenced by an aHR of 0.88 (95 % CI: 0.78–0.99).

The use of benzodiazepine-class sleep medications was associated with a higher risk of stroke in patients with insomnia, as indicated by aHR of 1.16 (95 % CI: 1.09–1.24). This association highlights the potential adverse effects of benzodiazepines on stroke risk among individuals suffering from insomnia.

The results in Table 3 demonstrated that acupuncture consistently lowered stroke risk across various demographic and health-related stratifications. For both sexes, the adjusted hazard ratios indicated a significant reduction in stroke risk with an aHR of 0.67 (95 % CI: 0.64–0.72) for females and 0.66 (95 % CI: 0.62–0.70) for males, with p-values less than 0.001. Age stratification further supported these results, with individuals aged 60–79 showing a notably reduced risk of stroke at an aHR of 0.64 (95 % CI: 0.61–0.68). Socioeconomic variables such as insurance amounts and urbanization levels also showed a consistent effect of acupuncture in reducing stroke risk. Patients from the highest urbanization category and the lowest insurance bracket demonstrated significant stroke risk reductions with aHRs of 0.68 (95 % CI: 0.63–0.72) and 0.65 (95 % CI: 0.62–0.69) respectively. The consistency of these effects across various comorbidities such as diabetes mellitus and hypertension, with aHRs of 0.63 (95 % CI: 0.59–0.68) and 0.67 (95 % CI: 0.64–0.70), emphasized the robustness of acupuncture's preventive benefits across different health contexts.

Moreover, the study explored the impact of acupuncture across different levels of urbanization and insurance coverage, reinforcing the treatment's effectiveness in various socioeconomic settings. For instance, urban dwellers in the highest category (Urbanization 1) experienced a substantial decrease in stroke incidence with an aHR of 0.68 (95 % CI: 0.63–0.72), and similar results were observed in the lowest urban category with an aHR of 0.72 (95 % CI: 0.64–0.81), demonstrating the treatment's efficacy regardless of urbanization level. Similarly, patients with varying insurance coverage levels showed consistent benefits, with those in the highest insurance bracket (≥40,000) showing a reduced stroke risk at an aHR of 0.68 (95 % CI: 0.59–0.78).

The effect of acupuncture on reducing stroke risk was also consistent across patients with different comorbidities. For example, the presence of hyperlipidemia and coronary artery disease did not diminish the effectiveness of acupuncture, with patients suffering from these conditions showing aHRs of 0.74 (95 % CI: 0.69–0.79) and 0.68 (95 % CI: 0.64–0.73), respectively.

The combined use of acupuncture with statins significantly reduced the risk of stroke in patients suffering from insomnia, as evidenced by an aHR of 0.76 (95 % CI: 0.69–0.84). Additionally, anticoagulant medications such as Aspirin and Clopidogrel were also associated with a marked decrease in stroke risk among the same patient population, with Aspirin showing an aHR of 0.67 (95 % CI: 0.63–0.72) and Clopidogrel demonstrating an aHR of 0.76 (95 % CI: 0.61–0.94). These findings underscore the potential therapeutic benefits of integrating acupuncture with specific pharmacological treatments to mitigate stroke risk in individuals with insomnia.

3.4. Other analyses

Table 4 presented a concise summary of the primary findings regarding stroke risk in patients with insomnia who received acupuncture treatment compared with those who did not. Acupuncture significantly reduced the risk of ischemic stroke by 27 % (aHR: 0.73, 95 % CI: 0.69–0.77) and hemorrhagic stroke by 31 % (aHR: 0.69, 95 % CI: 0.62–0.75). Additionally, acupuncture caused a 42 % risk reduction in other stroke types (aHR: 0.58, 95 % CI: 0.53–0.64). Table 5 presented the primary findings regarding the risk of stroke in patients with insomnia on the basis of the number of acupuncture sessions they received. The results indicated a clear dose–response relationship between acupuncture treatment and stroke risk reduction. Specifically, patients who received 6–11 acupuncture sessions exhibited a 24 % lower risk of stroke (aHR: 0.76 95 % CI: 0.71–0.81), whereas those who received 12–17 sessions had a 31 % lower risk (aHR: 0.69, 95 % CI: 0.63–0.75). Moreover, patients who received 18–29 or ≥30 sessions exhibited even greater risk reduction, with a 34 % lower risk (aHR: 0.66, 95 % CI: 0.61–0.72) and a 42 % lower risk (aHR: 0.58, 95 % CI: 0.55–0.62), respectively.

4. Discussion

4.1. Key results

The key findings of this study highlight a significant association between acupuncture treatment and a reduced risk of stroke among patients with insomnia, as evident in both crude and adjusted analyses. Notably, a clear dose–response relationship was established, indicating that acupuncture was significantly associated with a reduced risk of both ischemic and hemorrhagic stroke. Furthermore, patients with comorbidities such as DM, hypertension, hyperlipidemia, CAD, CHF, anxiety,

Table 2
Risk of stroke by acupuncture treatment and covariates among patients with insomnia or sleep apnea.

Variables	Event	Person-year	IR[a]	cHR	(95 % CI)	*p*-value	aHR	(95 % CI)	*p*-value
Acupuncture									
No	4913	716129.51	6.86	1.00	(reference)	–	1.00	(reference)	–
Yes	3668	812812.81	4.51	0.64	(0.62, 0.67)[d]	<0.001	0.66	(0.63, 0.69)[d]	<0.001
Sex									
Female	4555	976406.66	4.67	1.00	(reference)	–	1.00	(reference)	–
Male	4026	552535.66	7.29	1.56	(1.49, 1.63)[d]	<0.001	1.47	(1.41, 1.53)[d]	<0.001
Age									
20-39	272	417762.90	0.65	1.00	(reference)	–	1.00	(reference)	–
40-59	1900	691994.22	2.75	4.23	(3.73, 4.8)[d]	<0.001	3.32	(2.92, 3.78)[d]	<0.001
60-79	5254	381714.90	13.76	21.50	(19.04, 24.29)[d]	<0.001	11.40	(10.1, 13.07)[d]	<0.001
≥80	1155	37470.29	30.82	52.00	(45.64, 59.46)[d]	<0.001	22.40	(19.49, 25.85)[d]	<0.001
mean, (SD)				1.08	(1.081, 1.084)[d]	<0.001	1.07	(1.064, 1.068)[d]	<0.001
Insurance amount									
0–19999 (lowest)	6380	1008083.99	6.33	1.00	(reference)	–	1.00	(reference)	–
20,000-39999	1441	355716.66	4.05	0.64	(0.61, 0.68)[d]	<0.001	0.84	(0.8, 0.89)[d]	<0.001
≥40,000 (highest)	760	165141.67	4.60	0.73	(0.67, 0.78)[d]	<0.001	0.75	(0.7, 0.81)[d]	<0.001
Urbanization									
1 (highest)	4006	798695.32	5.02	1.00	(reference)	–	1.00	(reference)	–
2	2786	442391.26	6.30	1.25	(1.19, 1.31)[d]	<0.001	1.14	(1.08, 1.19)[d]	<0.001
3	617	92349.59	6.68	1.33	(1.22, 1.44)[d]	<0.001	1.14	(1.05, 1.24)[c]	0.002
4 (lowest)	1172	195506.15	5.99	1.19	(1.11, 1.27)[d]	<0.001	1.14	(1.06, 1.21)[d]	<0.001
Comorbidities									
Diabetes mellitus	3195	243526.03	13.12	3.21	(3.07, 3.36)[d]	<0.001	1.51	(1.44, 1.58)[d]	<0.001
Hypertension	6286	517386.81	12.15	5.42	(5.16, 5.68)[d]	<0.001	1.80	(1.7, 1.91)[d]	<0.001
Hyperlipidemia	3539	428337.96	8.26	1.87	(1.79, 1.95)[d]	<0.001	0.82	(0.78, 0.86)[d]	<0.001
Coronary artery disease	3543	270885.85	13.08	3.32	(3.18, 3.46)[d]	<0.001	0.99	(0.94, 1.04)	0.629
Congestive heart failure	727	33348.89	21.80	4.32	(4, 4.66)[d]	<0.001	1.37	(1.26, 1.48)[d]	<0.001
Anxiety	3002	519296.69	5.78	1.06	(1.01, 1.11)[b]	0.012	0.81	(0.77, 0.85)[d]	<0.001
Alcoholism	322	36530.22	8.81	1.62	(1.45, 1.81)[d]	<0.001	2.02	(1.8, 2.27)[d]	<0.001
Smoking	112	25587.60	4.38	0.82	(0.68, 0.99)[b]	0.039	0.98	(0.81, 1.18)	0.821
Obesity	88	20376.97	4.32	0.80	(0.65, 0.99)[b]	0.037	0.92	(0.74, 1.13)	0.414
Depression	1358	250877.72	5.41	0.97	(0.91, 1.02)	0.254	0.97	(0.9, 1.04)	0.336
Atrial fibrillation	1855	177752.49	10.44	2.13	(2.03, 2.25)[d]	<0.001	1.03	(0.98, 1.09)	0.258
Medication									
NSIADs	7392	1286508.22	5.75	1.17	(1.1, 1.25)[d]	<0.001	0.87	(0.81, 0.93)[d]	<0.001
Oral steroid	3632	600941.79	6.04	1.16	(1.11, 1.21)[d]	<0.001	0.93	(0.89, 0.97)[c]	0.002
Statin	1682	173463.15	9.70	1.99	(1.89, 2.1)[d]	<0.001	0.91	(0.86, 0.97)[c]	0.004
BZD	7398	1140504.18	6.49	2.08	(1.96, 2.21)[d]	<0.001	1.16	(1.09, 1.24)[d]	<0.001
non-BZD	4280	656770.46	6.52	1.31	(1.26, 1.37)[d]	<0.001	1.04	(1.00, 1.09)	0.059
MAOI	120	15233.92	7.88	1.37	(1.14, 1.64)[d]	<0.001	1.16	(0.97, 1.4)	0.107
SSRI	468	103734.48	4.51	0.81	(0.74, 0.89)[d]	<0.001	0.93	(0.84, 1.03)	0.190
Tricyclic	1429	162463.99	8.80	1.70	(1.6, 1.8)[d]	<0.001	1.06	(1.00, 1.13)	0.062
Other anti-depressant drugs	1216	185296.54	6.56	1.21	(1.14, 1.28)[d]	<0.001	1.07	(1.00, 1.14)[b]	0.050
Aspirin	3939	289218.39	13.62	3.68	(3.53, 3.84)[d]	<0.001	1.24	(1.18, 1.31)[d]	<0.001
Clopidogrel	324	19887.81	16.29	3.14	(2.81, 3.51)[d]	<0.001	0.88	(0.78, 0.99)[b]	0.032
Other anticoagulants	543	26533.93	20.46	4.02	(3.68, 4.38)[d]	<0.001	1.29	(1.18, 1.42)[d]	<0.001

DM: diabetes mellitus, CAD: coronary artery disease, CHF: congestive heart failure, SD: standard deviation, PY: person-years, IR: incidence rate, CI: confidence interval, HR: hazard ratio.
$: The adjusted HR was calculated using a model that incorporated the variables of sex, age, comorbidities, and medications.
[a] Per 1000 person-year.
[b] $p < 0.05$.
[c] $p < 0.01$.
[d] $p < 0.001$.

and alcoholism derived substantial benefits from acupuncture, resulting in substantially lower adjusted hazard ratios. Additionally, acupuncture was effective in reducing the risk of stroke among patients taking NSAIDs, statins, sedative medications, and antidepressant drugs.

4.2. Interpretation

The study findings suggest a potential link between acupuncture treatment and a reduced risk of stroke in patients with insomnia, which is consistent with findings of previous research on the health benefits of acupuncture. However, it is essential to interpret these findings with caution due to the study's retrospective design and associated limitations. These limitations include the risk of selection bias, potential confounders, reliance on electronic health records, limited generalizability, a relatively short follow-up period, and the potential for residual confounding. Furthermore, causality could not be established because of the study design, and potential reporting bias may have influenced the accuracy of data. Although these findings were promising, further research, ideally prospective studies with longer follow-up periods, diverse populations, and a randomized controlled design, are warranted to confirm and expand upon these observations.

This research represented a significant contribution to the field by validating the long-term efficacy of acupuncture in reducing the risk of stroke in patients suffering from insomnia. Utilizing a large-scale matched cohort over an extended period, this study not only addressed the gap left by previous randomized controlled trials that assessed only short-term outcomes but also built upon the foundation of numerous high-quality trials to demonstrate the potential of acupuncture as a viable public health intervention for the management of insomnia and the prevention of significant diseases. The research introduced a novel perspective by examining acupuncture's role as a preventative measure against stroke among insomnia patients, thereby

Table 3
Stratified incidence rates, hazard ratios, and confidence intervals for stroke among patients with insomnia or sleep apnea who did and did not receive acupuncture.

Variables	Non-acupuncture			Acupuncture			cHR	(95 % CI)	*p* -value	aHR[b]	(95 % CI)	*p*-value	Interaction *p* -value
	Event	Person-year	IR[a]	Event	Person-year	IR[a]							
Sex													0.908
Female	2606	456462.70	5.71	1949	519943.96	3.75	0.64	(0.61, 0.68)[e]	<0.001	0.67	(0.64, 0.72)[e]	<0.001	
Male	2307	259666.81	8.88	1719	292868.85	5.87	0.65	(0.61, 0.69)[e]	<0.001	0.66	(0.62, 0.7)[e]	<0.001	
Age													<0.001
20-39	134	191074.84	0.70	138	226688.06	0.61	0.83	(0.66, 1.06)	0.130	0.81	(0.63, 1.02)	0.077	
40-59	1057	325644.01	3.25	843	366350.21	2.30	0.69	(0.63, 0.76)[e]	<0.001	0.73	(0.66, 0.79)[e]	<0.001	
60-79	3058	180830.48	16.91	2196	200884.42	10.93	0.63	(0.6, 0.67)[e]	<0.001	0.64	(0.61, 0.68)[e]	<0.001	
≥80	664	18580.18	35.74	491	18890.11	25.99	0.69	(0.61, 0.77)[e]	<0.001	0.69	(0.61, 0.78)[e]	<0.001	
Insurance amount													<0.001
0–19999 (lowest)	3715	472151.47	7.87	2665	535932.51	4.97	0.62	(0.59, 0.65)[e]	<0.001	0.65	(0.62, 0.69)[e]	<0.001	
20,000-39999	775	165270.29	4.69	666	190446.37	3.50	0.73	(0.65, 0.81)[e]	<0.001	0.71	(0.64, 0.79)[e]	<0.001	
≥40,000 (highest)	423	78707.74	5.37	337	86433.93	3.90	0.71	(0.62, 0.82)[e]	<0.001	0.68	(0.59, 0.78)[e]	<0.001	
Urbanization													<0.001
1 (highest)	2229	372759.92	5.98	1777	425935.40	4.17	0.68	(0.64, 0.73)[e]	<0.001	0.68	(0.63, 0.72)[e]	<0.001	
2	1648	206717.41	7.97	1138	235673.86	4.83	0.59	(0.55, 0.64)[e]	<0.001	0.62	(0.57, 0.67)[e]	<0.001	
3	373	43007.25	8.67	244	49342.33	4.95	0.56	(0.47, 0.65)[e]	<0.001	0.66	(0.56, 0.78)[e]	<0.001	
4 (lowest)	663	93644.93	7.08	509	101861.22	5.00	0.70	(0.62, 0.78)[e]	<0.001	0.72	(0.64, 0.81)[e]	<0.001	
Comorbidities													
Diabetes mellitus	1839	114627.69	16.04	1356	128898.34	10.52	0.64	(0.6, 0.69)[e]	<0.001	0.63	(0.59, 0.68)[e]	<0.001	0.749
Hypertension	3585	245987.54	14.57	2701	271399.27	9.95	0.67	(0.64, 0.7)[e]	<0.001	0.67	(0.64, 0.7)[e]	<0.001	0.114
Hyperlipidemia	1908	206343.42	9.25	1631	221994.54	7.35	0.78	(0.73, 0.83)[e]	<0.001	0.74	(0.69, 0.79)[e]	<0.001	<0.001
Coronary artery disease	1993	128589.15	15.50	1550	142296.70	10.89	0.69	(0.64, 0.74)[e]	<0.001	0.68	(0.64, 0.73)[e]	<0.001	0.025
Congestive heart failure	412	15247.48	27.02	315	18101.42	17.40	0.62	(0.54, 0.72)[e]	<0.001	0.64	(0.55, 0.74)[e]	<0.001	0.499
Anxiety	1642	246356.75	6.67	1360	272939.94	4.98	0.73	(0.68, 0.79)[e]	<0.001	0.71	(0.66, 0.77)[e]	<0.001	<0.001
Alcoholism	184	16348.54	11.25	138	20181.68	6.84	0.58	(0.47, 0.73)[e]	<0.001	0.62	(0.5, 0.78)[e]	<0.001	0.352
Smoking	59	11555.65	5.11	53	14031.95	3.78	0.70	(0.48, 1.02)	0.061	0.69	(0.47, 1.00)	0.050	0.565
Obesity	52	9381.91	5.54	36	10995.07	3.27	0.57	(0.37, 0.87)[d]	0.009	0.58	(0.38, 0.89)[c]	0.013	0.578
Depression	754	117420.18	6.42	604	133457.55	4.53	0.69	(0.62, 0.77)[e]	<0.001	0.68	(0.61, 0.76)[e]	<0.001	0.174
Atrial fibrillation	1016	84224.14	12.06	839	93528.35	8.97	0.73	(0.67, 0.8)[e]	<0.001	0.72	(0.65, 0.79)[e]	<0.001	0.004
Medication													
NSIADs	4189	603836.66	6.94	3203	682671.56	4.69	0.66	(0.63, 0.69)[e]	<0.001	0.67	(0.64, 0.7)[e]	<0.001	0.001
Oral steroid	2055	286319.59	7.18	1577	314622.21	5.01	0.69	(0.64, 0.73)[e]	<0.001	0.68	(0.64, 0.73)[e]	<0.001	0.013
Statin	901	84827.47	10.62	781	88635.68	8.81	0.82	(0.74, 0.9)[e]	<0.001	0.76	(0.69, 0.84)[e]	<0.001	<0.001
BZD	4279	537849.83	7.96	3119	602654.35	5.18	0.64	(0.61, 0.67)[e]	<0.001	0.66	(0.63, 0.69)[e]	<0.001	0.078
non-BZD	2413	310901.23	7.76	1867	345869.22	5.40	0.69	(0.65, 0.73)[e]	<0.001	0.68	(0.64, 0.72)[e]	<0.001	0.010
MAOI	72	7240.39	9.94	48	7993.53	6.00	0.60	(0.42, 0.87)[d]	0.007	0.68	(0.46, 0.98)[c]	0.041	0.649
SSRI	244	48573.39	5.02	224	55161.09	4.06	0.79	(0.66, 0.95)[c]	0.013	0.78	(0.65, 0.93)[d]	0.006	0.020
Tricyclic	784	78671.94	9.97	645	83792.05	7.70	0.76	(0.69, 0.85)[e]	<0.001	0.73	(0.66, 0.82)[e]	<0.001	<0.001
Other anti-depressant drugs	698	87717.59	7.96	518	97578.95	5.31	0.66	(0.59, 0.74)[e]	<0.001	0.65	(0.58, 0.73)[e]	<0.001	0.753

(*continued on next page*)

Table 3 (*continued*)

Variables	Non-acupuncture			Acupuncture			cHR	(95 % CI)	*p* -value	aHR[b]	(95 % CI)	*p*-value	Interaction *p* -value
	Event	Person-year	IR[a]	Event	Person-year	IR[a]							
Aspirin	2262	138856.48	16.29	1677	150361.91	11.15	0.67	(0.63, 0.72)[e]	<0.001	0.67	(0.63, 0.72)[e]	<0.001	0.277
Clopidogrel	176	9721.18	18.10	148	10166.63	14.56	0.79	(0.63, 0.98)[c]	0.033	0.76	(0.61, 0.94)[c]	0.013	0.073
Other anticoagulants	305	12641.38	24.13	238	13892.54	17.13	0.69	(0.58, 0.82)[e]	<0.001	0.67	(0.57, 0.8)[e]	<0.001	0.437

DM: diabetes mellitus, CAD: coronary artery disease, CHF: congestive heart failure, SD: standard deviation, PY: person-years, IR: incidence rate, CI: confidence interval, HR: hazard ratio.

[a] Per 1000 person-year.

[b] The adjusted HR was calculated using a model that incorporated the variables of sex, age, comorbidities, and medications.

[c] $p < 0.05$.

[d] $p < 0.01$.

[e] $p < 0.001$.

Table 4

Incidence rates, hazard ratios and confidence intervals for ischemic and hemorrhage stroke.

Outcomes	Non-acupuncture			Acupuncture			cHR	(95 % CI)	p-value	aHR[b]	(95 % CI)	p-value
	Event	Person-years	IR[a]	Event	Person-years	IR[a]						
Ischemic stroke	3038	720448.01	4.21682	2484	816572.59	3.04198	0.71	(0.67, 0.74)[c]	<0.001	0.73	(0.69, 0.77)[c]	<0.001
Hemorrhagic stroke	992	728423.44	1.36185	767	824024.08	0.9308	0.67	(0.61, 0.73)[c]	<0.001	0.69	(0.62, 0.75)[c]	<0.001
Other	1103	727300.68	1.51657	712	823489.72	0.86461	0.56	(0.51, 0.61)[c]	<0.001	0.58	(0.53, 0.64)[c]	<0.001

IR: incidence rate, CI: confidence interval, HR: hazard ratio.

*$p < 0.05$, **$p < 0.01$.

[a] Per 1000 person-year.

[b] The adjusted HR was calculated using a model that incorporated the variables of sex, age, comorbidities, and medications.

[c] $p < 0.001$.

Table 5

Risk of stroke and number of acupuncture in patients with insomnia or sleep apnea.

Number of acupuncture	N	Event	PY	IR[a]	cHR	(95 % CI)	p-value	aHR[b]	(95 % CI)	p-value
0	108,678	4913	716129.51	6.86	1.00	(reference)	–	1.00	(reference)	–
6–11	34,507	1126	231984.74	4.85	0.71	(0.66, 0.76)[c]	<0.001	0.76	(0.71, 0.81)[c]	<0.001
12–17	18,503	608	133123.07	4.57	0.66	(0.6, 0.72)[c]	<0.001	0.69	(0.63, 0.75)[c]	<0.001
18–29	19,577	641	147375.21	4.35	0.62	(0.57, 0.67)[c]	<0.001	0.66	(0.61, 0.72)[c]	<0.001
≥30	36,091	1293	300329.79	4.31	0.60	(0.57, 0.64)[c]	<0.001	0.58	(0.55, 0.62)[c]	<0.001

IR: incidence rate, CI: confidence interval, HR: hazard ratio.

*$p < 0.05$, **$p < 0.01$.

[a] Per 1000 person-year.

[b] The adjusted HR was calculated using a model that incorporated the variables of sex, age, comorbidities, and medications.

[c] $p < 0.001$.

highlighting the therapeutic promise of acupuncture in the treatment of insomnia and its prospective utility in staving off stroke in affected individuals.

The study introduced several novel elements in comparison to the preceding study "Acupuncture is associated with reduced dementia risk in patients with insomnia: A propensity-score-matched cohort study of real-world data", which focused on acupuncture and dementia risk. The presented study shifted the research emphasis towards examining the efficacy of acupuncture in mitigating stroke risk among patients with insomnia, employing an expanded dataset from the years 2000–2017 and encompassing a larger sample size of 218,084 patients. The study distinctively investigated the dose-response relationship, elucidating how varying frequencies of acupuncture sessions correlated with reductions in stroke risk. Contrary to the prior study, this manuscript positioned acupuncture not merely as a therapeutic option for insomnia but also as a potential nonpharmacological preventive strategy against stroke, underscoring its wider implications for public health.

The therapeutic benefits of acupuncture across various comorbid conditions with insomnia demonstrate its versatility and efficacy in enhancing patient outcomes. In hypertensive patients with insomnia, acupuncture significantly outperformed controls in improving sleep quality, as evidenced by marked reductions in the PSQI scores. Furthermore, acupuncture showed notable benefits in lowering both systolic and diastolic blood pressure, suggesting its dual therapeutic effect on sleep disturbances and hypertension.[10]

For patients living with advanced cancer, acupuncture was explored as a means to alleviate pain and, by extension, improve associated conditions like fatigue and insomnia. The acupuncture was effective in enhancing overall quality of life and mitigating insomnia, with minimal adverse events reported.[11] Additional analysis in cancer-related insomnia highlighted acupuncture and moxibustion (including transcutaneous electrical acupoint stimulation) as superior to Western medicine and placebo in improving sleep, showcasing acupuncture's potential in this demographic.[12,13] Among hemodialysis patients, auricular acupressure was found to be effective in improving sleep quality and reducing hypnotic dependency, offering a safe and adherent complementary therapy for insomnia.[14] In isolated COVID-19 patients, auricular point pressure significantly improved sleep and reduced

anxiety, demonstrating its utility in managing insomnia and psychological distress under quarantine conditions without notable safety concerns.[15]

For post-stroke patients, acupuncture showed substantial efficacy in improving sleep quality, efficiency, and duration, suggesting its beneficial role in post-stroke insomnia rehabilitation. The long-term effectiveness and safety of acupuncture in this group, however, require further investigation.[16] Finally, in the context of perimenopausal depression and insomnia, acupuncture facilitated significant improvements in sleep quality and was well-tolerated by participants, indicating its promise as a therapeutic modality for managing these comorbid conditions.[17] Overall, these studies collectively affirm acupuncture's potential as a multifaceted treatment option for insomnia, particularly in the presence of comorbid conditions, offering a viable, effective, and safe alternative to conventional therapies.

Studies have investigated the efficacy of acupuncture for poststroke insomnia[18] and enhancing sleep quality,[16] several notable findings from this study indicate acupuncture's therapeutic value for managing insomnia and its potential preventive role against stroke. In a comprehensive systematic review and meta-analysis, Lee and Lim (2016) revealed that acupuncture surpassed pharmaceutical interventions in ameliorating insomnia symptoms.[18] Moreover, Cao et al. (2022) conducted a rigorously blinded randomized controlled trial and reported verum acupuncture resulted in substantial improvements in sleep quality compared with sham acupuncture.[19] Shi et al. (2023) conducted an extensive systematic review and meta-analysis involving a substantial number of participants, and their findings aligned with the notion that acupuncture outperformed the strategies in control groups for enhancing various sleep parameters.[16] Additionally, Zhao et al. (2022) investigated a specific acupuncture technique, demonstrating its ability to improve morning blood pressure and enhance sleep quality.[20]

Recent studies have explored various acupuncture and acupoint stimulation techniques for their efficacy in treating primary insomnia, yielding valuable insights into their comparative effectiveness and potential as therapeutic options.

A comprehensive systematic review and network meta-analysis by Lu et al. (2022) evaluated the comparative effectiveness of multiple acupuncture therapies in treating primary insomnia. This analysis, which included 57 randomized controlled trials and 4678 patients, found that several acupuncture therapies significantly improved the PSQI scores compared to usual treatments. Specifically, acupoints catgut embedding emerged as the most effective therapy, with moderate certainty of evidence. Other therapies such as auricular acupressure or auricular acupuncture plus manual acupuncture, electroacupuncture plus acupoint application, and intradermal needle were also among the most effective.[21] Wang et al. (2023) conducted a systematic review and meta-analysis on Traditional Chinese tuina therapy for insomnia, incorporating eighteen studies with 1471 patients. This analysis revealed that tuina alone, or in combination with other treatments like acupuncture or auricular acupuncture, showed superior efficacy in improving PSQI scores and overall treatment effectiveness compared to other treatments or therapies alone.[22] Luo et al. (2022) focused on the combination of acupuncture and tuina for treating insomnia, analyzing 29 studies with 2688 cases. This combination proved more effective in improving total clinical effectiveness, PSQI scores, and Statistical Self-Rating Anxiety Scale scores than either drugs or acupuncture alone, offering a compelling case for integrated treatment approaches in managing insomnia.[23] Garland et al. (2019) compared acupuncture with cognitive behavioral therapy for insomnia (CBT-I) in cancer survivors, finding that while CBT-I was more effective immediately post-treatment, both acupuncture and CBT-I yielded clinically meaningful reductions in insomnia severity and maintained these improvements up to 20 weeks. Interestingly, acupuncture was found to be more effective for pain management at the end of the treatment period.[24] Bergdahl et al. (2016) compared auricular acupuncture with CBT-I, demonstrating that while both treatments led to significant within-group improvements in insomnia severity, CBT-I showed more pronounced between-group improvements immediately after treatment and at the 6-month follow-up. This study suggested that although auricular acupuncture may alleviate some symptoms of insomnia, CBT-I might offer a more effective standalone treatment for insomnia disorder.[25] Together, these studies underscore the potential of acupuncture and acupoint stimulation techniques as effective treatments for insomnia, with varying levels of evidence supporting their efficacy alone or in combination with other therapies.

In the realm of traditional Chinese medicine, acupuncture has been reputed as a beneficial intervention for various ailments, including insomnia, which is a common precursor to more severe conditions such as stroke. Recent studies have elaborated on the efficacy and mechanisms behind acupuncture's role in mitigating insomnia and potentially reducing stroke risk.

A randomized controlled trial by Yin et al. (2017) substantiated that acupuncture significantly enhances sleep quality in individuals suffering from primary insomnia. This study detailed how acupuncture outperformed sham treatments, markedly improving scores on the Insomnia Severity Index, sleep efficiency, total sleep time, and even psychological health as measured by depression scales. The results suggested not only improvements in sleep metrics post-treatment but also sustained enhancements during the follow-up period, highlighting the potential of acupuncture as a long-term remedy for insomnia.[5]

Further elucidating the biological underpinnings, a study by Huang et al. (2023) on Ziwuliuzhu acupuncture—a specific rhythmic pattern of acupuncture—revealed its effects at the molecular level in insomnia-affected rats. This research pointed out significant increases in the expression of Clock and Bmal1 mRNAs and elevated melatonin levels in the hypothalamus, implying that acupuncture might modulate key elements of the circadian rhythm, which is crucial for maintaining sleep-wake cycles and overall neurological health.[26]

Additionally, Wu and Zhao (2024) explored the broader implications of acupuncture on circadian rhythm sleep-wake disorders (CRSWDs), emphasizing its neurochemical mechanisms. Their review suggested that acupuncture might influence central and peripheral biological clocks, offering a non-pharmacological option to recalibrate disrupted biological rhythms associated, thereby improving sleep and reducing related health risks such as stroke.[27]

The paradoxical relationship between factors like hyperlipidemia, anxiety, smoking, obesity, and decreased stroke risk may reflect multifaceted dynamics, including health behavior changes post-diagnosis, therapeutic effects of condition-specific medications, and selection bias inherent to the insomnia-affected study cohort. Such dynamics hint at underlying complexities in stroke risk modulation, possibly obscured by statistical variances or uncontrolled confounders. The influence of healthcare accessibility, particularly in more urban settings, might further skew risk assessments. This complexity necessitates advanced investigations to disentangle and understand the intricate web of interactions influencing stroke risk, highlighting the importance of nuanced research methodologies to elucidate these unexpected findings.

In the analysis of stroke risk among patients with insomnia or sleep apnea, the identification of atrial fibrillation (AF) as a significant risk factor was a crucial finding. The crude hazard ratio of 2.13 (95 % CI: 2.03–2.25) suggested a strong initial association between AF and increased stroke risk. However, the marked reduction in the adjusted HR to 1.03 (95 % CI: 0.98–1.09) upon controlling for anticoagulant therapy and other treatments warranted a nuanced interpretation.

The substantial difference between the crude and adjusted HR indicated that anticoagulant treatment was likely a significant mediator in the relationship between AF and stroke risk.[28] Anticoagulants are well-documented for their efficacy in reducing the risk of stroke in patients with AF by preventing clot formation.[29] This suggested that once appropriate anticoagulation was instituted, the intrinsic risk attributed solely to AF diminished substantially.

The reduced stroke risks associated with Clopidogrel, as reflected by

an adjusted hazard ratio (aHR) of 0.88 (95 % CI: 0.78–0.99), indicated a certain degree of protection. However, the increased risks associated with Aspirin and other anticoagulants, as evidenced by the adjusted hazard ratios of 1.24 (95 % CI: 1.18–1.31) for Aspirin and 1.29 (95 % CI: 1.18–1.42) for other anticoagulants, could be partly explained by potential confounding factors. Patients prescribed these anticoagulants often had underlying conditions such as atrial fibrillation or coronary artery disease, which were risk factors for stroke in themselves.

This observation was inconsistent with the results of past clinical trials,[30] possibly because the higher hazard ratios observed might reflect the baseline risk profile of these patients rather than a direct causal effect of the anticoagulants increasing stroke risk. Essentially, these patients might have already been at higher risk for strokes due to their underlying conditions, and the requirement for anticoagulant therapy was a marker of this increased risk rather than a cause.

Furthermore, the effectiveness of these medications in stroke prevention could vary based on a range of factors including patient adherence to medication, dosing, and individual patient response, which might also influence the observed hazard ratios. It was crucial in such analyses to ensure that these confounding factors were adequately controlled for to derive a more accurate estimate of the true effect of anticoagulants on stroke risk.

The association between benzodiazepine use and an increased stroke risk among individuals suffering from insomnia has previously been explored in previous studies. The study by Wei-Shih Huang et al. examined the link between benzodiazepine use and stroke risk using Taiwan's National Health Insurance data from 2000 to 2003. This cohort study included 38,671 new benzodiazepine users and an equal number of matched non-users, focusing on their stroke outcomes through 2009. The findings revealed that benzodiazepine use was associated with a reduced risk of hemorrhagic stroke, but an increased risk of ischemic stroke in younger adults aged 20–39 years. Moreover, lower doses and shorter durations of benzodiazepine use correlated with reduced stroke risk in older adults, while higher doses and longer durations increased stroke risk across all age groups. This study suggests that while low-dose, short-term benzodiazepine use might offer some neuroprotective effects, high-dose, prolonged use may increase stroke risk, indicating a need for cautious prescribing.[31]

In addition to the acupuncture discussed in our paper, changing lifestyle habits also emerged as a crucial method for reducing the risk of stroke. Hu et al.[32,33] emphasized the importance of the SEED intervention (sleep, emotion, exercise, diet), which was expanded in E(e)SEEDi to include environmental factors, forming a comprehensive approach to health management. This method aligned well with the principles of acupuncture and traditional Chinese medicine, which emphasize holistic treatment and prevention strategies. By integrating the E(e)SEEDi framework, which incorporates environmental supplementation and Hu's healthy lifestyles intervention, our discussion was broadened to include a multi-faceted approach to reducing the risk of stroke. These strategies were pivotal for the early evaluation of risk factors and proved critical in the prevention and management of human non-communicable diseases. These approaches addressed complex interactions such as the obesity and hypertension, which were particularly relevant in halting the progression of cardiovascular diseases, diabetes, and cancer.

4.3. Generalizability

The generalizability of the study results was constrained by several key factors related to the study population. First, the study exclusively focused on a population residing in Taiwan, predominantly consisting of Han Chinese and Indigenous peoples. Consequently, caution should be exercised when applying these findings to ethnically and culturally diverse populations, especially those in Western countries. Second, the study primarily included individuals aged 40–79 years, with 44 % and 26 % in the 40–59- and 60–79-years age groups, respectively. Consequently, the study outcomes may not be directly applicable to younger or older age groups. Third, the study population had a notably high prevalence of comorbidities and chronic illnesses, with a prevalence of more than 30 % for conditions such as hypertension, hyperlipidemia, and anxiety. Therefore, the study results may be more relevant to individuals with pre-existing chronic conditions and may have limited applicability to generally healthy populations. Lastly, the study primarily focused on patients with insomnia who were already receiving treatment, which may have made the findings less relevant to individuals with milder insomnia, who may only require lifestyle adjustments. In summary, the external validity of the study findings was limited, and caution should be exercised when attempting to extrapolate the findings to populations beyond the study population with specific demographic and clinical characteristics.

Distinguishing the effects of treating insomnia from those of acupuncture on stroke prevention using the National Health Insurance Research Database (NHIRD) presents challenges due to the database's limitations. The NHIRD primarily captures administrative data, lacking detailed clinical metrics such as the severity of insomnia and specific patient-reported outcomes, which are essential for accurately assessing the effects of any intervention. Additionally, the inherent non-randomized nature of the treatment assignments in NHIRD data leads to potential confounding by indication and selection bias. These biases occur because patients who undergo acupuncture may differ significantly in unmeasured ways from those who do not, influencing both their risk of receiving treatment and their subsequent risk of stroke.

Nevertheless, it is important to acknowledge the strengths of the study that contributed to its overall value. The study provided valuable insights into the relationship between acupuncture, insomnia, and stroke risk, exploring a novel research topic. Its comprehensiveness, characterized by a large sample size (over 200,000 matched patients with insomnia) and an extended follow-up period of 18 years, enhanced the robustness of its findings.

4.4. Limitations

This study faced several limitations that impacted its findings. The retrospective design introduced the possibility of selection bias and unidentified confounders. Reliance on electronic health records and claims data might have resulted in coding inaccuracies and data quality issues, potentially skewing results. The study's findings might have had limited applicability outside the study region or to diverse populations. The 18-year follow-up may not have adequately captured long-term effects of acupuncture on insomnia and stroke risk, and variations in acupuncture delivery could have introduced further confounding. Additionally, the observational nature of the study prevented establishing causality between observed associations, and loss to follow-up could have introduced bias. A critical limitation stemmed from using the NHIRD, which lacked detailed insomnia symptom descriptions and quantifiable metrics like the PSQI scores. This gap prevented a nuanced analysis of acupuncture's impact on different insomnia types and severities. Furthermore, the dataset did not include specific details about acupuncture treatment, such as needle locations, acupoint selections, and methods, limiting the depth of treatment analysis. These limitations suggested caution in interpreting the study's results.

5. Conclusions

This study demonstrated a significant association between acupuncture treatment and a reduced risk of stroke among individuals with insomnia. The presence of a clear dose–response relationship suggests that more frequent acupuncture sessions are associated with a lower risk of stroke. Given these findings, acupuncture may offer a valuable nonpharmacological preventive strategy against stroke for individuals with insomnia.

Ethics statement

The NHIRD encrypts patient personal information to protect privacy and provides researchers with anonymous identification numbers associated with relevant claims information, including sex, date of birth, medical services received, and prescriptions. Therefore, patient consent is not required to access the NHIRD. The Research Ethics Committee of China Medical University and Hospital, Taiwan, has approved the study [CMUH110-REC1-038(CR-2)].

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Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Sawadogo W, Adera T, Alattar M, Perera R, Burch JB. Association between insomnia symptoms and trajectory with the risk of stroke in the health and retirement study. *Neurology*. 2023;101(5):e475–e488.
2. Chen Y, Kartsonaki C, Clarke R, et al. Sleep duration and risk of stroke and coronary heart disease: a 9-year community-based prospective study of 0.5 million Chinese adults. *BMC Neurol*. 2023;23(1):327.
3. Zhao FY, Fu QQ, Kennedy GA, et al. Can acupuncture improve objective sleep indices in patients with primary insomnia? A systematic review and meta-analysis. *Sleep Med*. 2021;80:244–259.
4. Zhang L, Tang Y, Hui R, et al. The effects of active acupuncture and placebo acupuncture on insomnia patients: a randomized controlled trial. *Psychol Health Med*. 2020;25(10):1201–1215.
5. Yin X, Gou M, Xu J, et al. Efficacy and safety of acupuncture treatment on primary insomnia: a randomized controlled trial. *Sleep Med*. 2017;37:193–200.
6. Howard G, Banach M, Kissela B, et al. Age-related differences in the role of risk factors for ischemic stroke. *Neurology*. 2023;100(14):e1444–e1453.
7. Purohit R, Wang S, Dusane S, Bhatt T. Age-related differences in reactive balance control and fall-risk in people with chronic stroke. *Gait Posture*. 2023;102:186–192.
8. Lin CL, Chern A, Wang MJ, Lin SK. Incidence of nerve injury following acupuncture treatments in Taiwan. *Compl Ther Med*. 2024;80, 103007.
9. Hsieh HT, Chou HJ, Wu PY, Lin SK. Bleeding risk after acupuncture in patients taking anticoagulant drugs: a case control study based on real-world data. *Compl Ther Med*. 2023;74, 102951.
10. Zhang J, Zhou X, Jiang H, et al. Acupuncture for insomnia symptoms in hypertensive patients: a systematic review and meta-analysis. *Front Neurol*. 2024;15, 1329132.
11. Epstein AS, Liou KT, Romero SAD, et al. Acupuncture vs massage for pain in patients living with advanced cancer: the IMPACT randomized clinical trial. *JAMA Netw Open*. 2023;6(11), e2342482.
12. Ou Y, Lin D, Ni X, et al. Acupuncture and moxibustion in patients with cancer-related insomnia: a systematic review and network meta-analysis. *Front Psychiatr*. 2023;14, 1108686.
13. Wan Q, Luo S, Wang X, et al. Association of acupuncture and auricular acupressure with the improvement of sleep disturbances in cancer survivors: a systematic review and meta-analysis. *Front Oncol*. 2022;12, 856093.
14. Wu Y, Yang L, Zhong Z, et al. Auricular acupressure for hemodialysis patients with insomnia: a multicenter double-blind randomized sham-controlled trial. *J Integr Complement Med*. 2022;28(4):339–348.
15. Luo Y, Ling C, Liu Y, et al. The beneficial role of auricular point pressure in insomnia and anxiety in isolated COVID-19 patients. *Evid Based Complement Alternat Med*. 2021;2021, 6611942.
16. Shi M, Ji Z, Sun T, et al. Efficacy and safety of acupuncture on sleep quality for post-stroke insomnia: a systematic review and meta-analysis. *Front Neurol*. 2023;14, 1164604.
17. Zhao FY, Zheng Z, Fu QQ, et al. Acupuncture for comorbid depression and insomnia in perimenopause: a feasibility patient-assessor-blinded, randomized, and sham-controlled clinical trial. *Front Public Health*. 2023;11, 1120567.
18. Lee SH, Lim SM. Acupuncture for insomnia after stroke: a systematic review and meta-analysis. *BMC Compl Alternative Med*. 2016;16:228.
19. Cao Y, Yan YJ, Xu JY, et al. Acupuncture for insomnia after ischemic stroke: an assessor-participant blinded, randomized controlled trial. *Acupunct Med*. 2022;40 (5):443–452.
20. Zhao Q, Wang CT, Cao CC. [Effect of Tiaoshen Qianyang acupuncture on blood pressure and sleep quality in patients with stroke-related sleep disorders complicated with hypertension]. *Zhongguo Zhen Jiu*. 2022;42(2):126–130.
21. Lu Y, Zhu H, Wang Q, et al. Comparative effectiveness of multiple acupuncture therapies for primary insomnia: a systematic review and network meta-analysis of randomized trial. *Sleep Med*. 2022;93:39–48.
22. Wang Z, Xu H, Zhou H, et al. A systematic review with meta-analysis: traditional Chinese tuina therapy for insomnia. *Front Neurosci*. 2022;16, 1096003.
23. Luo SW, Huang NP, Xiang Q, et al. A systematic review and meta-analysis of acupuncture combined with Tuina in the treatment of insomnia. *Medicine (Baltim)*. 2022;101(51), e30703.
24. Garland SN, Xie SX, DuHamel K, et al. Acupuncture versus cognitive behavioral therapy for insomnia in cancer survivors: a randomized clinical trial. *J Natl Cancer Inst*. 2019;111(12):1323–1331.
25. Bergdahl L, Broman JE, Berman AH, Haglund K, von Knorring L, Markström A. Auricular acupuncture and cognitive behavioural therapy for insomnia: a randomised controlled study. *Sleep Disord*. 2016;2016, 7057282.
26. Huang A, Xiao G, Chen Y, et al. Ziwuliuzhu acupuncture modulates clock mRNA, Bmal1 mRNA and melatonin in insomnia rats. *J Acupunct Meridian Stud*. 2023;16(3): 109–118.
27. Wu J, Zhao Z. Acupuncture in circadian rhythm sleep-wake disorders and its potential neurochemical mechanisms. *Front Neurosci*. 2024;18, 1346635.
28. Bang OY, On YK, Lee MY, et al. The risk of stroke/systemic embolism and major bleeding in Asian patients with non-valvular atrial fibrillation treated with non-vitamin K oral anticoagulants compared to warfarin: results from a real-world data analysis. *PLoS One*. 2020;15(11), e0242922.
29. Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365(10):883–891.
30. Benz AP, Hohnloser SH, Eikelboom JW, et al. Outcomes of patients with atrial fibrillation and ischemic stroke while on oral anticoagulation. *Eur Heart J*. 2023;44 (20):1807–1814.
31. Huang WS, Muo CH, Chang SN, Chang YJ, Tsai CH, Kao CH. Benzodiazepine use and risk of stroke: a retrospective population-based cohort study. *Psychiatr Clin Neurosci*. 2014;68(4):255–262.
32. Hu CS, Tkebuchava T. SEEDi(1.0-3.0) strategies for major noncommunicable diseases in China. *J Integr Med*. 2017;15(4):265–269.
33. Hu CS, Wu QH, Hu DY, Tkebuchava T. Novel strategies halt cardiovascular, diabetes, and cancer strips. *Chronic Dis Transl Med*. 2017;3(3):159–164.