# Identifying Chinese Medicine patterns of Tension-type Headache (TTH) and its implication on understanding TTH subgroups

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# Abstract

Background Acupuncture is commonly used to relieve tension-type of headache (TTH), however, there is a lack of consistent approach of devising acupuncture interventions for TTH due to limited evidence for symptom patterns according to Chinese medicine. This study aimed to identity common Chinese medicine symptom patterns of TTH.

Methods We applied a validated Chinese Medicine Headache Questionnaire to a group of headache sufferers. The questionnaire consisted of information about headache, aggravating and relieving factors and accompanying symptoms. The Migraine Disability Assessment Test (MIDAS) was used to assess disability and the Perceived Stress Scale (PSS) for the level of stress. Information about comorbidities was collected. The modified International Headache Society TTH diagnostic criteria (ICHD-II) were used to screen the participants. Principal component analysis was used for factor extraction and Two-Step cluster analyses for clustering. One-way analysis of variance (ANOVA) was used to compare cluster groups in disability and stress.

Results In total 170 participants, including 114 females and 56 males, met the selection criteria. The commonest headache features were continuous pain (64%) and fixed location (74%). Headache was aggravated by overwork (74%), stress (74%), and mental strain (70%) and relieved by sleeping (78%). The commonest accompanied symptoms were fatigue (71%) and neck stiffness (70%). Four clusters were identified with 46, 34, 46 and 44 participants in Clusters 1-4, respectively. Assessed by experts, the four clusters could be assigned to three different patterns, including Ascendant hyperactivity of Liver-Yang (Cluster 1), Dual Qi and Blood deficiency (Cluster 2), Liver depression forming Fire (Cluster 3), and an Un-labelled group (Cluster 4). The four clusters differed in their key signs and symptoms. Additionally, over 75% participants in clusters 1 and 2 were episodic TTH, over one third in Cluster 3 having chronic TTH, and the majority in Cluster 4 were in-frequent TTH. The three patterns identified also differed in levels of disability and some elements of coping as measured with PSS.

Conclusion The three symptom patterns identified are common clinical presentations of TTH. The new information will contribute to further understanding of the subtypes of TTH and guide the development of targeted interventions, including acupuncture, for clinical practice and research.


# Background

Tension-type Headache (TTH) is the second most prevalent chronic disorders in the world[1]. It is a significant cause of distress and disruption to life [2], resulting in marked reductions in quality of life and engagement in social and family activities [3]. However, the treatment strategies for TTH remain unspecific as the mechanisms underlying this prevalent disorder are unknown [2–4]. Chinese medicine (CM) has a long history of treating headaches. Acupuncture, a key treatment modality of CM, is recommended as a prophylactic treatment for chronic TTH [5]. Since TTH is not a standardised disorder in CM, recognition and treatment of such a disorder in clinical practice have to be based on the CM classification of general headache. In CM, each health condition is sub-divided into a few common patterns or syndromes based on signs and symptoms. Those patterns are important as they guide the selection of the supposed optimal acupuncture protocol.

Identifying CM patterns involves a complicated process of synthesising and analysing clinical symptoms and signs of the patient's condition to determine the location, cause and nature of the condition [6]. Diagnosis of TTH largely relies on textbook information or expert opinion, and is not based on research evidence. Consequently, variations in the diagnosis of TTH among practitioners is common [7]. Such variations would hinder advancement in research and clinical practice. Nevertheless, studies have shown that it is possible to standardise and validate patterns using objective methods and evidence-based approaches [8–14]. Cluster analysis, a multivariate statistical method is commonly used to identify homogeneous subgroups and has been recognised as a suitable technique for identifying CM patterns of diseases [15–17].

The aims of this study were to: 1) explore CM patterns of TTH based on data collected using a validated Chinese Medicine Headache Questionnaire (CMHQ); and, (2) to explore if identified CM patterns differed on information collected in modern TTH headache research, including headache features, severity of headache-related disability assessed with Migraine Disability Assessment Test (MIDAS) and number of comorbidities, psychological profiles, such as anxiety, depression and self-perceived level of stress.

## Methods

## Study design

A bilingual cross-sectional survey was conducted from February 2011 to June 2012. To obtain a broad sample of the headache population, a paper-based survey and an online survey were delivered in parallel. The online survey, which was anonymous and general population-based, was performed via the SurveyMonkey® platform (www.surveymonkey.com). The paper-based survey involved a collaborative multi-site investigation. The questionnaires were administrated at three sites: Melbourne, Beijing and Chengdu. The survey conducted in Melbourne was nested in a clinical trial, which carried out at RMIT University Bundoora campus, Australia. The two Chinese sites were the Acupuncture and Moxibustion Department, Beijing Hospital of Traditional Chinese Medicine (TCM) Affiliated to Capital Medical University, and Affiliated Hospital of Chengdu University of TCM.

## Ethics

The survey protocol was reviewed and assessed by the relevant ethics departments. In Melbourne site, the online approach and the paper-based investigation obtained approval from the College Human Ethics Advisory Network (CHEAN) of the College of Science Engineering and Health, RMIT University. The other two collaboration sites of Beijing and Chengdu were granted permission by the Department of Science Research, of the Beijing TCM Hospital, and for the Chengdu site, by the Department of Science and Technology, Chengdu University of TCM respectively.

# Recruiting and inclusion criteria

Potential headache sufferers aged from 18 to 65 years old were eligible to participate if they: were able to read English or Chinese; met the ICHD-II criteria of TTH or probable TTH [18]; and, had one day or more of TTH attacks per month for at least one year. The modified International Headache Society TTH diagnostic criteria (ICHD-II) were used to screen the participants. Exclusion criteria were: TTH onset after 50 years old; had more than 4 migraine attacks without aura (ICHD-II 1.1 migraine) per month; had any migraine attack with aura (ICHD-II 1.2) per month; had been hospitalised because of the head or neck injury; or, had migraine attacks which were not able to be distinguished from TTH.

# Measurements

Demographic characteristics of the participants collected from this survey included gender, age, ethnicity, marital status and education. Each of the listed instruments included in the survey was available in two language versions, i.e., the English version of CMHQ (Appendix 1) was used at the Melbourne site whereas the Mandarin version (Appendix 2) was used at the Chinese sites. As to the online survey, both language versions were available.

Chinese Medicine Headache Questionnaire (CMHQ). The CMHQ is used to assist CM pattern identification for headache disorders and found to be reliable and valid in capturing essential clinical indicators for making a CM diagnosis [19]. It is a symptom-based data collection tool consisting of a total 193 items which are grouped into three broad categories of pain description, aggravating and relieving factors, and accompanying symptoms. Responses to each item presented were on a 5-point Likert scale rating from 0 to 4 indicating never, seldom, sometimes, often and almost always.

Migraine Disability Assessment (MIDAS) Questionnaire. The MIDAS was initially designed for the migraine population to evaluate the severity of migraine. Studies have shown it is also valid and reliable in evaluating disability associated with TTH [20–25].

Perceived Stress Scale (PSS). The PSS is a widely used instrument in measuring nonspecific psychological stress. Its 10-item version is among the most widely used tool to measure global perceived stress in relation to the health-related outcomes. Those questions were designed to tap how unpredictable, uncontrollable and overloaded respondents find their lives [26, 27].

Comorbidity checklist. A comorbidity checklist was used to assess both somatic and mental comorbidity of TTH. Development of the checklist was based on the Cumulative Illness Rating Scale (CIRS) [28] and the World Mental Health Composite International Diagnostic Interview (WMH-CIDI) [29]. The items in this checklist were reformatted in a coherent manner and the comorbidity checklist comprised two parts involving 18 checkboxes to tick, i.e., somatic comorbidity assessment evaluated by 15 CIRS items and the mental comorbidity assessment by 3 categories summarised from the WMH-CIDI.

# Statistical analysis

SPSS 18.0 was used for data analysis. A p value < .05 was considered to be statistically significant. First, descriptive statistics were conducted to summarise demographic characteristics and questionnaires answers. Chi-Squared tests were used to examine the difference in categorical outcomes, such as TTH associated disability level (MIDAS level), comorbidity checklist information, gender, age range, marital status, education level and ethnicity. Second, factor analysis and cluster analysis were conjunctively applied to obtain effective clusters and identify meaningful CM patterns for TTH. Specifically, the principal component analysis (PCA) was used for factor extraction in condensing respondents' responses to diagnostic information obtained from CMHQ items,whereas the Two-Step cluster algorithm then used for grouping these identified factors into clusters for further evaluation [30, 31]. ANOVA was used to assess the cluster difference in MIDAS levels and in PSS. Third, Chi-Squared tests and ANOVA were employed to compare the characteristics of the resulting clusters, which enables further examining the group differences among the CM pattern types, in MIDAS levels and in PSS levels of the participants. Multiple comparisons were performed to compare group means via post hoc tests with Bonferroni correction when significant differences were observed in means across groups. For missing data handling, both case deletion and imputation methods were applied. Cases having more than 30% missing values within the total 193 items in CMHQ were deleted from the dataset, whereas cases having less than 30% missing values were remedied via the expectation–maximisation algorithm [32].

# Multivariate methods for pattern identification

Evaluation and interpretation of data for pattern identification had four sequential steps (Fig. 1). The first step was to reduce the items of CMHQ into a smaller datasets using factor analysis; the second step was to assess the factors extracted and to label those factors in a clinical meaningful manner; the third step was to group (clinical meaningful) factors into clusters using cluster analysis; the final step was the identification of TTH patterns, that is to label the clusters into clinically meaningful CM patterns. Sixteen teaching and research staff across universities and hospitals with their professional backgrounds covering Chinese medicine, acupuncture, modern medicine, and statistics, etc., were invited to provide their experts' opinions in the 2nd and 3rd steps to ensure that the labels assigned to factors and clusters were of clinical relevance and significance. Only the labels that reached 70% agreement among 16 evaluators were retained.

# Results

From February 2011 to June 2012, a total of 565 respondents took part in the survey, and 497 completed it. After applying the selection criteria and excluding those ineligible and those with more than 30% of missing data, 170 participants were finally included for data analysis. **Figure 2** illustrates the participant selection process. Among them, 70.6% were female and 29.4% were male (M:F=1:2.4). The average age of the participants was 38 years (*SD*=12). Defined by headache days per month, a majority (63%) of the included participants were Episodic Tension-Type Headache (ETTH) sufferers, whereas 23% and 14% were of chronic TTH (CTTH) and infrequent subtypes, respectively. Sociodemographic characteristics including information such as ethnicity, marital status and education are shown in **Table 1**.

According to the CMHQ, the key features of the headaches were pain with a fixed location (74%), of continuous (66.7%) and intermittent (52.7%) nature, with tight (35.3%), heavy (34.1%) and pulsating (34.1%) sensations, and affecting the neck (61.3%) and eyes (57.2%). The majority of participants had frequent headache either being worse at the end of the day (31.2%) or at no particular time (35.9%). As to the aggravating and relieving factors, overwork (74.1%), stress (73.6%), mental strain (70%), being tired (68.1%), lack of sleep (68.1%), anger or irritability (65.8%), anxiety (excessive worry) (65.5%) nervousness (56.3%), and muscular strain (muscle tightness) (53.1%), were identified as the commonest aggravating factors of headache (≥50%), whereas sleeping (77.7%), medication (62.7%), lying-down (62.4%), pressing on the pain area (62.1%) and massage (50.9%) were the commonest relieving factors of the headaches (≥ 50%). Apart from headaches, neck (60%), shoulder (45.3%) and lower back (35.3%) were the most common painful areas. Of the female-related items, bright red colored menstrual blood (50.5%), dark colored menstrual blood (62.4%), headache before period (51.6%) and abdominal pain during periods (52.7%) were the most commonly referred items. Overall, the most common TTH accompanying symptoms were fatigue (71.3%), neck stiffness (70%) and neck pain (60%).

## TTH pattern identification

The exploratory analytic methods of factor analysis and cluster analysis were conjointly used given the relatively large number of CMHQ items. Firstly, PCA was applied and resulted in 41 clinical meaningful factors, including 12 from CMHQ part 1, 13 from part 2, and 16 from part 3, were labelled and retained for TTH pattern identification **(Table 2)**. Secondly, using the Two-Step cluster analysis, four distinct cluster groups were identified.. Lastly, based on the clinical characteristics of each cluster and expert opinions, the four clusters were labelled as Ascendant hyperactivity of Liver yang (Cluster 1), Dual Qi and Blood deficiency (Cluster 2), Liver depression forming fire (Cluster 3) and an Un-labelled group (Cluster 4) **(Table 3)**. The first three are common patterns of headache presented in Chinese medicine clinical practice.

## Cluster comparisons

**Table 4** summaries the characteristics of subjects according to the four clusters. The four clusters differed in aspects of demographic characteristics, stress levels, pain intensity (indicated by MIDAS item B), and disability levels (indicated by MIDAS), and TTH subtypes.

Disability level was classified based on the MIDAS scores. The disability level ranged from level 1 to level 4. The mean MIDAS score of the current sample was 22.64 lost days, at a severe disability level (≥21 lost days due to headache over the last three months). One-way ANOVA results indicated no cluster differences in the overall MIDAS scores. However, there were significant cluster group differences in MIDAS items 4 (days reduced in household work) and MIDAS B (degree of headache intensity). *Post hoc t* tests with Bonferroni correction found clusters 2 and 4 were statistically different, with Cluster 2 having more non-productive days at home (8.2 days) due to headache and more severe headache (6.3) than cluster 4 (mean: 3 days, mean intensity: 4.7) **(Appendix 3)**. Indicated by the Chi Square test results, there was a statistically significant cluster difference in the disability level ($p$=.017). This was largely due to about 50% the participants in Clusters 2 and 3 having a higher level of disability (levels 3 and 4), whereas 50% of Cluster 4 had the lowest level of disability (level 1).

The PSS scores were calculated by summing each item, an average score of 16.72 was found. A mean score of PSS-10 around 13 is considered to be the average of 2387 healthy respondents in the United States [16, 27], with the normative data ranging from 12.1 to 14.7. Comparing with the norm, the existing sample had a relatively higher perceived stress than the general population. The PSS does not provide a cut-point to quantify the level of stress. The score ranges from 0-40 were however interpreted arbitrarily by another study, i.e., a low perceived stress level of 0–13, moderate perceived stress of 14–26, and a high perceived stress of 27–40 [33]. The average scores for factors of “Perceived Distress” and “Perceived Coping” were 9.39 and 6.35 respectively. Based on a higher PSS score corresponding to a higher level of perceived stress, a higher score in factor of “Perceived Distress” indicates a higher degree of general distress. It is also necessary to aware that a lower score in “Perceived Coping” factor reflects better coping ability since the four positively stated items (4,5,7,8) in this factor are reversed scored (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1 and, 4 = 0) and then summing across all items when calculating the overall score of PSS-10. Like the PSS overall score, there are no cut-offs for the two factors either. One-way ANOVA results indicated there was a statistically significant cluster difference observed on PSS items of 3, 5, 8 **(Appendix 4)** and “Perceived Coping” factor. Detected by the *post hoc t* tests with Bonferroni correction, significant differences between Cluster 1 and Clusters 3 and 4 and between Cluster 2 and Clusters 3 and 4 were found **(Appendix 5)**. Participants in Clusters 1 and 2 seemed to cope with stress better than the other two clusters.

Comorbidities of TTH participants were calculated by counting the total number of somatic comorbidities and mental comorbidities separately. All participants had a low number of comorbidities. Of the somatic comorbidity, the body systems of upper gastrointestinal and ophthalmological and otorhinolaryngology had a higher response (9.4% and 8.8% respectively) than others. In regard to the mental comorbidity, anxiety disorders and mood disorders were reported by 12 participants each (7.1%). There were no significant differences in somatic comorbidities among the identified four TTH clusters. Although there was no statistically significant difference in mental comorbidity among clusters, cluster 4 participants suffered no mental comorbidity at all.

## Profile of the clusters

Cluster 1 (*n*=46) had a moderate level of pain, moderate level of disability, and moderate distribution in both physical and mental comorbidity. Participants in this pattern may have more emotional changes than others, such as reporting feeling nervous and “stressed” (Item 3). However, compared with others, they mostly often felt that things were going their way (Item 5) and tended to perform best in coping ability (PSS “Perceived Coping” factor) when compared with.

Cluster 2 (*n*=34) not only had the overall highest pain intensity and severest disability among all four patterns, it also had the largest number of participants having a physical comorbidity. Nevertheless, participants in this pattern mostly often felt on top of things (Item 8).

Cluster 3 (*n*=46) had a moderate headache intensity and severe disability, which was similar to Cluster 2. However, participants in this type of TTH pattern seemed to be impacted greatly by their headache. They could hardly feel on top of things (item 8) different to those in Cluster 2, nor could they feel that things were going their way (Item 5) when compared with Cluster 1.

Cluster 4 (n=44) was un-labelled as there were insufficient characteristics of the symptoms and signs for CM diagnosis. However, it may be the least affected cluster not only because it had the lowest level (mild) of pain among the four clusters, but also had no mental comorbidity. Although participants in this cluster had the least emotional problems as they rarely felt nervous and “stressed” (item 3), they however had a poor coping ability as indicated by “Perceived Coping” factor.

In summary, four clusters were identified, among them, participants in Cluster 2 experienced the most severe headache and had the highest disability level. In contrast, Cluster 4 presented mild headache intensity, moderate disability and was free from mental comorbidity. Based on the ANOVA results on MIDAS, PSS and comorbidity checklist, the characteristics of the identified four clusters of TTH participants are summarised in **Table 5**. The four clusters were not only distinguishable in CM patterns, they also differed in aspects of subtypes of TTH, stress level, pain intensity (indicated by MIDAS item B), and disability level (indicated by MIDAS).

# Discussion

The present study identified distinct CM patterns of TTH through a cluster analysis of 170 TTH participants in a bilingual cross-sectional survey. The results of this study suggest that TTH can be divided into four clusters based on symptoms and signs that are significant to the diagnostic process in Chinese medicine. The four clusters were not only distinguishable in CM patterns, but also differed in aspects of subtypes of TTH (ETTH, frequent ETTH, and CTTH), stress level, pain intensity, and disability level. These findings expand the existing understanding of TTH symptomatology in Western medicine and TTH patterns in Chinese medicine, which may help advance our understanding of the symptoms associated with TTH and subgroups of TTH.

TTH has been shown to be associated with a number of symptoms. The common TTH characteristics and associated symptoms identified in the present study are consistent with the findings of other studies [34–37]. The main similarities are the precipitating factors such as physical activity, stress/tension, when tired, lack of sleep, specific foods/drinks, alcohol, and skipping meals, and some accompanying symptoms such as fatigue, insomnia, and irritability. Emotion-related factors may have impacted on the presence of TTH. The present study found that stress and/or tension (73.6%) was the leading precipitating factors, and the finding is consistent with others (49.4% [34], 74.5% [38], 63% in men and 77% in women [39], 52.5% [37]). Only a small percentage of anxiety disorders and mood disorders were detected (7.1% respectively). This is probably due to more than three-quarters of the respondents were ETTH sufferers, as it has been shown that psychiatric comorbidities are more common in CTTH patients [40, 41] whereas those having less frequent TTH tend to having a lesser degree of psychiatric comorbidity

[42]. These results expand the common understanding of TTH symptomatology in terms of its pain description, trigger factors, and accompanying symptoms, as it provides better understanding of symptomology of TTH. With this knowledge, it is possible that more targeted treatments could be developed.

In summary, a considerable similarity of reported features and associated symptoms on TTH were observed between the present study and studies investigating factors and symptoms associated with TTH from western medical aspects. Inevitably, due to the differences in sampling, methods of studies, and the time points when each study took place, there are some discrepancies in the results reported by the above-mentioned studies and the present studies. For example, specific foods/drinks, as an aggravating factor, varied from 2–35%, skipping meals from 24.8–52.9%, smoking from 8.6 to 38%. In addition, the present study observed that bilateral headache was the most common location of TTH (71%) and followed by pain experience in the forehead (52.7%). Although the study by Li et al. [35] also listed bilateral and forehead headache being the commonest TTH, their findings were different with bilateral headache being 79.9% and forehead 34.1%.

In CM, TTH is not a recognised disorder. Literature in CM diagnosis of TTH is limited, yet there is no golden CM standard to classify TTH, since none established TTH eligibility criteria in CM diagnosis. Due to this, differentiation diagnostic criteria of pattern identification in treatment varied, which may also indicate a need to establish the CM differentiation diagnosis of TTH in helping identify the significance of clinical outcome led by the variation from practitioners [43]. The CMHQ contains a series of accompanying symptoms that may be similar to other studies, a major difference between our investigation and other studies were that most CMHQ items detecting signs and symptoms were originally set for diagnosis purposes for distinguishing CM patterns. The present study captured a series of accompanying symptoms that are seldom mentioned by others. For instance, sore eyes (43.5%), thirst (40.6%), bloating (30.0%), joint stiffness (40.6%), muscle twitching (31.8%), increased forgetfulness (50.0%), sighing often (41.1%), and, inability to concentrate (47.1%) were common symptoms experienced by TTH suffers in this sample.

The aim of cluster analysis is to differentiate a group of individuals into subgroups with homogeneous attributes that are diverse from other subgroups [44]. For example, using the hierarchical clustering, one study identified subgroups of individuals with headache who self-medicate which could be helpful to tailor intervention strategies for prevention of medication-overuse headache[45]. Another recent study on diabetic peripheral neuropathy (DPN) using cluster and factor analysis identified distinct groups of patients with respect to its clinical impacts on symptom patterns and comorbidities. Such comprehensive approaches could endorse the subgrouping to individualise the evaluation of patients with DPN. In CM syndrome research, exploratory analysis methods were valuable in understanding and verifying the CM patterns in a series of diseases and conditions defined by modern medicine. Those studies covers a range of topics such as Chronic obstructive pulmonary disease (COPD) [46–48], metabolic syndrome [49], chronic fatigue syndrome [50, 51], diabetic nephropathy [52], acquired immune deficiency syndrome (AIDS) [53, 54], lung cancer [55], preoperative colorectal cancer [56], stroke [57, 58], diabetes mellitus [59], diabetic retinopathy [60], excessive menstruation [61], functional constipation [62], uterus myoma [59], acute myocardial infraction [63], acute pancreatitis [64], posthepatitic cirrhosis [15], chronic low back pain [65], fibromyalgia [66–69], and coronary heart disease [70–72]. Generally, those studies identified explainable CM patterns and interpreted those modern diseases in a reasonable way. In the present study, the use of other measurements enhanced the understandings to the identified patterns in aspects of headache features, severity of headache-related disability, comorbidities, and psychological profiles, which reflect the multidimensional perspectives of TTH. The patterns identified were not only different in symptom manifestations, but also in disability and self-perceived stress and coping.

Very few studies have examined the differences between ETTH and CTTH beyond headache days. In modern medicine, identification of subtypes of TTH under ICHD-II is mainly distinguished by the frequency of headache attacks on the basis of epidemiological studies [73]. Within ETTH, its infrequent subtype occur at lower frequency (< 1 day a month) than the frequent subtype (≥ 1 day a month). The present study indicated that the infrequent ETTH reported much lower headache intensity (mild, mean of 2.78) than other two (moderate, mean of 5.85 and 5.81 respectively) and showed the lowest level of disability. This is in line with the description of ICHD-II that such infrequent subtype has very little impact on the individual whereas the chronic subtype in the present study is associated with a high level of disability[74]. Since ETTH and CTTH also differ in the level of disability and some symptomatology.it is possible to sub-categorise TTH from a multi-dimensional perspective, but not just limited to the frequency of headache.

In the present study, the four CM patterns differed from the current TTH subtypes. The three patterns not only differ in headache frequency, but also in headache intensity and disability. Over three-quarters of participants in Clusters 1 and 2 had frequent ETTH and about one-fifth had CTTH, whereas one-third in Cluster 3 had CTTH, and half had frequent ETTH. All these three clusters had very few participants with infrequent ETTH, whereas one-third of Cluster 4 was having infrequent ETTH (< 1 day). Those results indicate that the CM pattern identification goes beyond headache frequency as it focuses on symptoms and signs that TTH sufferers experience in addition to their headache frequency.

Currently, there is a significant gap in understanding sub-types of TTH. On one hand, the IHS diagnostic criteria for TTH are designed to distinguish TTH from other types of headaches to some degree, and to classify TTH into three subtypes based upon attack frequency only. Non-headache symptoms associated with TTH are, however, not explained or accounted for. On the other hand, despite several epidemiological studies observing a series of aggravating and relieving factors and accompanying symptoms of TTH, clinical practice to date has not given adequate attention to TTH symptoms. The current study fills those gaps by further understanding non-headache symptoms in TTH and using knowledge of pattern identification and advanced statistical methods to identify three clinically-meaningful subgroups of TTH. The presence of these subgroups of TTH sufferers indicates that there is a need to go beyond frequency and relieving factors of TTH. Addressing headache as well as accompanying non-headache symptoms may lead to more efficient treatment strategies.

This study has important strengths. To the best of authors' knowledge, the present investigation is the first study using exploratory statistical method to research TTH-related symptoms as well as identifying CM patterns of TTH. Our study presented an original statistical methodology that allowed the identification of clinical CM patterns. The method applied, that is using objective exploratory analytic approaches to the symptom-based clinical variables of TTH participants, provides an alternative to current modern medicine approaches in understanding the symptoms associated with TTH and subgroups of TTH. The survey was both hospital-based and general population-based. As a result, it should be applicable to the majority of TTH population.

In summary, the findings expand the existing understanding of TTH symptomatology and TTH patterns. They provide essential information for future research on subgroups of TTH. Nevertheless, several limitations of the current study should be considered. Firstly, the present results could be limited due to its sample size, as some other possible patterns may be observed with a larger sample size. Secondly, relying on exploratory analysis has its drawbacks, since statistically-determined clusters can be affected by many factors. Although we conducted exploratory analysis, we relied on experts' opinions when interpreting the generated factors and labelling the grouped symptoms and signs. However, expert opinions may be subjective. The present study minimised this potential limitation by a combined approach of exploratory analysis and expert opinions. Both internal and external experts were consulted during the processes of evaluation, determination and labelling of clusters. Finally, this study is a cross-sectional study, which only analysed the symptom distribution collected at a specific duration over the last 3 months. The presence and the severity of symptoms observed may change over time. Future studies may use longitudinal cohort approaches to evaluate the stability of the identified CM patterns over time, and to assess the effect of interventions.

# Conclusions

This study provides new and critical information for determining the symptom patterns of TTH. Through cluster analysis of information relevant to Chinse medicine. The identified patterns not only differed in symptoms and signs, but also in level of disability and stress. The subgroup classification will guide targeted intervention design, including acupuncture, for clinical practice and research.

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# Declarations

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## Abbreviations

ANOVA: One way analysis of variance

CHEAN: College Human Ethics Advisory Network

CIRS: Cumulative Illness Rating Scale

CM: Chinese medicine

CMHQ: Chinese Medicine Headache Questionnaire

CTTH: Chronic Tension-type headache

ICHD-II: Headache Society TTH diagnostic criteria (2nd edition)

IHS: International Headache Society

MIDAS: Migraine Disability Assessment Test

PCA: Principal component analysis

PSS: Perceive Stress Scale

SD: Standard Deviation

TCM: Traditional Chinese medicine

TTH: Tension-type Headache

ETTH: Episodic Tension-Type Headache

WMH-CIDI: World Mental Health Composite International Diagnostic Interview

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## Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. All requests to access personal data will be handled in accordance with the procedures by the Ethics Committee.

## Authors' contributions

Xinyu Hao: first author; study conception and design, data analysis, manuscript drafting

Fanrong Liang & Linpeng Wang: data collection, data interpretation

Ken Greenwood: methodology, CMHQ validation

Charlie Xue: study conception and funding acquisition, methodology, data interpretation, critical review of the MS

Ying Li & Zhen Zheng: co-corresponding authors; study conception, data analysis, manuscript revision

## Ethics approval and consent to participate

The study was approved by the College Human Ethics Advisory Network (CHEAN) of Science Engineering and Health, RMIT University (protocol approval number: BSEHAPP 10-11, May 23, 2011) and subsequently ratified by collaboration sites. Participation to the study was on a voluntary basis: all participants were provided information explaining the purpose of the study and they were informed consent before inclusion. All data were anonymous.

## Consent for publication

Not applicable

### Competing interests

The authors declare that they have no competing interests.

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### Disclosure

No conflict of financial interest to declare.

### Additional file

(see: Supplementation files)

## Tables

Table 1. Sociodemographic characteristics of the included subjects

| | Frequency (n) | Percent (%) |
|---|---|---|
| **Gender (n=170)** | | |
| Women | 120 | 70.6 |
| Men | 50 | 29.4 |
| **Age range (n=166)** | | |
| 20-29 | 55 | 33.1 |
| 30-39 | 44 | 26.5 |
| 40-49 | 31 | 18.7 |
| 50-59 | 26 | 15.7 |
| 60+ | 10 | 6.0 |
| **Marital status (n=165)** | | |
| Single | 64 | 38.8 |
| Married | 77 | 46.7 |
| Partnered | 9 | 5.5 |
| Divorced | 13 | 7.9 |
| Separated | 2 | 1.2 |
| **Ethnicity distribution (n=164)** | | |
| Chinese Asian | 79 | 48.2 |
| Australian Peoples | 42 | 25.6 |
| British | 13 | 7.9 |
| New Zealand Peoples | 3 | 1.8 |
| Southern European | 3 | 1.8 |
| Irish | 3 | 1.8 |
| Western European | 3 | 1.8 |
| South Eastern European | 1 | .6 |
| Northern European | 1 | .6 |
| Eastern European | 1 | .6 |
| Maritime South-East Asian | 1 | .6 |
| Arab | 1 | .6 |
| Central Asian | 1 | .6 |
| Mainland South-East Asian | 1 | .6 |
| Southern Asian | 1 | .6 |
| Other north-east Asian | 1 | .6 |
| Other Asian | 1 | .6 |
| Had more than one ethnicity | 8 | 4.9 |
| **Level of education (n=164)** | | |
| Postgraduate degree level | 40 | 24.4 |
| Graduate diploma and graduate certificate level | 8 | 4.9 |
| Bachelor degree level | 72 | 43.9 |
| Advanced diploma and diploma level | 18 | 11.0 |
| TAFE level | 10 | 6.1 |
| Secondary education | 14 | 8.5 |
| Primary education | 2 | 1.2 |

Table 2. Extraction of factors

| CMHQ PART1<br><br>**Pain description** | CMHQ PART2<br><br>**Aggravating & relieving factors** | CMHQ PART3<br><br>**Accompanying symptoms** |
|---|---|---|
| FAC1.1F1CentralHead | FAC 2.1F1Mental | FAC 3.1F1LiverQi&Fire |
| FAC 1.1F2WholeHead | FAC 2.1F2Food | FAC 3.1F2Eye |
| FAC 1.1F3LateralHead | FAC 2.1F3WeatherChange | FAC 3.1F3BoneJointWind |
| FAC 1.3F1RhythmHeadache | FAC 2.1F4NoFood&Drink | FAC 3.1F4PoorDigestion |
| FAC 1.3F2ExplosiveNotDull | FAC 2.1F5MentalStrain | FAC 3.1F5LiverSpleenFire |
| FAC 1.3F3SharpHeadache | FAC 2.1F6MuscularStrain | FAC 3.1F6YinDeficiency |
| FAC 1.3F4TightHeadache | FAC 2.1F7Oil&Spicy | FAC 3.1F7LiverAttackStomach |
| FAC 1.3F7DistendingHeadache | FAC 2.1F8WindDamp | FAC 3.1F8ENT |
| FAC 1.3F8EmptyHeadache | FAC 2.1F9PhysicalStrain | FAC 3.1F9LightSound |
| FAC 1.5F1LateOfDay | FAC 2.1F10Alcohol-DragCigar | FAC 3.1F10TemperatureSensitivity |
| FAC 1.5F2BothEnd | FAC 2.2F1Rest | FAC 3.1F11Constipation |
| FAC 1.5F3AllDay | FAC 2.2F2PhysicalStimulation | FAC 3.1F12BloodDeficiency |
| | FAC 2.2F3EatingRelated | FAC 3.1F13YangDeficiency |
| | | FAC 3.1F14SpleenDeficienyOfBowel |
| | | FAC 3.1F16Tinnitus |
| | | FAC 3.1F17Insomnia |
| Included: n=12 | Included: n=13 | Included: n=16 |

* In this table, “FAC” is the abbreviation of “factor”, whereas the numbers 1.X after it indicate their section number. For instance, FAC1.6F1 denotes the extracted first factor of Section 1.6, which summarised items of Forehead, Back of the head, and Top of the head.

Table 3. Summary of cluster characteristics based according to the CMHQ data

| | Cluster 1 (n=46) | Cluster 2 (n=34) | | Cluster 3 (n=46) | Cluster 4 (n=44) |
|---|---|---|---|---|---|
| Location & Quality | • Forehead; Back of the head; Top of the head<br>• PAIN QUALITY: Throbbing; Pulsating; Pounding; Tight; A “band-like” sensation | • Forehead, Back of the head, Top of the head; Both side of the head<br>• PAIN QUALITY: Throbbing; Pulsating; Pounding<br>• Worse in the morning and at night; All day | | Whole head;<br>No particular location | Explosive;<br>NOT Dull;<br>Sharp; Piercing |
| Aggravating & Relieving factors | AGGRAVATING BY:<br>Dehydration<br>Hunger / Being hungry<br>Chocolate<br>Muscular strain(muscle tightness)<br>Poor posture in sitting, standing or sleeping<br>Teeth grinding | AGGRAVATING BY:<br>Change of weather;<br>Change in temperature;<br>Hot weather; Cold weather; Dehydration; Hunger; Chocolate | RELIEVING BY:<br>Exercise; Massage<br>Pressing the pain area; Warmth<br>Coldness; Medication; Eating | AGGRAVATING BY:<br>Stress; Nervousness<br>Irritability<br>Excessive worry; Depression<br>Tension or conflict related | AGGRAVATING BY:<br>Windy days<br>Damp weather / Humid weather<br>Rainy days |
| Accompanying symptoms | Sensitivity to light (or to bright lights)<br>Sensitivity to sound | “Pins and needles” or numbness in the hands and feet; Faintness; Dizziness; Watery bowel motion; Loose bowel motion | | Dry mouth; Thirst; Bitter taste in the mouth | Belching; Bloating;<br>Indigestion;<br>Fear of being hot |

Table 4. Cluster comparisons of demographic data, TTH subtypes, MIDAS, PSS, and CIRS items

| | | TTH clusters | | | | Total (n) | p-value† Chi-Square | p-value† ANOVA |
|---|---|---|---|---|---|---|---|---|
| | | C1 | C2 | C3 | C4 | | | |
| | | 44 [v.34] | 33 [v.4] | 37 [v.1] | 29 [v.12] | 143 | N/A | **0.000*[05]** |
| | F | 35 | 27 | 30 | 28 | 120 | .307 | N/A |
| | M | 11 | 7 | 16 | 16 | 50 | | |
| | 20-29 | 6 | 8 | 17 | 24 | 55 | **.001*[0125]** | N/A |
| | 20-29 | 10 | 12 | 10 | 12 | 44 | | |
| | 20-29 | 10 | 8 | 6 | 7 | 31 | | |
| | 20-29 | 14 | 4 | 8 | 0 | 26 | | |
| | 20-29 | 5 | 2 | 2 | 1 | 10 | | |
| atus | Single | 13 | 10 | 16 | 25 | 64 | .047 | N/A |
| | Married | 22 | 15 | 25 | 14 | 77 | | |
| | Partnered | 3 | 4 | 0 | 2 | 9 | | |
| | Divorced | 6 | 4 | 1 | 2 | 13 | | |
| | Separated | 0 | 1 | 0 | 1 | 2 | | |
| evel | Postgraduate | 13 | 8 | 8 | 11 | 40 | .968 | N/A |
| | Graduate | 3 | 2 | 1 | 2 | 8 | | |
| | Bachelor | 17 | 14 | 21 | 20 | 72 | | |
| | Diploma | 4 | 5 | 3 | 6 | 19 | | |
| | TAFE | 4 | 1 | 3 | 2 | 10 | | |
| | Secondary Edu | 4 | 4 | 4 | 2 | 14 | | |
| | Primary Edu | 0 | 0 | 1 | 1 | 2 | | |
| | Oceania | 19 | 18 | 4 | 4 | 45 | **.000*[0125]** | N/A |
| | European | 14 | 7 | 2 | 2 | 25 | | |
| | Arab | 0 | 0 | 1 | 0 | 1 | | |
| | Asian | 7 | 5 | 35 | 38 | 85 | | |
| | had > 1 ethnicity | 5 | 3 | 0 | 0 | 8 | | |
| es | Infrequent ETTH | 1(2%) | 1(3%) | 7(15%) | 15(34%) | 24(14%) | **.000*[0125]** | N/A |
| | Frequent ETTH | 36(78%) | 26(76%) | 23(50%) | 22(50%) | 107(63%) | | |
| | CTTH | 9(20%) | 7(21%) | 16(35%) | 7(16%) | 39(23%) | | |
| | Q1 | 44(1.07) | 33(2.30) | 43(2.74) | 44(3.86) | 164(7.771) | N/A | .408 |
| | Q2 | 44(5.34) | 33(9.67) | 43(9.81) | 44(5.50) | 164(7.43) | N/A | .157 |
| | Q3 | 44(3.95) | 33(6.82) | 43(4.00) | 44(3.23) | 164(4.35) | N/A | .209 |
| | Q4 | 44(6.05) | 33(8.15) | 43(4.35) | 44(2.93) | 164(5.19) | N/A | **.038*[05]** |
| | Q5 | 44(2.18) | 33(4.24)) | 432.65 | 443.86 | 164(3.17) | N/A | .606 |
| | MIDAS A | 44(20.45) | 33(26.73) | 43(20.53) | 44(15.82) | 164(20.49) | N/A | .259 |
| | MIDAS B | 44(5.45) | 33(6.30) v.4 | 43(5.42) | 44(4.68) v.2 | 164(5.41) | N/A | **.015*[05]** |
| | MIDAS SUM (mean score) | 44(18.59) | 33(31.18) | 43(23.56) | 44(19.39) | 164(22.64) | N/A | .310 |
| bility | Level 1 | 12(27%) | 3(1%) | 14(33%) | 22(50%) | 51(31%) | **.017*[05]** | N/A |
| | Level 2 | 5(11%) | 7(21%) | 3(7%) | 4(9%) | 19(12%) | | |
| | Level 3 | 14(32%) | 8(24%) | 8(19%) | 7(16%) | 37(23%) | | |
| | Level 4 | 13(30%) | 15(45%) | 18(42%) | 11(25%) | 57(35%) | | |
| | Sum | 16.68 | 16.19 | 18.79 | 15.11 | 16.72 | N/A | .092 |
| em) | Perceived Distress | 9.85 | 10.06 | 10.22 | 7.52 | 9.39 | N/A | .066 |
| | Perceived Coping | 5.04 [v.3,4] | 5.18 [v.3,4] | 7.35* v.1,2 | 7.59* v.1,2 | 6.35 | N/A | **.000*[017]** |
| umber of | Somatic comorbidity | 46 | 34 | 46 | 44 | 42.9% | .588 | N/A |
| | Mental comorbidity | 8 | 9 | 5 | 0 | 12.9% | .060 | N/A |

tralia is a county of immigration. In section of ethnicity, the category of “had more than 1 ethnicity” indicated a group
nts in this country share more than one ethnicity. For example, an Australian person may have his/her mother of Irish
d father of Greek. In such case, these participants may tick two options and in data analysis, he/she was classified as
nad more than one ethnicity.

n Chi-Square and ANOVA were applied to access cluster differences for comparison. Chi-Square tests examine
outcomes, whereas ANOVA assess the means of each cluster. *p* values correspond to comparisons between the
ng Chi-square test or ANOVA, as appropriate

an difference is significant at the 0.05 level.

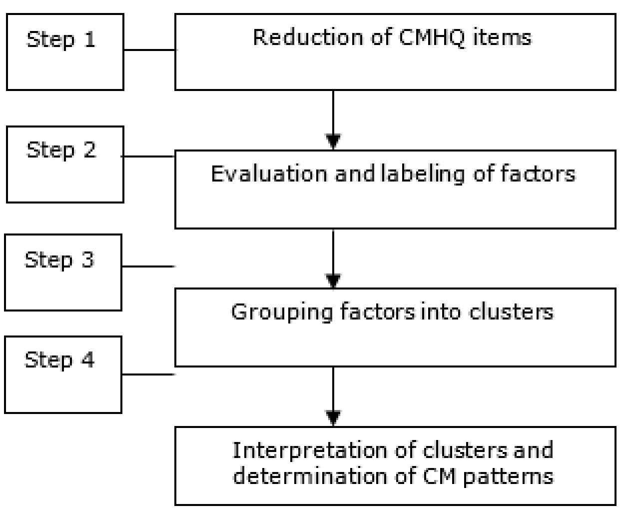
ean difference is significant at the 0.0125(0.05/4) level.

an difference is significant at the 0.017(0.05/3) level.

s the clusters differed with post-hoc Bonferroni correction, whereas the “x(figure)” after “v.” indicates specific
r clusters.

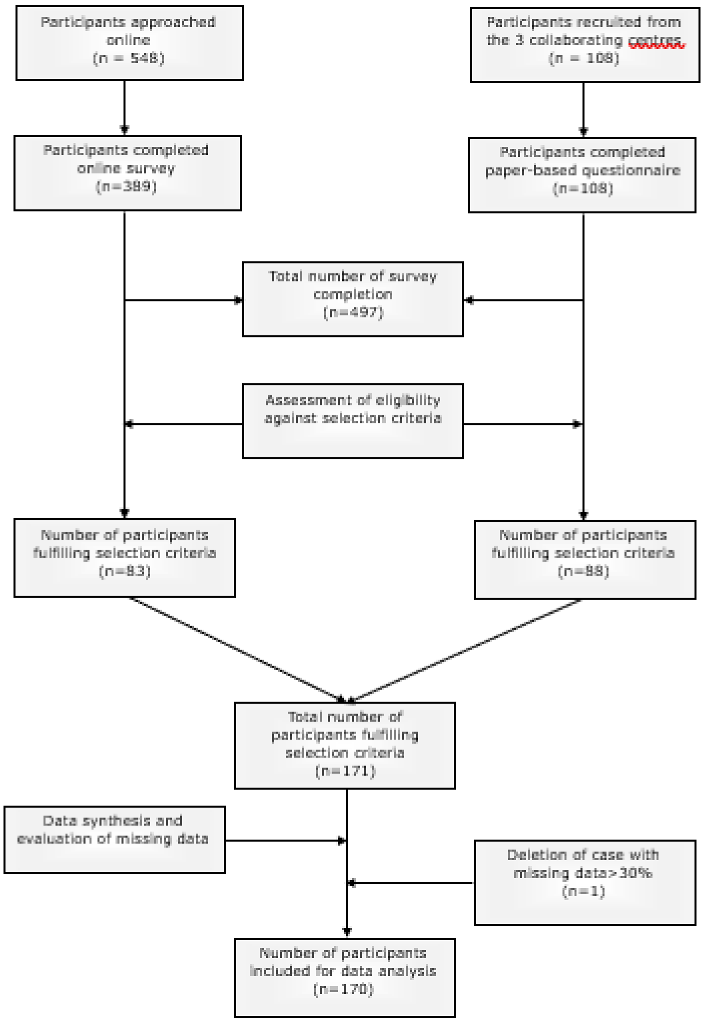
[Due to technical limitations, table 5 could not be displayed here. Please see the supplementary files section to access table 5.]

## Figures




### Figure 1

Process of CM pattern identification




### Figure 2

Flow chart of participant recruitment and screening process

# Supplementary Files

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