Clinical Rheumatology (2019) 38:1393–1400
https://doi.org/10.1007/s10067-018-04425-w

ORIGINAL ARTICLE

A survey of traditional Chinese medicine use among rheumatoid arthritis patients: a claims data–based cohort study

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Received: 19 October 2018 / Revised: 18 December 2018 / Accepted: 28 December 2018 / Published online: 22 January 2019

Abstract

Introduction/objectives Traditional Chinese medicine (TCM) is commonly used for symptom relief in patients with chronic diseases. Nevertheless, large-scale surveys focusing on the utilization of TCM among patients with rheumatoid arthritis (RA) are limited, especially in Taiwan, where TCM is highly popular. This cohort study aimed to describe the utilization of TCM and determine the factors related to TCM usage among RA patients.

Method A national health insurance database was used to identify 6532 newly diagnosed RA patients aged between 20 and 70 years, together with 12,246 subjects without RA matched by sex, age, and index year between 2000 and 2010. Incidence density of TCM use and its related factors was calculated by the Poisson regression model.

Results Findings indicated that RA patients experienced higher incidence density of TCM use than non-RA patients, with an adjusted incidence density ratio of 1.30 (95% confidence interval = 1.21–1.36). Multivariate analysis showed that RA patients who were female, were young, had high monthly income, had high Charlson-Deyo comorbidity index scores, and lived in the highly urbanized area with high TCM density were more likely to use TCM services. The top three reasons for seeking TCM services were diseases of the musculoskeletal system and connective tissue, the respiratory system, and the digestive system.

Conclusions The findings allow healthcare providers to identify the pattern of TCM use and characterize the factors that affect TCM utilization. Further research is required to fully address the efficiency and safety of TCM in treating RA patients.

Keywords Incidence density · Rheumatoid arthritis · Traditional Chinese medicine · Utilization

Ming-Chi Lu, Hanoch Livneh and Lei-Mei Chiu contributed equally to this work.

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Introduction

Rheumatoid arthritis (RA) is a chronic disease that often affects adults at any age, resulting in a wide range of disabling conditions and inability to work, thus imposing enormous burdens [1]. In the USA, the total annual costs for RA amounted to $19.3 billion, and the total annual costs including intangible costs exceeded $39 billion [2].

Due to the systemic inflammation, RA is a critical risk factor for many chronic conditions, such as cancer, cardiovascular disease, and respiratory disease [3]. A study by Lassere and colleagues further indicated that people with RA had a lower life expectancy by 6–7 years compared with the general population [4]. Although pharmacotherapy, including nonsteroidal anti-inflammatory drugs (NSAIDs) and nonbiologic or biologic disease-modifying antirheumatic drugs (DMARDs), is currently the most commonly used treatment for RA, the severity of the side effects may insidiously occur and affect their adherence to treatment [5, 6]. Therefore, alternative therapies have become increasingly popular as adjunctive treatments for patients with chronic diseases [7–9]. One of the most popular of these alternative treatments is traditional Chinese medicine (TCM).

Over the past few years, a number of studies have investigated the role of TCM in treating RA. A review article indicated that the extracts from the root of *Tripterygium wilfordii* Hook F (TwHF) could suppress the production of cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-2 (IL-2) [10]. Another study comparing TwHF with methotrexate (MTX) revealed that the combination of two methods (MTX and TwHF) showed greater effectiveness than MTX alone in controlling disease activity in RA patients [11]. Another study indicated that a candidate compound of TCM, calycosin, had a potent binding affinity with interleukin (IL)-6 receptor protein involved in the development of RA [12].

Although many studies have suggested that TCM might be safer and more effective in the treatment of RA than routine therapies alone, it is unclear if RA patients have used TCM services more frequently than the general population. Additionally, it is not yet known what specific factors influence the use of TCM, and how this may impact the use of medical resources and, therefore, the promotion of better treatment for RA. To fill this gap in the literature, the present study used the national insurance claims database to investigate how TCM is used in treating patients with RA in Taiwan and what factors influence TCM use.

Patients and methods

Data source

This retrospective cohort study used the Longitudinal Health Insurance Database (LHID) 2000, which has been maintained by the Bureau of National Health Insurance (NHI) and provided to Taiwanese scientists for research purposes. Since 1995, Taiwan has had a single-payer NHI program to remove financial barriers of medical care for all legal residents. As of 2010, over 99% of the population of Taiwan were enrolled in this program [13]. The LHID 2000, a subset database of the NHI program, contains the entire original claims data from 1996 to 2012 of 1,000,000 beneficiaries randomly sampled from the year 2000 registry for beneficiaries of the NHI program. Because a multistage stratified systematic sampling method was used, no statistically significant differences regarding sex or age occurred between the one million insured individuals and the general population [13]. This database contains all NHI enrolment files, claims data, and the registry for prescription drugs to provide comprehensive utilization information for subjects covered by the insurance program. To date, more than 300 published papers have used this database as the basis for their studies [13, 14]. This study was approved by the local institutional review board and ethics committee of Buddhist Dalin Tzu Chi Hospital, Taiwan (No. B10004021-2).

Study population

Diagnoses in the insurance claims data were coded with the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM). After employing a 4-year washout period, we included patients aged between 20 and 70 years, and with newly diagnosed RA within the 2000–2010 time period for ICD codes of 714.0. To reduce the potential for disease misclassification, only those with catastrophic illness certification (CIC) due to RA were eligible. In Taiwan, insured persons with major diseases, such as schizophrenia, mood disorders, immune disease, or cancer can apply for a CIC that grants exemption from co-payment. The date when RA patients gained the approval for catastrophic illness registration was considered as the index date. In order to ensure that all patients with RA in this study were incident cases, only new-onset RA cases were included. The database search identified 6503 RA patients who were included in the study.

In observational studies, it is crucial to reduce baseline imbalance prior to conducting data analysis. In this regard, we used propensity score matching to select the non-RA cases. The propensity score is the probability of assignment of treatment conditional on the basis of subjects' demographics and baseline comorbidities at enrollment as listed in Table 1. One-to-one nearest neighbor matching within 0.2 caliper distance, in which pairs of user and nonuser groups were formed, such that matched subjects have similar values of the propensity. The logistic regression, including these confounders, yielded a *c*-statistic of 0.74 in this study, indicating fair discrimination between the two cohorts [15]. Thereafter, each subject in the control group was assigned the same index

Table 1 Demographic and clinical characteristics of enrolled RA patients

Variable	Non-RA $N = 6503$ (%)	RA $N = 6503$ (%)	P
Gender			0.16
Female	4689 (72.1)	4617 (71.0)	
Age			0.89
≤ 50 years	2920 (44.9)	2913 (44.8)	
Mean (± SD)	51.01 (± 11.62)	51.10 (± 11.63)	0.90
Monthly income			0.96
High	286 (4.4)	293 (4.5)	
Median	3544 (54.5)	3538 (54.4)	
Low	2673 (41.1)	2672 (41.1)	
Residential area			0.98
Urban	3727 (57.3)	3726 (57.3)	
Suburban	1040 (16.0)	1034 (15.9)	
Rural	1736 (26.7)	1743 (26.8)	
CCI			0.88
< 2	832 (12.8)	826 (12.7)	
Density of TCM physicians			0.90
High	1457 (22.4)	1463 (22.5)	

RA, rheumatoid arthritis; *SD*, standard deviation; *CCI*, Charlson-Deyo comorbidity index; *TCM*, traditional Chinese medicine

date as the corresponding RA patient. A total of 6503 non-RA subjects were identified for further analysis.

In this study, the incidence density was used to describe the utilization of TCM services, which includes the prescription of Chinese herbal medicines, acupuncture, manipulative therapy, and traumatology, all of which have been part of healthcare and are fully reimbursed under the NHI system. All subjects were followed up from index date to the date of withdrawal from insurance or the end of 2012 to determine the counts of TCM use. Thereafter, the incidence density of TCM use was calculated with the numbers of TCM visits identified during the follow-up, divided by the total person-years (PYs) for each group under the Poisson assumption [16].

Baseline demographic characteristics and comorbidity

The sample's demographic characteristics included age, gender, income for estimating insurance payment, the availability of TCM healthcare resources, and urbanization level of the subject's residential area. The monthly incomes were stratified into three levels: ≤ New Taiwan Dollar (NTD) 17,880, NTD 17,881–NTD 43,900, and ≥ NTD 43,901. Urbanization levels were divided into three strata: urban (levels 1–2), suburban (levels 3–4), and rural (levels 5–7) areas. Level 1 refers to the "most urbanized" and level 7 refers to the "least urbanized" communities [17]. Additionally, we also calculated the level of TCM physician density using the numbers of TCM clinician per 1,000,000 residents for each of the administrative units. Areas that were above 50% percentile were regarded as the high TCM physician density. Baseline comorbidities were evaluated by using the established Charlson-Deyo comorbidity index (CCI) [18] that is based on the individual medical records 1 year prior to the beginning of cohort entry.

Statistical analysis

Intergroup differences were evaluated using the independent sample t test for continuous variables, and the χ^2 test for categorical variables. The incidence density of TCM use between RA and non-RA cohorts was presented with the number of cases per 1000 PYs. To compare the difference in TCM use between RA and non-RA subjects, the incidence density ratio (IDR) and 95% confidence interval (CI) were calculated by the Poisson regression model. In addition, the incidence density of TCM use for all-cause and cause-specific diseases in the RA cohort was also done to clarify the common reasons for TCM consultation. To determine the factors that might predict TCM usage among RA cohort, a multivariate Poisson regression was performed to evaluate the adjusted relative risk, with 95% CI, after consideration of the baseline characteristics of the study subjects. A P value < 0.05 was considered statistically significant. All analyses were performed with the SAS software version 9.3 (SAS Institute, Cary, NC).

Results

The RA cohort and non-RA cohort provided data for 6503 and 6503 cases, respectively. After matching procedure with propensity score, there was no significant difference between the two groups in age, sex, monthly income, residential area, density of TCM physicians, and CCI score, indicating the two groups to be comparable on these characteristics (Table 1).

Of the enrolled subjects, 80.1% of RA patients ($N = 5207/6503$) and 70.1% of non-RA cases (4559/6503) had previously used TCM. Overall, after adjustment for potential confounders, patients with RA were found to have higher utilization of TCM services than those without RA (2723.77 vs 2052.73, respectively, per 1000 PYs), with an adjusted IDR of 1.30 (95% CI, 1.21–1.36) (Table 2).

Furthermore, with regard to TCM outpatient visits (Table 3), we found that herbal remedies (49.6%) constituted the most commonly used therapeutic approach, followed by combined therapy (32.7%) and acupuncture or traumatology manipulation alone (17.7%). As for the frequency of visits, the majority of RA patients visited TCM clinics more than six times (66.2%). The analysis of the major disease categories for all TCM visits among them is summarized in Table 4. It

Table 2 Incidence of TCM treatment for RA patients compared with non-RA controls

Patient group	TCM visits	PYs	Incidence	Incidence density ratio† (95% CI)
Controls	199,978	97,420.70	2052.73	1
RA patients	139,870	51,351.72	2723.77	1.30 (1.21–1.36)

† Adjusted for the variables listed on Table 1

RA, rheumatoid arthritis; *PYs*, person-years; *CI*, confidence interval; *TCM*, traditional Chinese medicine

showed the category of "musculoskeletal system and connective tissue" was the most common reason for using TCM services (778.61 per 1000 PYs), followed by " respiratory system" (493.62 per 1000 PYs) and "digestive system" (374.83 per 1000 PYs).

Table 5 reveals the factors affecting TCM usage in RA patients as determined by the Poisson regression analysis. Gender, age, monthly income, residential area, CCI scores, and the density of TCM physicians were, all, significantly related to TCM use. Female gender (adjusted RR = 1.45; 95% CI = 1.42–1.46), being ≤ 50 years of age (adjusted RR = 1.24; 95% CI = 1.21–1.25), having highest monthly income (adjusted RR = 1.06; 95% CI = 1.02–1.09), higher CCI scores (adjusted RR = 1.28; 95% CI = 1.26–1.31), and living in an urban area (adjusted RR = 1.12; 95% CI = 1.10–1.14) and in a high TCM physicians density area (adjusted RR = 1.18; 95% CI = 1.16–1.20) increased the likelihood that patients are prone to use TCM services.

Discussion

This is the first large-scale survey to focus on characterizing the factors that impact the use of TCM in RA patients in Taiwan. Findings of our study showed a significantly higher use of TCM in people with RA than in the general population. As this is the first study to address this issue, it is not possible to compare our findings with previous research. However, we can infer that patients with autoimmune diseases may require more intensive treatment and, therefore, be inclined to utilize alternative treatments with fewer side effects to improve therapeutic efficacy [12, 19]. Despite the fact that many potent anti-arthritic drugs are available for managing arthritis, their prolonged use is associated with severe adverse effects, such as nausea, skin rash, infections, and depressive symptom [2, 20, 21].

In practice, some commonly used Chinese herbal medicines for the treatment of RA, such as TwHF [10], San-qi [22], or Chuan-niu-xi [23], have been shown to stimulate blood circulation and to promote physiological function in the autoimmune system through lowering the serum levels of inflammatory markers containing TNF-α and IL-6 and to reduce the Matrix metalloproteinase expression, which is reported to play an important role in the pathogenesis of RA. Given that the randomized trials in RA patients receiving both DMARD treatment and TCM are lacking, further research may be needed to more carefully evaluate the effects of TCM among RA patients, in particular if they also concurrently receive DMARDs. This could be used, then, as a reference in the integration of TCM services into standard of care to promote better prognosis for this population.

The data we reviewed suggested that the common reasons for TCM visits were diseases of the musculoskeletal system and connective tissue, respiratory system, and digestive system. It can be speculated that the chronic inflammatory reaction of the immune system may insidiously affect other extra tissues, containing muscles, lung, or vascular organs, thus causing comorbidities [12]. Additionally, the DMARDs were shown to be related to the occurrence of gastrointestinal-related symptoms due to significant toxicities [24]. These concerns may have further heightened the use of TCM among RA patients.

Results of the multivariate Poisson regression analysis indicated that females were more likely to use TCM services

Table 3 Treatment modalities of TCM received for RA patients

Number of TCM visits	No. of patients			Total cases received TCM (*N* = 5207)
	Acupuncture or traumatology manipulation only (*N* = 923)	Chinese herbal medicine only (*N* = 2579)	Combination of both treatment modalities (*N* = 1705)	
1–3	349 (37.8%)	251 (9.7%)	238 (14.0%)	838 (16.1%)
4–6	277 (30.0%)	319 (12.4%)	326 (19.1%)	922 (17.7%)
> 6	297 (32.2%)	2009 (77.9)	1141 (66.9%)	3447 (66.2%)

TCM, traditional Chinese medicine

Table 4 Incidence of TCM treatment by major disease categories among the RA patients (PYs = 51,351.72)

Disease (ICD-9-CM)	Frequency	Incidence (per 1000 PYs)
All diseases	139,870	2723.76
Musculoskeletal system and connective tissue (710–739)	39,983	778.61
Respiratory system (460–519)	25,348	493.62
Digestive system (520–579)	19,248	374.83
Circulatory system (390–459)	15,150	295.02
Nervous system (320–389)	13,791	268.56
Genitourinary system (580–629)	6780	132.03
Skin and subcutaneous tissue (680–709)	4406	85.80
Endocrine, nutritional and metabolic disease and immunity disorder (240–279)	3481	67.79
Neoplasms (140–239)	3074	59.86
Congenital anomalies (740–759)	2445	47.61
Infectious and parasitic disease (001–139)	1219	23.74
Complications of pregnancy, childbirth and the puerperium (630–676)	514	10.01
Symptoms, signs and ill-defined conditions (780–799)	473	9.21
Injury and poisoning (800–999)	70	1.36
Certain conditions originating in the perinatal period (760–779)	0	0.00

ICD-9-CM, International Classification of Disease, 9th Revision, Clinical Modification

than males, which is consistent with previous reports [25, 26]. We speculate that women may have better knowledge and more positive attitudes regarding self-care than men and therefore are more likely to select other treatment options to address negative changes in their well-being [25, 26]. Additional reports indicated that Chinese herbal formulas were helpful in alleviating discomfort during the menstrual periods [27, 28], which may also account for the high utilization of TCM services in females.

Consistent with the findings on the association between age and TCM use among patients with other medical conditions [25, 26], the present results support earlier findings that showed younger patients to be more likely to use TCM than older patients. It can be inferred that younger patients may have easier access to social resources, better knowledge of their benefits, and more open attitudes regarding practices of physical rehabilitation and disease prevention [29]. In this regard, younger individuals may be more willing to use TCM for symptom relief and health maintenance after RA onset. However, our findings differ from those reported by Liu and colleagues [30]. This inconsistency may be attributed to the difference in the nature of study participants, i.e., patients, in Liu et al.'s study, had hepatitis C, as well as the different age classifications used in the study.

Those from high socioeconomic status, as indicated by higher monthly income or residing in highly urbanized areas, had the higher likelihood of using TCM services, which was consistent with prior findings [25, 26, 31]. Typically, economic elements play an important role in physician supply and medical utilization [32]. We assumed that the residents who lived in urban areas or had higher household income also had more opportunities to access other therapeutic services. On the other hand, a former report indicated that highly urbanized areas were linked to higher density of TCM-providing physicians in Taiwan [33], which may account for the positive relationship observed between the greater TCM use and the density of TCM physicians.

The present study found that higher CCI score was associated with higher tendency for TCM use, implying that people who suffered from multiple comorbid conditions were more likely to use TCM services. This finding is in accordance with previous work which showed that comorbidity burden is an important determinant of healthcare utilization among patients with chronic diseases, regardless of the use of Western medicine or TCM [19, 34]. This may be explained by the fact that patients with high-risk conditions may be more willing to seek alternative therapeutic modalities to improve their physical functions [30].

While our study is the first to investigate the utilization pattern of TCM services among individuals with RA, there are important limitations to consider. First, coding error of disease is inevitable in an administrative database. To minimize this bias, we only enrolled subjects with RA following at least three outpatient visits that reported consistent diagnoses or after they had at least one inpatient admission. It should also be noted that the NHI of Taiwan randomly samples claims from hospitals, interview patients, and review medical charts to verify the accuracy of medical records. Second, information on social network relationships, coping strategies, family factors, religious beliefs, and educational levels was not available

Table 5 Poisson regression analysis of the association of baseline characteristics with TCM use among RA patients (n = 6503)

Variable	Crude RR (95% CI)	Adjusted RR† (95% CI)
Gender		
Female	1.44 (1.42–1.46)**	1.45 (1.42–1.46)**
Male	1	1
Age		
≤ 50 years	1.22 (1.21–1.23)**	1.24 (1.21–1.25)**
> 50 years	1	1
Monthly income		
High	1.06 (1.03–1.09)**	1.06 (1.02–1.09)**
Median	0.99 (0.97–1.03)	1.03 (1.01–1.07)*
Low	1	1
Residential area		
Urban	1.18 (1.16–1.21)**	1.12 (1.10–1.14)**
Suburban	1.17 (1.16–1.19)**	1.09 (1.07–1.11)**
Rural	1	1
CCI		
≥ 2	1.25 (1.22–1.27)**	1.28 (1.26–1.31)**
< 2	1	1
Density of TCM physicians		
High	1.23 (1.21–1.25)**	1.18 (1.16–1.20)**
Low	1	1
Visits seeking medical care	1.01 (1.00–1.03)*	1.01 (0.99–1.02)

*$P < 0.05$

**$P < 0.01$

† Adjusted for the other variables in this table

RA, rheumatoid arthritis; *RR*, relative risk; *CI*, confidence interval; *CCI*, Charlson-Deyo comorbidity index; *TCM*, traditional Chinese medicine

from the claims data and may have influenced the accuracy of our findings. Future research via a national survey to recruit the entire population of RA is needed to better assess if the present findings are replicable and to further examine the annual trend of TCM use among them. Third, we were unable to contact the enrolled patients directly about the use of Chinese herbs due to the anonymity of identification numbers in the database; thus, the use of TCM might have been underestimated. Fourth, evidence derived from any observational cohort study is generally less robust than that obtained from randomized control trials since cohort studies are subject to various biases related to confounding effects. Despite our careful efforts to maintain adequate control of potentially confounding factors, unpredictable biases could still have remained. Notwithstanding these limitations, the strengths of this study must also be acknowledged and these include the availability of billing data from health insurance that provide estimates of validity with reference to enrollees' demographics and resource utilization. In addition, the patterns of TCM use and their difference between the sample of RA patients and the general population were determined by the IDR, which allowed for a more precise comparison regarding healthcare service utilization [16].

In conclusion, we conducted a nationwide, population-based study to compare the incidence density of TCM use between RA and non-RA cohorts in Taiwan. The findings indicated that RA patients had a higher tendency of TCM use by a magnitude of 30% as compared to the general population. Factors leading to the higher use of TCM services among RA patients included being female, being of younger age, having higher monthly income and higher CCI scores, living in urbanized areas, and living in higher TCM physician density. The data from this population-based study provide further insight, for healthcare providers, into the actual patterns of TCM use in treating RA patients. We propose that these promising findings may have important implications for future research and clinical practice. Faced with increased interest in TCM services, further research is recommended to evaluate the efficacy and safety of TCM in treating RA patients, which in turn can also serve as a groundwork to instituting more appropriate interventions to improve medical prognosis.

Acknowledgements The study is based in part on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance, Department of Health, and managed by National Health Research Institutes.

Role of authors All the authors approved the contents of the submitted article. Conceived and designed the experiments: LMC, YCC, TTY. Analyzed the data: TTY. Contributed reagents/materials/analysis tools: TTY, CLM, LH, LMC. Wrote the paper: TTY, LH. Final approval of manuscript: LMC, LH, CLM, LNS, YCC, TTY.

Funding information This research was supported by Dalin Tzuchi Hospital (Grant Number DTCRD103(2)-E-05).

Compliance with ethical standards

Disclosures None.

Ethics approval This study was approved by the local institutional review board and ethics committee of Buddhist Dalin Tzu Chi Hospital, Taiwan (No. B10004021-2).

Disclaimer The interpretation and conclusions contained herein do not represent those of the Bureau of National Health Insurance, Department of Health, or National Health Research Institutes.

References

1. Lenssinck ML, Burdorf A, Boonen A, Gignac MA, Hazes JM, Luime JJ (2013) Consequences of inflammatory arthritis for workplace productivity loss and sick leave: a systematic review. Ann Rheum Dis 72(4):493–505
2. Birnbaum H, Pike C, Kaufman R, Marynchenko M, Kidolezi Y, Cifaldi M (2010) Societal cost of rheumatoid arthritis patients in the US. Curr Med Res Opin 26(1):77–90
3. Gabriel S, Michaud K (2009) Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther 11(3):229
4. Lassere MN, Rappo J, Portek IJ, Sturgess A, Edmonds JP (2013) How many life years are lost in patients with rheumatoid arthritis? Secular cause-specific and all-cause mortality in rheumatoid arthritis, and their predictors in a long-term Australian cohort study. Intern Med J 43(1):66–72
5. Da Silva JAP, Jacobs JWG, Kirwan JR, Boers M, Saag KG, Inês LB et al (2006) Safety of low dose glucocorticoid treatment in rheumatoid arthritis: published evidence and prospective trial data. Ann Rheum Dis 65(3):285–293
6. Lin MC, Lu MC, Livneh H, Lai NS, Guo HR, Tsai TY (2017) Factors associated with sexual dysfunction in Taiwanese females with rheumatoid arthritis. BMC Womens Health 17:12
7. Lee YW, Chen TL, Shih YR, Tsai CL, Chang CC, Liang HH et al (2014) Adjunctive traditional Chinese medicine therapy improves survival in patients with advanced breast cancer: a population-based study. Cancer 120(9):1338–1344
8. Chen KH, Yeh MH, Livneh H, Chen BC, Lin IH, Lu MC, Tsai TY, Yeh CC (2017) Association of traditional Chinese medicine therapy and the risk of dementia in patients with hypertension: a nationwide population-based cohort study. BMC Complement Altern Med 17(1):178
9. Tsai TY, Li CY, Livneh H, Lin IH, Lu MC, Yeh CC (2016) Decreased risk of stroke in patients receiving traditional Chinese medicine for vertigo: a population-based cohort study. J Ethnopharmacol 184:138–143
10. Bao J, Dai SM (2011) A Chinese herb Tripterygium wilfordii Hook F in the treatment of rheumatoid arthritis: mechanism, efficacy, and safety. Rheumatol Int 31(9):1123–1129
11. Lv QW, Zhang W, Shi Q, Zheng WJ, Li X, Chen H, Wu QJ, Jiang WL, Li HB, Gong L, Wei W, Liu H, Liu AJ, Jin HT, Wang JX, Liu XM, Li ZB, Liu B, Shen M, Wang Q, Wu XN, Liang D, Yin YF, Fei YY, Su JM, Zhao LD, Jiang Y, Li J, Tang FL, Zhang FC, Lipsky PE, Zhang X (2015) Comparison of tripterygium wilfordii hook f with methotrexate in the treatment of active rheumatoid arthritis (TRIFRA): a randomised, controlled clinical trial. Ann Rheum Dis 74:1078–1086
12. Lee WY, Chen HY, Chen KC, Chen CYC (2014) Treatment of rheumatoid arthritis with traditional Chinese medicine. Biomed Res Int 2014:528018
13. National Health Insurance Research Database, Taiwan. http://nhird.nhri.org.tw/date_cohort.html (accessed 25 Dec 2016)
14. Wu CY, Hu HY, Pu CY, Huang N, Shen HC, Li CP, Chou YJ (2011) Pulmonary tuberculosis increases the risk of lung cancer. Cancer 117(3):618–624
15. Baek S, Park SH, Won E, Park YR, Kim HJ (2015) Propensity score matching: a conceptual review for radiology researchers. Korean J Radiol 16(2):286–296
16. Wu TH, Hsieh PC, Li CY, Su HF (2013) Emergency department utilization by national health insurance home-care recipients. Taiwan J Public Health 32(1):18–30
17. Liu CY, Hung YT, Chuang YL, Chen YJ, Weng WS, Liu JS et al (2006) Incorporating development stratification of Taiwan townships into sampling design of large scale health interview survey. J Health Manag 4(1):1–22
18. Deyo RA, Cherkin DC, Ciol MA (1992) Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 45(6):613–619
19. Busato A, Dönges A, Herren S, Widmer M, Marian F (2006) Health status and health care utilisation of patients in complementary and conventional primary care in Switzerland - an observational study. Fam Pract 23(1):116–124
20. Moudgil KD, Berman BM (2014) Traditional Chinese medicine: potential for clinical treatment of rheumatoid arthritis. Expert Rev Clin Immunol 10(7):819–822
21. Zhang P, Li J, Han Y, Yu XW, Qin L (2010) Traditional Chinese medicine in the treatment of rheumatoid arthritis: a general review. Rheumatol Int 30(6):713–718
22. Zhang C, Jiang M, Chen G, Lu A (2012) Incorporation of traditional Chinese medicine pattern diagnosis in the management of rheumatoid arthritis. Eur J Integr Med 4(3):e245–e254
23. Li HQ, Wei JJ, Xia W, Li JH, Liu AJ, Yin SB, Wang C, Song L, Wang Y, Zheng GQ, Fan JP (2015) Promoting blood circulation for removing blood stasis therapy for acute intracerebral hemorrhage: a systematic review and meta-analysis. Acta Pharmacol Sin 36(6):659–675
24. Jiang M, Zhao J, Lu A, Zha Q, He Y (2010) Does gastrointestinal adverse drug reaction influence therapeutic effect in the treatment of rheumatoid arthritis? J Altern Complement Med 16(2):143–144
25. Shih CC, Liao CC, Su YC, Tsai CC, Lin JG (2012) Gender differences in traditional Chinese medicine use among adults in Taiwan. PLoS One 7(4):e32540
26. Liao CC, Lin JG, Tsai CC, Lane HL, Su TC, Wang HH et al (2012) An investigation of the use of traditional Chinese medicine in stroke patients in Taiwan. Evid Based Complement Alternat Med 2012:387164
27. Haines CJ, Lam PM, Chung TK, Cheng KF, Leung PC (2008) A randomized, double-blind, placebo-controlled study of the effect of a Chinese herbal medicine preparation (Dang Gui Buxue Tang) on menopausal symptoms in Hong Kong Chinese women. Climacteric 11(3):244–251

28. Kwee SH, Tan HH, Marsman A, Wauters C (2007) The effect of Chinese herbal medicines (CHM) on menopausal symptoms compared to hormone replacement therapy (HRT) and placebo. Maturitas 58(1):83–90
29. Cornwell B, Laumann EO, Schumm LP (2008) The social connectedness of older adults: a national profile. Am Sociol Rev 73(2): 185–203
30. Liu CY, Chu JY, Chiang JH, Yen HR, Hsu CH (2016) Utilization and prescription patterns of traditional Chinese medicine for patients with hepatitis C in Taiwan: a population-based study. BMC Complement Altern Med 16:397
31. Liao YH, Lin CC, Li TC, Lin JG (2012) Utilization pattern of traditional Chinese medicine for liver cancer patients in Taiwan. BMC Complement Altern Med 12:146
32. Cooper RA, Getzen TE, Laud P (2003) Economic expansion is a major determinant of physician supply and utilization. Health Serv Res 38(2):675–696
33. Shih CC, Su YC, Liao CC, Lin JG (2010) Patterns of medical pluralism among adults: results from the 2001 National Health Interview Survey in Taiwan. BMC Health Serv Res 10:191
34. Schneeweiss S, Maclure M (2000) Use of comorbidity scores for control of confounding in studies using administrative databases. Int J Epidemiol 29(5):891–898