

# A Real-World Data Analysis of The Distribution of Traditional Chinese Medicine Syndromes and Their Elements Among Bronchiectasis Patients

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## Research

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# Abstract

**Introduction:** We sought to investigate the distribution of traditional Chinese medicine (TCM) syndromes and their elements among bronchiectasis patients using real-world data.

**Methods:** A real-world study was performed to explore the relationship between TCM syndrome and bronchiectasis using electronic medical information from 1,113 patients in China. Factor analyses were used to reduce the dimensions of TCM syndrome elements and to detect common factors. Additionally, cluster analyses were employed to assess combinations of TCM syndrome elements. Finally, association rule analyses were performed to investigate the structures of TCM syndrome elements in order to estimate the patterns of TCM syndromes.

**Results:** A total of 17 TCM syndrome elements were extracted using this method. There were four Shi TCM syndromes of Tan\_Re\_Yong\_Fei (36.39%), Tan\_Zhuo\_Zu\_Fei (12.94%), Gan\_Huo\_Fan\_Fei (11.59%), and Feng\_Re\_Fan\_Fei (11.32%) with >5.0% distribution frequency in total sample. The highest Xu TCM syndrome was Fei\_Yin\_Xu (18.24%). Factor analysis, cluster analysis, and association rule analysis found that Tan, Huo, Feng, Yin\_Xu, Fei, and Gan were the core TCM syndrome elements.

**Conclusion:** In this study, TCM Shi syndromes of Tan\_Re\_Yong\_Fei, Tan\_Zhuo\_Zu\_Fei, Gan\_Huo\_Fan\_Fei, and Feng\_Re\_Fan\_Fei were detected with a high frequency among bronchiectasis patients using real-world data, as was the TCM core Xu syndrome of Fei\_Yin\_Xu. The core elements of Huo, Tan, Feng, Yin\_Xu, Fei and Gan were found across the entire sample.

## Introduction

Bronchiectasis is defined as chronic inflammatory bronchial disease with irreversible dilation of the bronchial lumen (1). Clinically speaking, it usually presents with chronic recurrent cough, expectoration, hemoptysis, progressive dyspnea, pulmonary functional deterioration, recurrent respiratory infections, and a reduced quality of life and life expectancy (2). Pathologically, patients have abnormally dilated bronchi leading to impairment of host defenses, chronic infection with bacteria, and airways inflammation. A retrospective cohort study showed there was a high prevalence of bronchiectasis in the United States (3), and the prevalence of bronchiectasis in China is 1.5% in men and 1.1% in women (4, 5). Moreover, the prevalence of bronchiectasis appears to be increasing in recent years (6).

Since a significant proportion of patients fail to get satisfactory treatment from modern medicine, many patients seek help from complementary and alternative medicine, especially traditional Chinese medicine (TCM) (7, 8). TCM uses a classification system developed over thousands of years wherein different “syndromes” are used to summarize the cause, nature, and location of pathological changes at various stages of disease(9),(10). These syndromes stratify diseases according to groups of specific symptoms that are regarded as a summary of the body’s condition in the disease process (11). They describe differences in etiology and pathogenesis of a disease and emphasize the variation in individual bodies’ constitutions(12). Thus, patients with the same disease may present with different syndromes because

of individual differences in physiological responses; TCM considers these differences vital for prescribing appropriate treatment(9). Syndromes are thus used as the foundation for diagnosis and prescription in TCM, and are the key concept of TCM theory (9).

TCM treatment for bronchiectasis has a long history, and numerous basic and clinical studies have found that TCM has curative effects on bronchiectasis (8). Since applying TCM to the treatment of bronchiectasis must be based on syndrome differentiations for optimum efficacy, it is especially important to identify the TCM syndromes commonly identified with bronchiectasis. However, such information is currently limited to textbooks and individual expert counseling(7), and there is limited clinical evidence of the TCM syndromes that typically present with bronchiectasis. A better understanding of TCM syndrome distribution in bronchiectasis patients may help healthcare providers improve the clinical efficacy of Chinese medicine treatment.

The advent of big data creates both opportunities and challenges for TCM (13). Real-world studies (RWS), in which data are collected in real-life practical circumstances, have become hotspots for clinical research (14), (15). Clinical data collected in the hospital, at home or abroad, are more accessible due to the development of information technology and wide use of hospital information systems (HIS) and electronic medical records (EMRs)(16). It is crucial to perform RWS on TCM syndromes, using large clinical datasets with modern data-mining and machine-learning techniques, to produce a scientific and reliable evidence base for TCM, thereby transforming TCM from experience-based medicine to evidence-based medicine (16),(17).With this in mind, the present study attempted to investigate common distribution patterns and core elements of TCM syndromes in patients with bronchiectasis by searching real-world medical records for evidence of TCM treatment in patients with bronchiectasis.

## Methods

### Study design and participants

We performed a RWS to explore the distribution of common TCM syndromes in patients with bronchiectasis by using patient medical records, mainly including EMR and HIS. All medical records from 2013 to 2016 in respiratory disease wards at five Chinese hospitals were collected. Bronchiectasis was identified using a centralized database of patients with bronchiectasis All adult patients with a physician-established diagnosis of bronchiectasis were eligible for inclusion. Bronchiectasis was diagnosed to include blood tests, sputum cultures, and on review of imaging, which recommends all non-cystic-fibrosis-related bronchiectasis be confirmed by CT scan (18). The institutional review board of each participating site approved the study, as did an administrative institutional review board for the data collection center. After patients provided informed consent, medical records were queried by a study coordinator or principal investigator using standardized recording forms. Participants with other comorbid pulmonary diseases (e.g., asthma or chronic obstructive pulmonary disease), or any other comorbid diseases and conditions that might confound data interpretation (e.g., cancer, immune diseases, endocrine diseases,

cardiovascular, hematologic, hepatic, renal, or neurological diseases, oral contraceptive use, or pregnancy) were excluded from the study.

## Data collection and preparation

The contents of patient medical records were based on EMR and standard Chinese guidelines. General information, complaints, medical histories, modern medicine diagnoses, and TCM diagnoses were extracted. Medical record data were transferred from the EMR systems of five hospitals and loaded onto electronic platforms capable of handling large datasets at the Institute of Biomedical Informatics and Biostatistics, the Institute of Integrative Medicine at Fudan University. Demographic information, hospitalization records, and clinical outcomes were extracted using Python 3.5 programs. Standard common data models for integrative medical treatment of bronchiectasis, including diagnosis of TCM syndromes, were created to establish uniform standard codes for data analysis. A total of 1,113 medical records with complete data, consisting of general information, TCM syndrome features, and final TCM and modern medicine diagnoses were available for analysis.

## Data analysis

Standard TCM syndrome guidelines were used to establish the elements of each TCM (19). Data analyses were carried out to estimate the distribution of different TCM syndromes and their associated elements among bronchiectasis patients, including frequency of individual distribution, frequency of different combinations, and difference analysis of TCM syndromes and combinations of their elements. Differences in variables among gender were determined by one-way analysis of variance (ANOVA), and differences in properties were detected by  $\chi^2$  analysis among the groups. Tests were two-sided, and a  $p$ -value of  $< 0.05$  was considered significant. Frequency analyses were employed to explore the proportion of TCM syndrome diagnoses for bronchiectasis. Moreover, frequency analyses were performed to assess the proportion of TCM syndrome elements present in different diagnoses. Results were analyzed using the Statistical Package for Social Sciences for Windows, version 16.0 (SPSS, Chicago, IL, USA).

We performed factor analyses to reduce the dimensions of TCM syndrome elements and to explore the structures of these elements. The Kaiser-Meyer-Olkin (KMO) test and Bartlett's test of sphericity were used to evaluate the suitability of the collected TCM syndrome elements for factor analysis(20). Common factors were extracted using principal component analyses (20). Varimax rotation was used to allow for factor load absolute value of the new common factor (factor load absolute value was  $\geq 0.20$ ) (20). Hierarchical cluster analyses were used to classify TCM syndrome elements using Ward's method to generate a dendrogram for estimation of similar clusters(21). Association rule analyses were carried out to investigate the structures of TCM syndrome elements in order to estimate the distribution of TCM syndromes. A set of frequent rules was generated, and the strength of these rules was then evaluated using three parameters of support, confidence, and lift.(22). Rules having a support percentage value of  $> 10$  and a confidence percentage value of  $> 80$  were reported. The Apriori algorithm was used to evaluate

the pattern of association within TCM syndrome elements. Data mining was performed using the SPSS Modeler (version 18.0, Chicago, IL, USA) and packages in Python 3.5.

## Results

### Demographic characteristics

The baseline demographics for the 1,113 individuals were listed in Table 1. The proportion of females was 60.02%, and the mean age was 65.31 years. The average duration of hospitalization was 12.06 days in total sample. There was no difference in duration of hospitalization in male than females (10.03 vs. 12.23,  $p = 0.115$ ). The primary ethnicity of the participants was Han Chinese (94.79%). The vast majority (98.74%) of patients experienced improvements in their condition or were cured.

### Frequency of TCM syndromes and their elements among bronchiectasis patients

The distribution of TCM syndromes among the bronchiectasis patients in our study is shown in Table 2. A total of 17 TCM syndromes were identified. The four most common Shi syndromes were Tan\_Re\_Yong\_Fei (36.39%), Tan\_Zhuo\_Zu\_Fei (12.94%), Gan\_Huo\_Fan\_Fei (11.59%), and Feng\_Re\_Fan\_Fei (11.32%). These can be translated respectively as phlegm-heat obstructing the lung, phlegm-turbidity obstructing the lung, liver fire invading the lung, and wind-heat obstructing the lung. The most common Xu syndrome was Fei\_Yin\_Xu (18.24%), which can be translated as Yin-deficiency of the lung. There was no Mix syndromes present in more than 5% of the total sample.

Fifteen TCM syndrome elements were identified and are listed in Table 3. Four pathogenesis elements met the 5% inclusion threshold: Huo ("fire," 22.25%), Tan ("phlegm," 19.28%), Yin Xu ("Yin deficiency," 6.93%), and Feng ("wind," 4.79%). Two location elements were present in significant proportion: Fei ("lung," 36.25%) and Gan ("liver," 4.26%).

### Factor analysis of TCM syndrome elements

Using the entire sample, the KMO value of the partial correlation of variables was 0.731, and the approximate chi-square value of Bartlett's test of sphericity was 672.74 ( $p < 0.001$ ). Similar results were obtained using the Shi and Xu groups of elements (KMO  $> 0.50$  and  $p < 0.001$  for Bartlett's test for both). The results of the factor load matrix after rotation transformation are listed in Table 4. In the entire sample, characteristic root values of the first eight common factors were  $> 1.0$ , and their cumulative variance contribution rates reached 81.93. A scree plot was used to show the relevance of common factors and characteristic root values (Figure 1A), indicating that the scatter location of the first eight common factors was steep and that the characteristic root values for the rest of the common factors were small. Varimax rotation was used for factor rotation and transformation, and absolute factor load

values that were  $\geq 0.20$  are listed in Table 4. Similarly, four and two common factors were extracted from the Shi and Xu syndrome groups, respectively (Figures 1B and 1C).

## Cluster analysis of TCM syndrome elements

Using the entire sample, hierarchical cluster analysis found that TCM syndrome elements were significantly different among three clusters (Figure 2A). Cluster 1 was comprised of the Huo, Tan, and Fei elements; Cluster 2 consisted of the Shi, Pi, Qi\_Zhi, Xue\_Yu, Du, Xue\_Xu, and Han elements, while Cluster 3 was comprised of the rest of the elements. Additionally, in the Shi syndrome group, three further clusters were identified: Cluster 1 included the Qi Zhi, Xue\_Yu, Fei, and Han elements; Cluster 2 included the Gan, Feng, Han, and Tan elements (Figure 2B). In the Xu syndrome group, Cluster 1 consisted of the Fei and Yin\_Xu elements, while Cluster 2 consisted of the Shen, Qi\_Xu, and Xue\_Xu elements (Figure 2C).

## Association rule analysis of TCM syndrome elements

An association rule analysis indicated associations among the Tan, Huo, Feng, Yin Xu, Fei, and Gan elements (Table 5). Using the rule algorithm, eight rules were found and are listed in Table 5. The strongest support percentage parameter was between the Fei and Huo elements (60.907%). Three rules were established which applied to the full set of elements: Huo => Gan and Fei; Fei => Tan and Huo; and Fei => Yin Xu. In the Shi syndrome group, three further rules were identified, suggesting associations among the Huo, Feng, Tan, Fei, and Gan elements. In the Xu syndrome group, one association was identified: Fei => Yin\_Xu.

## Discussion

Although TCM is widely used in the treatment of bronchiectasis in China, a system of syndrome differentiation using evidence-based medicine has not been established (16). Since syndrome diagnosis is key to TCM therapy, there is an urgent need for TCM researchers to perform more epidemiological studies of high methodological quality on syndrome distribution in bronchiectasis patients. To our knowledge, this is the first study to investigate TCM syndrome distribution in bronchiectasis patients using real-world data. RWS offer insights into the interactions between patient characteristics, preferences, lifestyles, and treatment outcomes that are often excluded from double-blind clinical randomized controlled trials (RCTs) (23). This type of study also offers the opportunity to explore how these interactions differ between therapies and treatment modalities and to evaluate important clinical outcomes, such as bronchiectasis exacerbations, that can be underpowered in RCTs owing to their short duration and their pre-selection of idealized patients in whom negative outcomes are often relatively infrequent (24).

Through comprehensive summary, the results of the present study demonstrate that the four most common Shi syndromes among bronchiectasis patients, in decreasing order of frequency, were

Tan\_Re\_Yong\_Fei, Tan\_Zhuo\_Zu\_Fei, Gan\_Huo\_Fan\_Fei, and Feng\_Re\_Fan\_Fei. Frequency analyses showed all four Shi syndromes were present with > 5.0% frequency. These results suggest that the four Shi syndromes are the most common in bronchiectasis. Similarly, the Xu syndrome of Fei\_Yin\_Xu was identified in a significant proportion of bronchiectasis patients. Additionally, frequency analyses, factor analyses, cluster analyses, and association rule analyses for different syndrome elements demonstrated that the predominant elements in the pathogenesis of bronchiectasis were Huo, Tan, Yin\_Xu, and Feng, representing the four elements phlegm, fire, Yin-deficiency, and wind, respectively. The main disease locations were Fei (lung) and Gan (liver), indicating that bronchiectasis can be attributed to functional disorders of the lungs and liver. However, it should be pointed out that the “liver” in TCM refers not only to the anatomical organ but also to a complex system which includes a series of functions which modern medicine ascribes to the metabolic system, central nervous system, endocrine system, blood system, digestive system, and others (25).

According to TCM theory, bronchiectasis arises from the invasion of evils (i.e., wind, heat, and dampness, which conceptually resemble pathogenic infection in western medicine) (26). Our results indicate that bronchiectasis can be divided into five overlapping categories based on TCM syndromes. In the first type of bronchiectasis cases, bronchiectasis may lead to retention of body fluids in all meridians and collaterals, leading to the production of sputum, which clinically manifests as Tan\_Zhuo\_Zu\_Fei (phlegm-turbidity obstructing the lung) (27). In the second type of cases, the accumulation of phlegm and heat readily results in bronchial necrosis (27). This type of bronchiectasis is the end result of a pathological process involving a vicious circle of inflammation, recurrent infection, and bronchial wall damage caused by phlegm and heat (28). This phlegm-heat obstructing the lung has been associated with exaggerated inflammatory responses secondary to airway destruction (28). In the third type of cases, bronchiectasis is the result of stagnated wind evils, particularly in patients with frailty (27). In these cases, wind and heat (the pathogenetic causes) stagnate in the lungs; this usually occurs in the early stage of bronchiectasis (26). In the fourth type of cases, liver-fire invading the lung syndrome appears in cases of bronchiectasis with hemoptysis, which is consistent with the traditional understanding (7). In the fifth type of cases, prolonged courses of bronchiectasis, coupled with evil stagnation and frailty, can render a substantial loss of primordial Yin (29). According to TCM theory, a deficiency of bodily fluid in the respiratory system, especially in the mucous epithelium, is the mechanism behind the Yin-deficiency in the lung syndrome (29). Therefore, these patients presented with Yin-deficiency in the lung syndrome. In the present study, Yin-deficiency syndrome is the most common Xu TCM syndrome with bronchiectasis patients, suggesting the importance of nourishing Yin and moisturizing the lungs(30).

In terms of distribution of the TCM syndrome in bronchiectasis, the detected frequency of phlegm-heat syndrome was significantly higher than that of other syndromes, indicating that phlegm-heat is a major contraindication in the treatment of bronchiectasis. The frequency of Yin-deficiency was also significantly higher than the other three syndromes (phlegm turbidity, liver-fire, and wind-heat). It can therefore be inferred that Yin-deficiency has a wide distribution as a fundamental syndrome pattern with a high frequency of occurrence in bronchiectasis patients, especially in the elderly, frail, and patients with long illness durations.

Identification of the aforementioned five syndrome categories suggests that they form the core pathogenesis of bronchiectasis and should thus be the fundamental diagnostic elements taken into account during differentiation of bronchiectasis. It follows that, when formulating a prescription to treat bronchiectasis, the five strategies that should be considered depending on the presenting syndrome pattern are removing sputum and clearing heat, resolving phlegm turbidity, clearing away liver-fire, and nourishing Yin. Furthermore, the target organs of treatment should be the lung and liver (as defined by TCM).

This study achieved three primary results of significance. First, this study identified the distribution of TCM syndromes in patients with bronchiectasis using objective parameters from real-world datasets. This method may help reduce bias and may also encourage more practitioners to use this syndrome differentiation approach. Second, results from this study can guide clinical trials in evaluating the efficacy of TCM treatments for bronchiectasis. Once the most common TCM syndromes of bronchiectasis are identified, further interventional research can investigate the efficacy and safety of TCM treatments for bronchiectasis based on the specific syndromes identified. Third, since this study established that wind-heat syndromes usually occur in the early stage of bronchiectasis, effective treatment can be targeted to this population to slow down the progression of the disease, ultimately reducing the burden for both patients and the medical system caused by advanced complications.

There are some limitations of this study. First, selection bias may exist because the present study was based on a RWS design. All data were derived from participants in hospitals in five cities using a relatively small sample, and therefore may not be representative of the distribution of TCM syndromes in bronchiectasis patients in the rest of China. Additional multi-center studies with larger samples are required to verify the conclusions of the present study. Second, the different causes, severity, and stages of bronchiectasis in the original sample population were unclear because we did not subdivide the data. Third, the associations between TCM syndromes and modern medicine indicators were not explored in this work. Future research should focus in greater depth on the objective evidence of TCM syndromes in bronchiectasis patients.

## Conclusion

In summary, the TCM Shi syndromes of Tan\_Re\_Yong\_Fei, Tan\_Zhuo\_Zu\_Fei, Gan\_Huo\_Fan\_Fei, and Feng\_Re\_Fan\_Fei were detected with a high frequency among bronchiectasis patients using real-world data, as was the TCM core Xu syndrome of Fei\_Yin\_Xu. The core elements of Huo, Tan, Feng, Yin\_Xu, Fei and Gan were found across the entire sample.

Interpretation for items

Fei - the lung; Pi - the spleen; Shen - the kidney; Xin - the heart; Nao - the brain; Shi - the excess; Xu-the deficiency; Huo - the fire; Tan - the phlegm; Feng - the wind;

## Abbreviations

Traditional Chinese medicine (TCM)

Real-world studies (RWS)

Hospital information systems (HIS)

Electronic medical records (EMRs)

One-way analysis of variance (ANOVA)

Kaiser-Meyer-Olkin (KMO)

Randomized controlled trials (RCTs)

## Declarations

Ethical approval

This study was approved by the Committee of Huashan Hospital, Shanghai, China. The methods were carried out in accordance with the approved guidelines.

Consent for publication:

All authors read and approved the final manuscript.

Availability of data and material:

The datasets generated and/or analyzed during the current study are not publicly available due to private information but are available from the corresponding author on reasonable request. Dataset are from the study whose authors may be contacted at Institute of Bioinformatics and Biostatistics, Institutes of Integrative Medicine, Fudan University.

Competing interests:

None declared of conflict of interest

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Author's contributions:

Y.D and C.W drafted the manuscript. Y.J and Q.K participated in the design of the study and performed the statistical analysis. Z.T and J.D conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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#### Author Disclosure Statement

No competing financial interests exist.

## References

1. Bergin DA, Hurley K, Mehta A, Cox S, Ryan D, O'Neill SJ, et al. Airway inflammatory markers in individuals with cystic fibrosis and non-cystic fibrosis bronchiectasis. *J Inflamm Res*. 2013;6:1-11.
2. Martinez-Garcia MA, Perpina-Tordera M, Roman-Sanchez P, Soler-Cataluna JJ. Quality-of-life determinants in patients with clinically stable bronchiectasis. *Chest*. 2005;128(2):739-45.
3. Weycker D, Hansen GL, Seifer FD. Prevalence and incidence of noncystic fibrosis bronchiectasis among US adults in 2013. *Chron Respir Dis*. 2017;14(4):377-84.
4. Zhou YM, Wang C, Yao WZ, Chen P, Kang J, Huang SG, et al. [The prevalence and risk factors of bronchiectasis in residents aged 40 years old and above in seven cities in China]. *Zhonghua Nei Ke Za Zhi*. 2013;52(5):379-82.
5. Qi Q, Wang W, Li T, Zhang Y, Li Y. Aetiology and clinical characteristics of patients with bronchiectasis in a Chinese Han population: A prospective study. *Respirology*. 2015;20(6):917-24.
6. Aksamit TR, O'Donnell AE, Barker A, Olivier KN, Winthrop KL, Daniels MLA, et al. Adult Patients With Bronchiectasis: A First Look at the US Bronchiectasis Research Registry. *Chest*. 2017;151(5):982-92.
7. Li X, Wu YG, Zhang HY, Shao CR. [Typing of bronchiectasis according to syndrome differentiation]. *Zhong Xi Yi Jie He Xue Bao*. 2004;2(4):255-7.
8. Zhang ZM, Ren PH, Guan WJ. Symptom-based treatment with Traditional Chinese Medicine in bronchiectasis patients with hemoptysis. *J Thorac Dis*. 2017;9(9):E884-E6.
9. Su SB, Lu A, Li S, Jia W. Evidence-Based ZHENG: A Traditional Chinese Medicine Syndrome. *Evid Based Complement Alternat Med*. 2012;2012:246538.
10. Li Q, Yang GY, Liu JP. Syndrome differentiation in chinese herbal medicine for irritable bowel syndrome: a literature review of randomized trials. *Evid Based Complement Alternat Med*.

- 2013;2013:232147.
11. Chen WX, Wu QY, Chen BC, Ke MY, Guo LC, Liu XJ. [Measurement study of disease differentiation treatment based on standard syndrome differentiation]. *Zhong Xi Yi Jie He Xue Bao*. 2009;7(5):401-6.
  12. Lu AP, Chen KJ. Chinese medicine pattern diagnosis could lead to innovation in medical sciences. *Chin J Integr Med*. 2011;17(11):811-7.
  13. Zhang J, Zhang B. Clinical research of traditional Chinese medicine in big data era. *Front Med*. 2014;8(3):321-7.
  14. Tian F, Xie YM. [Real-world study: a potential new approach to effectiveness evaluation of traditional Chinese medicine interventions]. *Zhong Xi Yi Jie He Xue Bao*. 2010;8(4):301-6.
  15. Birring SS, Brew J, Kilbourn A, Edwards V, Wilson R, Morice AH. Rococo study: a real-world evaluation of an over-the-counter medicine in acute cough (a multicentre, randomised, controlled study). *BMJ Open*. 2017;7(1):e014112.
  16. Zhang R, Wang Y, Liu B, Song G, Zhou X, Fan S, et al. Clinical data quality problems and countermeasure for real world study. *Front Med*. 2014;8(3):352-7.
  17. Zhao K, Tian JF, Zhao C, Yuan F, Gao ZY, Li LZ, et al. Effectiveness of integrative medicine therapy on coronary artery disease prognosis: A real-world study. *Chin J Integr Med*. 2016.
  18. Hill AT, Pasteur M, Cornford C, Welham S, Bilton D. Primary care summary of the British Thoracic Society Guideline on the management of non-cystic fibrosis bronchiectasis. *Prim Care Respir J*. 2011;20(2):135-40.
  19. Wei J, Wu R, Fau - Zhao D, Zhao D. Analysis on traditional Chinese medicine syndrome elements and relevant factors for senile diabetes. 2013.33(4)(0255-2922 (Print)):473-8.
  20. McSweeney LB, Koch EI, Saules KK, Jefferson S. Exploratory Factor Analysis of Diagnostic and Statistical Manual, 5th Edition, Criteria for Posttraumatic Stress Disorder. *J Nerv Ment Dis*. 2016;204(1):9-14.
  21. Kheifets LI. Cluster analysis: a perspective. *Stat Med*. 1993;12(19-20):1755-6.
  22. Goh DH, Ang RP. An introduction to association rule mining: an application in counseling and help-seeking behavior of adolescents. *Behav Res Methods*. 2007;39(2):259-66.
  23. New JP, Bakerly ND, Leather D, Woodcock A. Obtaining real-world evidence: the Salford Lung Study. *Thorax*. 2014;69(12):1152-4.
  24. Wilk N, Wierzbicka N, Skrzekowska-Baran I, Mocko P, Tomassy J, Kloc K. Study types and reliability of Real World Evidence compared with experimental evidence used in Polish reimbursement decision-making processes. *Public Health*. 2017;145:51-8.
  25. Li XQ, Zhang H, Li XW. [Study on reference laboratory diagnostic index of liver-fire ascending syndrome]. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2001;21(3):190-2.
  26. Chiang PJ, Li TC, Chang CH, Chen LL, Lin JD, Su YC. SEED: the six excesses (Liu Yin) evaluation and diagnosis scale. *Chin Med*. 2015;10:30.

27. Jiao Y, Liu J, Jiang L, Liu Q, Li X, Zhang S, et al. Guidelines on common cold for traditional Chinese medicine based on pattern differentiation. *J Tradit Chin Med.* 2013;33(4):417-22.
28. Chotirmall SH, Al-Alawi M, Mirkovic B, Lavelle G, Logan PM, Greene CM, et al. Aspergillus-associated airway disease, inflammation, and the innate immune response. *Biomed Res Int.* 2013;2013:723129.
29. Chen RQ, Wong CM, Cao KJ, Lam TH. An evidence-based validation of traditional Chinese medicine syndromes. *Complement Ther Med.* 2010;18(5):199-205.
30. Chen Z, Wang P. Clinical Distribution and Molecular Basis of Traditional Chinese Medicine ZHENG in Cancer. *Evid Based Complement Alternat Med.* 2012;2012:783923.

## Tables

Table 1: characteristics of individuals with bronchiectasis				
Variable	Male	Female	Total	P Value***
N	445	668	1113	0.001
Age, year	57.03±14.54	65.31±12.55	64.68±14.1	0.001
Duration, day	10.03±5.82	12.23±8.2	12.06±8.06	0.115
Married, yes (%)	415(93.26%)	613(91.77%)	1028(92.36%)	0.488
Ethnic, han (%)	417(93.71%)	638(95.51%)	1055(94.79%)	0.414
Entrance*, (%)	439(98.65%)	665(99.55%)	1104(99.19%)	0.315
Outcome**, (%)	440(98.88%)	659(98.65%)	1099(98.74%)	0.364
Note: *entrance from outpatient clinic, **outcome to include improved or cured, ***difference analyses for variables between male and female.				

Table 2: Distribution of traditional Chinese medicine syndrome pattern for bronchiectasis				
ID	TCM syndrome type	TCM syndrome pattern	Frequency	Percent (%)
1	Shi	Tan_Re_Yong_Fei	405	36.39
2		Tan_Zhuo_Zu_Fei	144	12.94
3		Gan_Huo_Fan_Fei	129	11.59
4		Feng_Re_Fan_Fei	126	11.32
5		Feng_Han_Xi_Fei	19	1.71
6		Tan_Yu_Zu_Fei	6	0.54
7		Re_Du_Yong_Fei	5	0.45
8		Qi_Zhi_Xue_Yu	2	0.18
9	Xu	Fei_Yin_Xu	203	18.24
10		Fei_Qi_Xu	13	1.17
11		Qi_Xue_Kui_Xu	13	1.17
12		Fei_Shen_Qi_Xu	12	1.08
13		Fei_Shen_Qi_Yin_Liang_Xu	7	0.63
14	Mix	Fei_Pi_Qi_Xu_Tan_Shi_Yun_Fei	16	1.44
15		Fei_Shen_Qi_Xu_Tan_Re_Yong_Fei	8	0.72
16		Fei_Shen_Qi_Xu_Tan_Shi_Yun_Fei	4	0.36
17		Fei_Pi_Qi_Xu_Tan_Re_Yong_Fei	1	0.09
Total			1113	100
Note: TCM-traditional Chinese medicine				

Table 3: Distribution of traditional Chinese medicine syndrome element for bronchiectasis in total sample				
ID	TCM syndrome element type	TCM syndrome element	Frequency	Percent (%)
1	Pathogenesis	Huo	674	22.25
2		Tan	584	19.28
3		Yin_Xu	210	6.93
4		Feng	145	4.79
5		Qi_Xu	74	2.44
6		Shi	20	0.66
7		Han	19	0.63
8		Xue_Xu	13	0.43
9		Xue_Yu	8	0.26
10		Du	5	0.17
11		Qi_Zhi	2	0.07
12	Location	Fei	1098	36.25
13		Gan	129	4.26
14		Shen	31	1.02
15		Pi	17	0.56
Total			3029	100

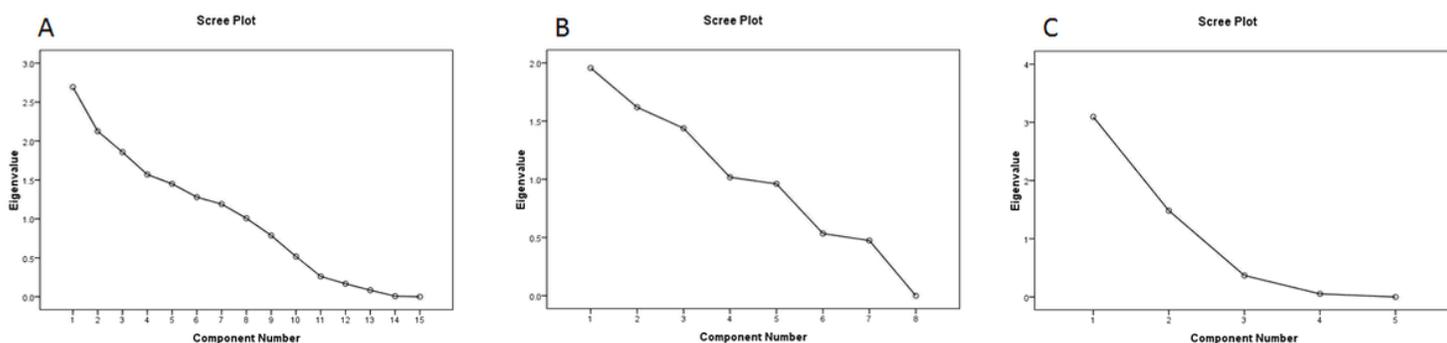
Note: TCM-traditional Chinese medicine

Table 4: Common factors and their corresponding traditional Chinese medicine syndrome elements of interpretation of cause, and location of disease			
Group	Common factor	TCM syndrome element variable of interpretation of cause	Location of disease
Entire	F1	Qi_Xu(0.482), Shi(0.947)	Pi(0.97)
	F2	Qi_Xu(0.399), Xue_Xu(0.987)	Fei(0.962)
	F3	Huo(0.838), Tan(0.5), Yin_Xu(0.931)	Gan(0.226)
	F4	Qi_Zhi(0.869), Xue_Yu(0.856)	Fei(0.247)
	F5	Qi_Xu(0.73)	Shen(0.978)
	F6	Feng(0.875), Han(0.742)	
	F7	Huo(0.22), Tan(0.713)	Gan(0.891)
	F8	Du(0.994), Tan(0.756)	
Shi	F1	Feng(0.862), Han(0.733), Tan(0.649)	Fei(0.399)
	F2	Han(0.256), Huo(0.601), Tan(0.73)	Gan(0.858)
	F3	Huo(0.268), Qi_Zhi(0.85), Xue_Yu(0.856)	
	F4	Huo(0.299)	Gan(0.217), Fei(0.911)
Xu	F1	Qi_Xu(0.866), Yin_Xu(0.725)	Fei(0.979), Shen(0.228)
	F2	Xue_Xu(0.979), Yin_Xu(0.562)	Fei(0.979)
Note: values in parentheses are results of factor load matrix after rotation transformation, factor load values that were positive and larger or equal to 0.20			

Table 5: Association rule analysis for traditional Chinese medicine syndrome element on bronchiectasis						
Group	Consequent	Antecedent	Support %	Confidence %	Lift	
Entire	Huo	Gan	11.59	100	1.651	
	Huo	Gan and Fei	11.59	100	1.651	
	Huo	Feng	13.028	86.897	1.435	
	Huo	Feng and Fei	13.028	86.897	1.435	
	Fei	Huo	60.557	100	1.014	
	Fei	Tan	52.471	100	1.014	
	Fei	Tan and Huo	37.197	100	1.014	
	Fei	Yin_Xu	18.868	100	1.014	
	Shi	Huo	Gan	15.431	100	1.257
		Huo	Feng	17.344	86.897	1.092
Fei		Tan and Huo	14.197	81.067	1.054	
Xu	Fei	Yin_Xu	84.677	100	1.055	

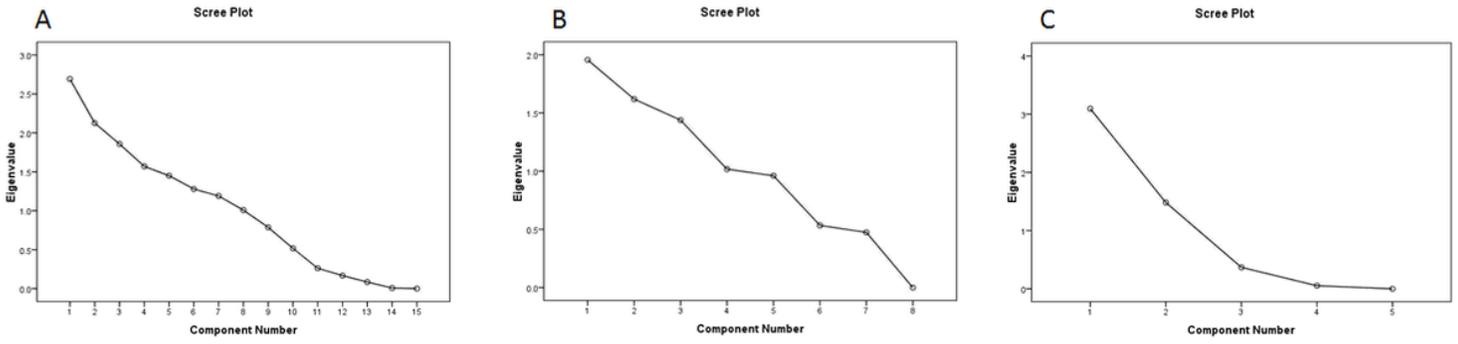
Note: Support% >20% and confidence%>80%

## Figures



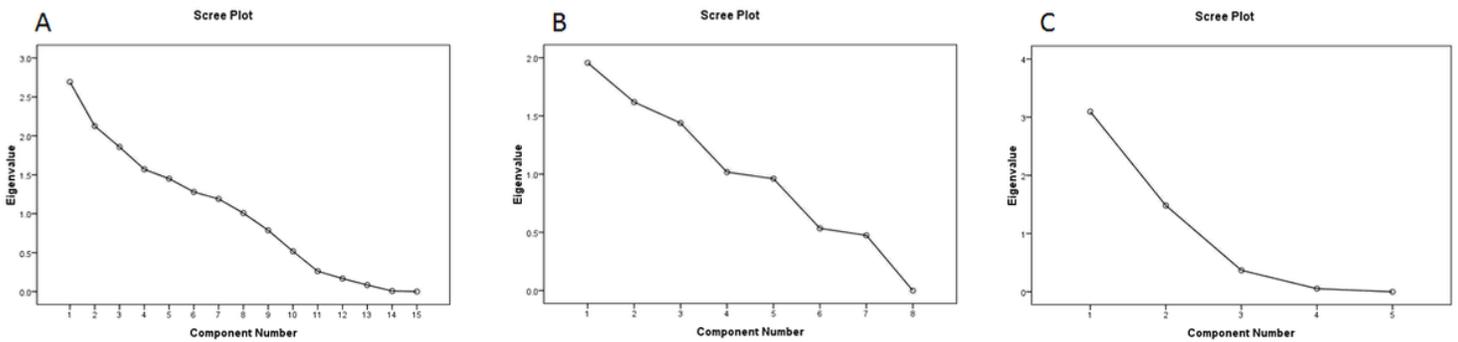
**Figure 1**

Scree plot of characteristic root value of common factors. A: Scree plot of characteristic root value of common factors for total sample; B: Scree plot of characteristic root value of common factors for Shi TCM syndrome group; C: Scree plot of characteristic root value of common factors for Xu TCM syndrome group.



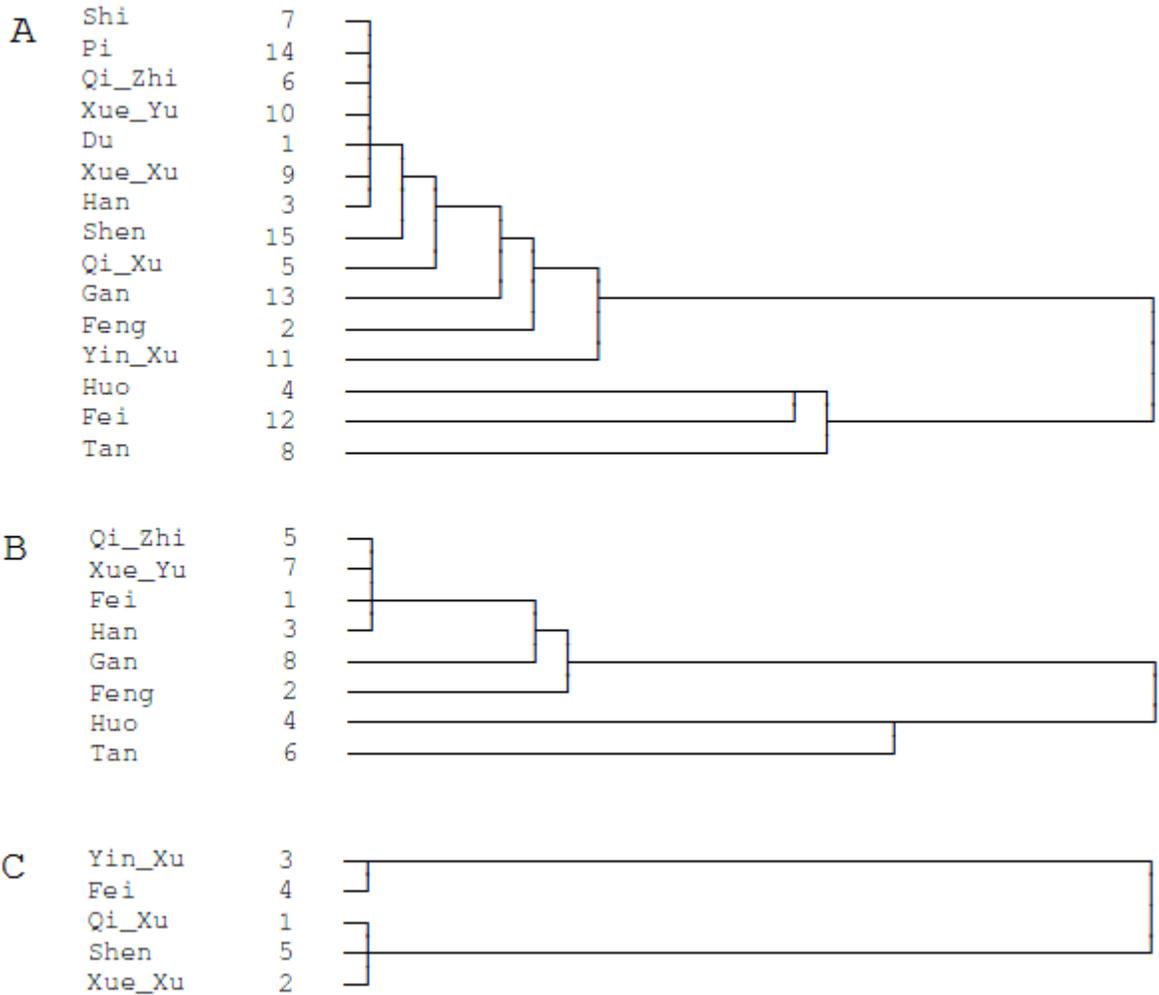
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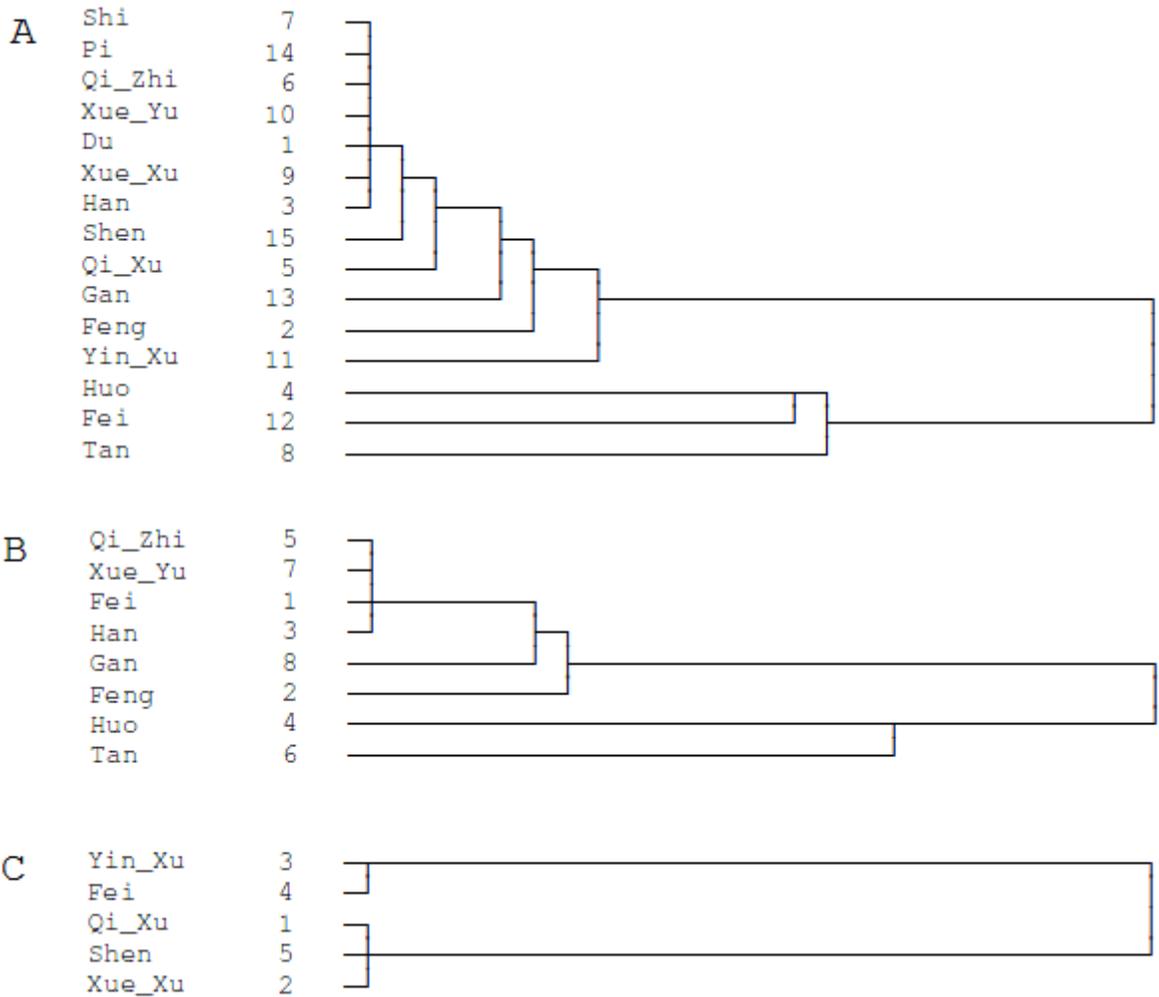
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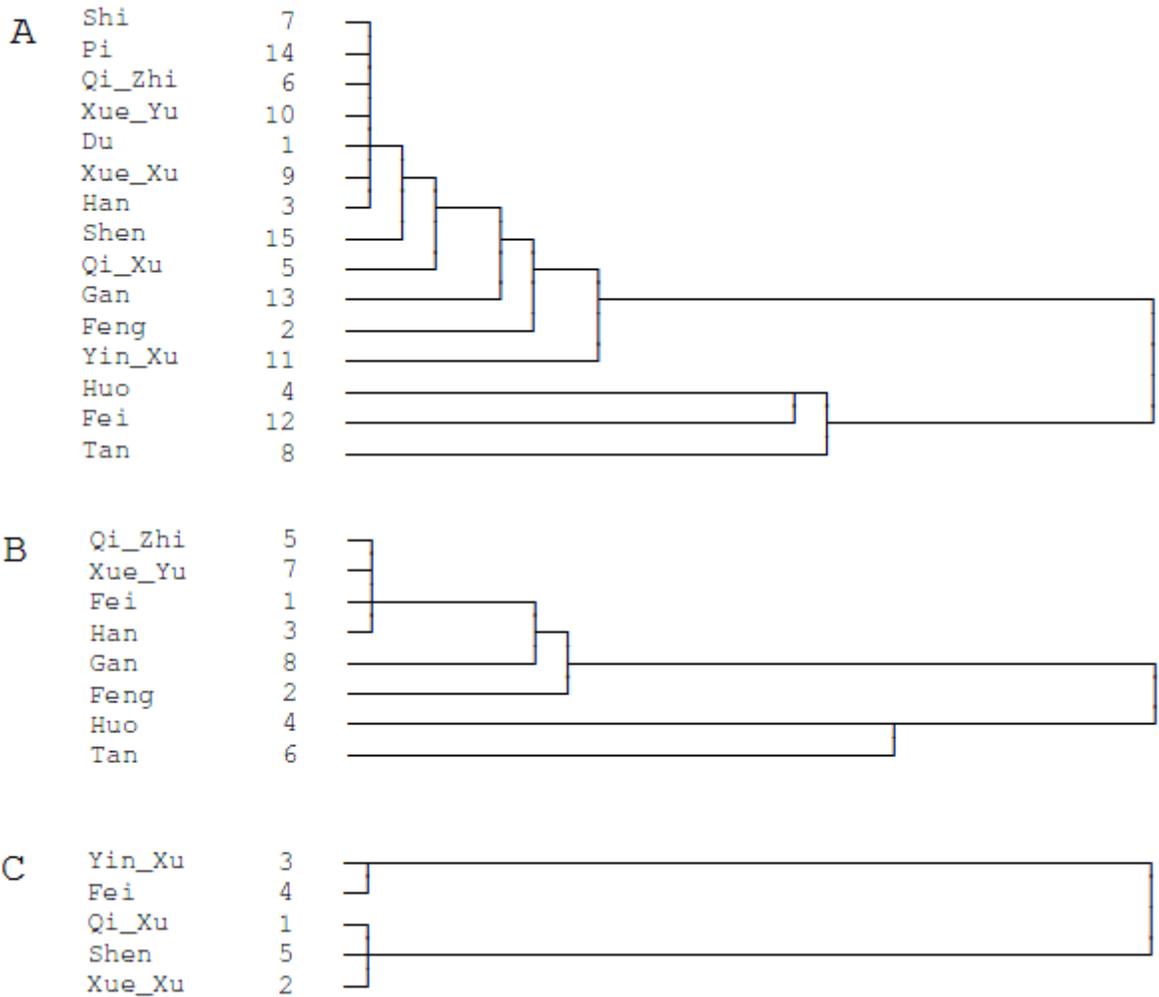
**Figure 2**

Cluster analysis for traditional Chinese medicine (TCM) syndrome element on bronchiectasis. A: results of cluster analysis for TCM syndrome element in total sample; B: results of cluster analysis for TCM syndrome element in Shi TCM syndrome group; C: results of cluster analysis for TCM syndrome element in Xu TCM syndrome group.



**Figure 2**

Cluster analysis for traditional Chinese medicine (TCM) syndrome element on bronchiectasis. A: results of cluster analysis for TCM syndrome element in total sample; B: results of cluster analysis for TCM syndrome element in Shi TCM syndrome group; C: results of cluster analysis for TCM syndrome element in Xu TCM syndrome group.



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Cluster analysis for traditional Chinese medicine (TCM) syndrome element on bronchiectasis. A: results of cluster analysis for TCM syndrome element in total sample; B: results of cluster analysis for TCM syndrome element in Shi TCM syndrome group; C: results of cluster analysis for TCM syndrome element in Xu TCM syndrome group.