Classification of Non-Specific Chronic Low Back Pain on Symptoms and Signs Based on Traditional Chinese Medicine

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A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Epidemiology

Prince of Songkla University

2010

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Academic year 2010

Abstract

This thesis consists of 3 studies. The abstract of each study is given here with

Study 1

Title: Application of Delphi technique in identification of appropriate screening questions for chronic low back pain from Traditional Chinese Medicine experts' opinions

Objective: The goal of the present study was to obtain a standard list of Traditional Chinese Medicine (TCM) symptoms and signs for screening chronic low back pain (CLBP) from a group of experts and to assess agreement and consistency among their opinions on the items of a questionnaire.

Design, settings, and subjects: The study design involved three rounds of modified Delphi technique, and it was carried out by 13 experts in orthopedics, massage, and acupuncture working in four hospitals affiliated with Yunnan University of Traditional Chinese Medicine, China.

Outcome measures: The outcome was measured on the 5-score Likert-scale self-administered checklists.

Results: A review of eight textbooks identified 12 pain characteristics, 11 associated factors, and 25 physical and tongue diagnostic expressions as important factors in the TCM diagnosis of CLBP. These 48 diagnostic characteristics were rated by 13 experts as "not important" to "very important" on a scale of 1-5. After three rounds of rating, 13 characteristics were eliminated from the list, with the final numbers for each group being 8, 11, and 16, respectively. Seven items based on Western medicine were also added by the experts. The intra-class correlation (ICC) coefficient for agreement among the experts was 0.2 at the end. Intra-rater, between rounds, consecutive pair-wise median kappa values were 0.53 and 0.66. Analysis of variance using items appearing in all three rounds revealed significant effects of expert and group of symptoms and signs ($p < 0.001$) and nonsignificant differences among scores of the same expert in the three rounds ($p = 0.97$). Mean score of physical and tongue expressions were significantly ($p < 0.001$) lower than that of all other groups of symptoms and signs.

Conclusions: Modern TCM experts have de-emphasized the items on physical and tongue expressions and have adopted instead those from Western medicine. Intra-expert agreement across items was low, and each expert tended to stick to her/his original opinions.

Study 2

Title: Factor analysis on symptoms and signs of chronic low back pain based on Traditional Chinese Medicine theory

Objective: To use factor analysis to explore patterns of symptoms and signs from patients with chronic low back pain (CLBP) based on the Traditional Chinese Medicine (TCM) theory.

Design, settings, and subjects: A cross-sectional study was carried out among 513 patients with CLBP in four hospitals affiliated with Yunnan University of Traditional Chinese Medicine, China.

Outcome measures: 31 symptoms and signs on a 6-level self-report questionnaire.

Results: Four factors were extracted. They were eventually interpreted as (1) "qi and/or blood stagnation", which includes 8 items such as piercing pain; activity limited by feeling of local heaviness, lumbar and flank stiffness with bending limitation and purple tongue etc., (2) "cold/damp", which has 7 items for example cold/damp pain, pallid face and greasy coating, etc., (3) a part of "kidney deficiency", which includes 2 items - "dull pain and

recurrent vague pain", (4) "warmth/heat", which is related to 3 items viz. yellow tongue coating. The four factors accounted for 12.7%, 8.2%, 8.2% and 7.8% of the total variance, respectively. There are 7 items with uniqueness over 0.8.

Conclusions: Four TCM major groups of pathophysiology could explain 37% of variance of 31 symptoms and signs of the CLBP patients. Thirteen items were not groupable.

Study 3

Title: Cluster analysis for patients grouping

Methodology: The data set used in the second study was further analyzed using cluster analysis. A dendrogram was obtained from hierarchical cluster analysis. The number of clusters was identified from k-means cluster analysis. Means factor score for each factor was computed for each cluster of subjects to characterize the groups by underlying symptoms and signs. Cluster was then tabulated against socio-ecomic characteristics and other clinical settings. Finally, multinomial logistic regression was used to adjust for confounders.

Results: Four clusters was identified: Cluster 1 was mostly suffering cold/damp, cluster 2 had no predominating factors of symptoms and signs, cluster 3 was by qi and/or blood stagnation and warmth/heat, cluster 4 was by kidney deficiency. Independent predictors for the clusters included hospital, age, education and smoking but not gender or drinking.

Conclusion: Four of main underlying TCM pathophysiology explained 4 groups on clusters. Within the study sample of CLBP patients, socio-economic are other clinical setting may determine what group the patient will belong to.

Conclusion of the whole thesis: Different TCM experts had their own independent opinions on the checklist for symptoms and signs of CLBP. Using the most acceptable list, we were able to document that four main underlying factors explain 37% of the pathophysiology. Four clusters of patients were classified by these underlying factors and they were associated with various socio-economic characteristics.

Key words: chronic low back pain, Traditional Chinese Medicine, Delphi technique, factor analysis, symptoms and signs, cluster analysis

Structure of this thesis

Chapter 1 starts with introduction of definition of chronic low back pain used in this thesis, perspective of western and Traditional Chinese Medicine (TCM) on chronic low back pain (CLBP). Modern research techniques such as the Delphi method, factor analysis and cluster analysis, which are used in this thesis, are reviewed.

Chapter 2 is the result of the first study using Delphi technique to develop a checklist of symptoms and signs, which were subsequently used in the following chapter. This chapter was published in the Journal of Alternative and Complementary Medicine. (study 1)

Chapter 3 is based on data collection of the 513 real patients to identify the construct of the symptoms and signs using factor analysis. (study 2)

Chapter 4 continues to analyze the data by using cluster analysis to group the subjects into clusters or groups. Determination of the clusters based on socio-demographic and other clinical data were finally identified. (study 3)

Chapter 5 concludes all findings and gives recommendations.

ACKNOWLEDGEMENTS

It is a pleasure to thank the many people who made this thesis possible.

I would like to express deep and heartfelt gratitude to my supervisor, Professor Virasakdi Chongsuvivatwong M.D., Ph.D., Head of the Epidemiology Unit, Medicine Faculty, Prince of Songkla University, for his continuous support in the Ph.D program. Professor Virasakdi always guided me patiently and gave me detailed and constructive comments. He not only taught me how to generate the meaningful hypothesis in public health, but also guided me to synthesize own my novel viewpoints of the research. His wide knowledge and his logical way of thinking have been of great value for me. His ideals and concepts have had a remarkable influence on my entire career in the field of health research.

I am grateful to my co-advisor, Dr. Alan Geater, whose enthusiasm, inspiration, and great efforts to explain things clearly and simply, helped to make statistics fun for me.

I wish to express my warm and sincere thanks to my colleagues and my classmates for their support and kind cooperation throughout my study period.

My warm thanks are due to the teaching staff of Epidemiology Unit of Prince of Songkla University, who gave me new understanding of Epidemiology, Research Methodology and Statistics.

I wish to thank all my best friends, for helping me get through the difficult times and for all the emotional support, comradeship, entertainment and caring they provided.

Lastly, and most importantly, I wish to thank my father and my family. They bore me, raised me and supported me at all times. To them I dedicate this thesis.

Xiong Guangyi

LIST OF ABBEVIATIONS

ANOVA	Analysis of Variance
BMI	Body Mass Index
CAM	Complementary and Alternative Medicine
CFA	Confirmatory Factor Analysis
CI	Confidence Interval
CLBP	Chronic Low Back Pain
CT	Computer Tomography
EFA	Exploratory Factor Analysis
ICC	Intra-class Correlation Coefficient
ICD	International Classification of Disease
LBP	Low Back Pain
LR-test	Likelihood Ratio test
MRI	Magnetic Resonance Imaging
RRR	Ratio of Relative Risk
SS	Sum of Squares
TCM	Traditional Chinese Medicine

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Chapter 1

Literature review

1. Background

In order to tackle the problem of classification of chronic low back pain (CLBP), the present study reviews Traditional Chinese Medicine (TCM) literatures on a CLBP to obtain a list of candidate symptoms and signs, and then we will use a qualitative method of knowledge assembling and organization, namely "Delphi method" to refine the list. After data collection from patients to group signs and symptom in the list two major statistical methods (factor analysis and cluster analysis) are applied to the data. They are briefly defined here.

1.1 Definitions

1.1.1 Low back pain (LBP)

LBP manifests itself as pain, muscle tension, or stiffness; localized below the costal margin and above the inferior gluteal folds; with or without leg pain; and is not attributed to recognizable pathology. According to the duration of pain, it is

classified as acute pain (< 4 weeks), sub-acute pain (4 weeks - 12 weeks) and chronic pain (>12 weeks).[1]

LBP with least and moderate intensity and pain duration has an annual incidence in the adult population of 10-15%, and a point prevalence of 15-30%. The prevalence rises with increasing age up to 65 years, after which age it drops off for unknown reasons. Lifetime prevalence of LBP exceeds 70%, with peak point prevalence between ages 35 to 55 years. Furthermore, recurrent episodes of LBP occur very frequently whereas a considerable number of people suffer permanently from LBP. Chronic LBP (CLBP) is present in 3% to 7% of the population in western industrialized countries and is one third to half of LBP.[2]

The total costs of LBP to industry in 1988 in the United States were estimated to be between US$26.8 and US$ 56 billion. In the Netherlands, the total costs of absenteeism and disablement due to back pain and the indirect costs - were estimated at US$ 3.1 billion and US$ 1.5 billion, respectively, in 1991, while the total direct medical costs were estimated at US$ 368 million. Most of costs in CLBP patients were spent on repeated treatments and absenteeism.[3]

Above all, CLBP is the main parts of LBP. CLBP and related disabilities are major public health problems and a major cause of medical expenses, absenteeism and disablement.[1]

1.1.2 Traditional Chinese Medicine (TCM) symptoms and signs

TCM is an ancient medical system. It is composed of thousands of clinic experiences, cultural tradition and philosophical concepts in China.

The core of TCM theory is holistically integrated whole namely, the human body as an integrated whole and inseparable from nature. Each part of the body is seen as a complete system. Basically, human body is composed of three concentric cylinders. The first and innermost cylinder contains the internal organs, known as Visceral systems. The second cylinder symbolizes the flow of energy or qi through the body, or the meridian systems. The third and outermost cylinder is the surface of the body which serves as the environmental interface and the signalling system of inner dysfunction.

TCM postulates that any manifestation of disease is considered a sign of imbalance in the Visceral systems or meridian systems. The TCM therapeutists collect symptoms and signs of the surface of the body with four methods including (1) observation, (2) listening and smelling, (3) interview of symptoms, (4) palpation and pressure. They classify the diseases by those four methods using in Chinese herbal medicine, acupuncture, massage and qigong, etc.

LBP is defined, similarly in TCM, as pain, muscle tension, or stiffness; localized below the costal margin and above the inferior glustea; folds; with or without leg pain. It is

classified into syndromes according to different symptoms and signs, such as the cold/damp LBP; the kidney deficiency LBP. An understanding of syndrome would provide new avenues for interventions to minimize the impact of symptoms on health-related outcomes.

There have been a few studies trying to classify LBP in the western medicine prospect.[4-6] It is important to have a similar study examining whether TCM could also have the same role in this disease classification. Moreover, it is useful to link the group of symptom and sign with concurrent disability so that priority could be set in management of those symptoms and signs.

This chapter consists of reviewing existing data on how western medicine experienced in classification of LBP. A brief TCM theory on LBP is also reviewed in order to come up with group of symptoms and signs based on TCM theory. After that, relevant candidate research methodology used for disease classified qualitative aspect, such as Delphi technique and quantitative analysis such as factor analysis and cluster analysis are reviewed.

1.2 Western medicine perspective in CLBP

1.2.1 Diagnosis:

Of all adults complaining of back pain, only around 5% can be classified as having nerve root pain (using strict diagnostic criteria) with the remainder having back pain with or without

referred leg pain, which is commonly referred to as non-specific low back pain.[7] Of those who develop acute LBP, 30% develop chronic LBP. The past 15 years have seen an intensive research effort to identify effective treatments and management strategies for low back pain.[8] In spite of the small number of pathological conditions that can give rise to back pain, most cases (85%) are classified as "non-specific" because a definitive diagnosis cannot be achieved by current ratiological methods.[9]

Even when a specific diagnosis is made, the validity of diagnosis can often be questioned. This leaves a diagnostic and management vacuum. This situation commonly results in the "signs and symptoms" of the disorder being treated without consideration for the underlying basis or mechanism for the pain disorder. It is well recognized that the classification of chronic low back pain (CLBP) disorders into homogenous groups, and the application of specific interventions tailored for these groups is likely to enhance treatment efficacy. [10] The etiology of low back pain may be difficult to determine at times because of the number of diverse anatomic structures located in or near the low back region.

It is established that LBP is a multi-dimensional problem.[11,12] These dimensions consist of pathoanatomical, neurophysiological, physical and psychosocial factors.[7] Classification of CLBP pain disorders can be based on the mechanism(s) underlying and driving the disorder, such as lumbosacral (LS) radiculopathies, spondylolisthesis, vertebral compression fractures, ankylosing

spondylitis, referred pain from the pelvic girdle, discities (prolapsed disc) and vertebral osteomyelities, psoas abscess and arachnoiditis, diffuse idiopathic, skeletal hyperostosis and cancer pain etc. [13] Back and spine impairments are the most common impairment among young and middle-aged people.[14]

Although history, clinical examination, and radiological studies may be able to provide sufficient information for diagnosis of a pain generator causing LBP, the need for specific diagnoses in several cases still remains. Diagnostic interventions performed under fluoroscopic guidance by an experienced and knowledgeable practitioner are required for patients who present a diagnostic challenge.[15] LBP, especially CLBP disorders, must be considered within a biopsychosocial framework. The presence and dominance of the potential pathoanatomical, physical, neurophysiological, psychological and social factors that may impact on these disorders is different for each individual with CLBP.

1.3 Traditional Chinese Medicine perspective on LBP

Traditional Chinese Medicine is based on a number of philosophical concepts, one of which postulates that any manifestation of disease is considered a sign of imbalance between the Yin and Yang force within the body. Vital energy (qi and blood) circulates throughout the body along the so-called meridians, which have either yin or yang characteristics.

The other one is nature consisting of five basic elements: fire, wood, water, metal and earth. Body and mind have their corresponding parts. This system is also called the Visceral syndrome Differentiation Theory, which classifies five systems: heart system, liver system, kidney system, lung system and spleen system. These five systems are analogous of the five nature elements viz. heart system is analogous with fire, kidney with water, liver with wood, lung with metal and spleen with earth.

Another important theory is the Eight Principle Syndrome Differentiation Theory. The Eight Principle Syndrome Differentiation Theory classifies syndromes, using 4 different dimensions: yin vs yang, exterior vs interior, cold vs heat and deficiency vs excessive states.

These theories are clinical reasoning tools for classifying specific health states and syndromes, and for diagnosing illnesses. By using these two classification systems on various syndromes, diagnosis of imbalance of these systems is made. Subsequently, treatment can be planned.

Regarding to TCM, the low back region is under control of the kidney system. The influence of kidney however flows throughout the whole body affecting all parts. Bladder, for example is in the flow path.

1.3.1 The TCM diagnosis of CLBP

TCM clinical data collections include (1) observation, (2) listening and smelling, (3) interview of symptoms, (4) palpation and pressure.

Diagnosis of disease by TCM is based on these clinical data collection combined with the three cylinders theory (mentioned in 1.1.2). The explanations, however, contain a lot of subjectivity of clinician. TCM doctors use 4-diagnosis to collect medical records and they consider that everything is correlated. For example there is an obvious correlation between skin colour and the pattern of disharmony. Red colouration usually indicates stagnation or heat, brown implies more chronic stagnation, purple means stagnation of blood, and pale or even bluish indicates cold. This situation commonly results in the "symptoms and signs" of the disorder being treated without consideration for the underlying basis for the pain disorder. Since the strongest evidence for efficacy is largely empirical in nature, this leaves a diagnostic and management vacuum.

The pain in TCM is considered as a blockage of meridians or disorders of Visceral Syndrome Differentiation systems. Lower part of the back is the home of the kidney and it is traversed by the Bladder meridians. Therefore, LBP, being in lower part of the back, would be the result of blockage of qi and /or blood of the Bladder meridians, or disorders of kidney system. These can be caused by three primary factors, one is derangement of either

wind, cold and damp, the other is disorders of the emotion and another is injury. This conception is different from western medicine which uses muscle, intervertebral disc and nerves to explain the symptoms. [16]

When these physical sensations are chronic, there are clearly manifestations of some disharmony and imbalance. Further, there are in addition to being an integral modality within the practice of TCM.

Now in mainland China, all colleges of TCM have 50-60% course within modern medicine. In Western Country, 60% of doctors practicing Chinese acupuncture and TCM are western medicine doctors as well. Whereas, more than 85% of practitioners considered symptoms or signs were "very" or "exceptionally" important by TCM for making a diagnosis.[17] They record and describe patient's pain characteristics or location, a cause that relieved or exacerbated the pain, history of pain onset, and pratitioner's palpation findings in TCM term.[18]

Classical categorization of LBP from the TCM point of view

According to TCM, LBP can be divided into four groups:

1 寒湿腰痛：腰部冷痛重着，转侧不利，逐渐加重，每遇阴天或腰部感寒后加剧，痛处喜温，体乏力，或肢末欠温，食少腹胀，舌淡体大，苔白腻而润，脉像沉紧或沉迟。

1 Cold/Damp LBP: This group is characterized by: dull low back pain, movement-induced pain, pain worsened by cold, pain relieved

by warmth, body fatigue, feeling of cold in the extremities, weakness of appetite, indigestion and flatulent, large tongue with lightened colour and whiter and oily surface, deepened, tightened or delayed pulse

2 温热腰痛：腰髋驰痛，牵制拘争，痛处伴有热感，每于热天或腰部着热后痛剧，遇冷痛减，口渴不欲饮，尿色黄赤，或午后身热，微汗出，舌红苔黄腻，脉濡数或洪数。

2 Warm and Heat LBP: This group is characterized by: throbbing pain on waist and hip area, local feeling of tightness and burning sensation, worsened by hot weather or local heat, relieved by cooling, thirsty but does not want to drink, deep yellow or red urine, afternoon fever and tiny drop perspiration, red tongue colour with yellow moistened surface, fast but jerky or strong pulse

3 瘀血腰痛：痛处固定，或胀痛不适，或痛如锥刺，日轻夜重，或持续不解，活动不利，甚则不能转侧，痛处拒按，面晦唇暗，舌质阴青或有瘀斑，脉多弦涩或细数。病程迁延，常有外伤，劳损史。

3 Qi and/or Blood Stagnation LBP: This group is characterized by: fixed pain, or radiating and swelling pain, or pin-pick like pain, mild in day and worsening in night, or continuing pain, unable to move or rotate, unbearable to pressure on the pain area, gloomy face and dull lip, slightly blue tongue or with petechia, non-smooth and tense or thread rapid pulse, lengthy course of pain, usually accompanying trauma and injury.

4 肾虚腰痛：腰痛以酥软为主，喜按喜揉，腰膝无力，遇劳更甚，卧则减轻，常反复发作。偏阳虚者，则少腹拘争，面色恍白，手足不温，舌淡，脉沉细；偏阴虚者，则心烦失眠，口燥咽干，面色潮红，手足心热，舌红少苔，脉弦细数。

4 Kidney Deficiency LBP: dull pain, pain relieved by pressure and massage, fatigue at leg and knee, pain worsened by movement, relieved by bed rest, often recurring. Subgroups of these include yang deficiency and yin deficiency. Yang deficiency is associated with tightening of lower abdomen, pale face, feeling of cold in the extremities, breathing with tiredness and fatigue, lighted colour tongue, deepened and thin pulse; Yin deficiency is associated with perturbed and insomnia, dry mouth and throat, flashing red face, heat in the central part of feet and hands, red tongue and surface with little, tense and thin pulse.

The above clinical descriptions are taken from classic TCM teaching textbook. With clinical epidemiology and modern statistics, there is an opportunity to examine in-depth the grouping of domain of symptoms of LBP. It may come up with a new insight on the nature of these diseases.[19]

1.3.2 TCM classification of CLBP

Current approaches or models used for the diagnosis and classification of CLBP have continued to only refer to a single dimension of the disorders of the lower back pain, limiting their validity and integrated whole. Because of this, even when a specific diagnosis can been made, there is still a need to

classify the disorder based on the TCM theories that drive the pain disorder to ensure appropriate management.

One research in USA investigated 50 acupuncturists who practiced TCM. They classified patients with CLBP into 8 syndromes: (1) qi and/or blood stagnation, (2) any of four types of kidney deficiency and (3) wind/cold/damp, etc.[20] But there are only 4 kinds of syndromes described in Chinese textbooks. So TCM about CLBP symptoms and signs is no clearly and lack of scientific basis for criterion of classification standard.

The primary aim of this research is to classify CLBP latent symptoms and signs factors and cluster correlated subgroup syndromes. After getting the results, we will use it as outcome to measure the efficacy of TCM treatment and construct quality of life result for CLBP.

1.4 The Delphi method

The names "Delphi" obviously comes from the Oracle of Delphi. She sang her predictions, which she received from Gaia. The Delphi method is a form of evaluation. It recognizes human judgment as legitimate and useful inputs in generating forecasts.[21]

The Delphi method recognizes the value of expert opinion, experience and intuition and allows using the limited information available in these forms, when scientific knowledge is lacking.

Questions are usually formulated as hypotheses, and experts' state the time when they think these hypotheses will be fulfilled. Each round of questioning is follow by the feedback on the preceding round of replies of other members of the group. It is believed that during this process the range of the answers will decrease and the group will converge toward the "correct" answer. After several rounds the process is complete and the median scores determine the final answer.

In general, the Delphi method is useful in centralizing the opinions in the panel. It avoids the negative effects of face-to-face panel discussions and solves the usual problems of group dynamics, and the panel director controls the interactions among the participants by processing the information and filtering out irrelevant content. At the same time, it allows them to freely express their opinions, encourage open critique and admitting errors by revising earlier judgments.[22]

In this study we will use modified Delphi method by consulting the panel of therapists and experts on symptoms of CLBP based on TCM. It will help us judge the main of domains factor in CLBP symptoms and construct pools of symptoms and signs of CLBP based on TCM.

1.4.1 Modified Delphi method

1.4.2 Historical Background

The Delphi method aims to assess the direction of long-range trends, with special emphasis on science and technology, and their

probable effects on society. The first applications of the Delphi method carried out at the RAND Corporation was illustrated in the publication by Gordon and Helmer (1964) to forecast the impact of technology on warfare.

In terms of technology forecasting, Levary and Han (1995) stated the objective of the Delphi method as to combine expert opinions concerning the likelihood of realizing the proposed technology as well as expert opinions concerning the expected development time into a single position. Later on, the notion of cross impacts was introduced to overcome the shortcomings of this simplistic approach.

Since the 1950s several research studies have used the Delphi method, particularly in public health issues (such as, policies for drug use reduction and prevention of AIDS/HIV) and education areas. The Delphi method is an exercise in group communication among a panel of geographically dispersed experts It has been used since then in various national foresight processes to design roadmaps of future technological developments.[23]

The Delphi method has traditionally been a technique aimed at building an agreement, or consensus about an opinion or view, without necessarily having people meet face to face, such as through surveys, questionnaires, emails etc. This technique, if used effectively, can be highly efficient and generate new knowledge.

To build consensus, the Delphi method often uses the Hegelian dialectic process of thesis (establishing an opinion or view), antithesis (conflicting opinion or view) and finally synthesis (a new agreement or consensus), with synthesis becoming the new thesis. All participants in the process shall then either change their views to align with the new thesis, or support the new thesis, to establish a new common view. The goal is a continual evolution towards 'oneness of mind', or consensus on the opinion or view.

1.4.3 Application of the Delphi method

The Delphi method is used to apply:

1 Forecasts a specific, single-dimension future issue

2 Consensus building

3 Avoid groupthink and spiral of silence

4 Generating creative ideas

1.4.4 The Basic of the Delphi Method

The basic of the Delphi Method describes the following ten steps for the Delphi method: [24]

1 Formation of a team to undertake and monitor a Delphi on a given subject

2 Selection of one or more panels to participate in the exercise customarily, the panelists are experts in the area to be investigated.

3 Development of the first round Delphi questionnaire

4 Testing the questionnaire for proper wording (e.g., ambiguities, vagueness)

5 Transmission of the first questionnaires to the panelists

6 Analysis of the first round responses

7 Preparation of the second round questionnaires (and possible testing)

8 Transmission of the second round questionnaires to the panelists

9 Analysis of the second round responses (Steps 7 to 9 are reiterated as long as desired or necessary to achieve stability in the results.)

10 Preparation of a report by the analysis team to present the conclusions of the exercise

A number of questions need to be asked before making the of selecting or ruling out the Delphi technique:

What kind of group communication process is desirable in order to explore the problem at hand?

Who are the people with expertise on the problem and where are they located?

What are the alternative techniques available and what results can reasonably be expected from their application?

1.4.5 Strengths and limitations

Strengths include

1 Rapid consensus

2 Participants can reside anywhere in the world

3 Coverage of wide range of expertise

4 Avoid groupthink

5 Forecasts the specific, single-dimension question

Limitations include

1 Cross impact is neglected in the original form.

2 Does not cope well with paradigm shifts.

3 Success of the method depends on the quality of participants.

4 One should watch out for:

Imposing preconceptions or monitor's own view

Ignoring and not sufficiently investigating disagreements

Underestimating the demanding nature of the Delphi method

The key problems reported include: poor internal consistency and reliability of judgements among experts, and therefore low reproducibility of forecasts based on the results elicited; sensitivity of results to ambiguity and respondent reactivity in the questionnaires used for data collection; difficulty in assessing the degree of expertise held by participating experts. [25]

1.4.6 Assumptions of the Delphi method

1 Well-informed individual, using their insights and experience, are better equipped to predict the future than theoretical approaches or extrapolation of trends.

2 Complex problems

3 Participating experts have no history of adequate communication.

4 Experts should represent diverse backgrounds with respect to experience or expertise.

5 Disagreements are grave or politically unpleasant.

1.4.7 Application of the Delphi method to our research

After a list of symptoms and signs is generated through literature review of the standard TCM textbooks, the method will be applied.

1.5 The factor analysis to CLBP symptoms and signs

1.5.1 Factor analysis

Factor analysis is applied as a data reduction and/or structure detection method.[26]

The factor analysis is classified into exploratory factor analysis (EFA) and confirmatory factor analysis (CFA). The exploratory factor analysis (EFA) is used to summarize data by grouping together variables that are intercorelated. The direct purpose of exploratory factor analysis is to reduce a large set of variable in to a smaller number of factors so that they may be described and used easily. The confirmatory factor analysis (CFA) tests hypotheses about the structure of variables, and may follow an exploratory factor analysis or come directly from theory. The factor analysis procedures are extraction, rotation, addressing the number of factor and calculating the factor score.[27]

Factor analysis is used to define a set of latent factor that are responsible for covariance among a group of symptoms and signs. It is the most common approach for grouping symptoms and examining the relationship among a number of variables based on the matrix of correlation coefficients between the variables. In the current study, the symptom of patients with CLBP will be analyzed by exploratory factor analysis to group symptoms and signs. Later cluster analysis will be used to identify different groups of CLBP.[28]

1.5.2 History and concept

The term "symptom" refers to a single subjective indicator of disease or physical disturbance. In fact, from the Middle Ages to the late 19th century, symptoms were generally thought of as the bodily or mental phenomena that constituted specific illness. In the 20th century, it became known and accepted that underlying pathophysiologic mechanisms were responsible for the pattern of symptoms that typified different diseases. As the diagnosis of diseases became more sophisticated, symptom-based diagnostic criteria were supplanted by laboratory and imaging tests and symptoms have received less attention.[29]

However, symptom observation continues to play a role in the identification and development of diagnostic criteria for some mental illnesses and chronic diseases. Symptom observation is developed by selecting homogeneous groups of clinical.

Characteristics, primarily symptoms, and defining the diagnosis on the basis of treatment response and/or specific outcomes.

The most common approach for grouping symptoms and signs is factor this latent factor would covary more strongly with each other than they would with symptoms that are affected by a different latent factor.

The factor analysis can be executed with different methods using principal factor, principal axis factoring, least squares approach, maximum likelihood, alpha factoring and image analysis

criterion, and displays the eigenvalues and the factor loadings or eigenvectors, etc. This procedure is also called methods of extracting initial factors.

Rotation modifies the results of the initial factor solution to create a set of loadings that are more interpretable for factors or easier pattern of factor loadings, while keeping the number of factors. There are two rotation methods. One is the method of orthogonal rotation and the other is oblique rotation.

There are many distinct alternative rule to detect the number of factors include: significance tests, eigenvalue specification, criterion of substantive importance, scree-test and criteria of interpretability and invariance, etc.

If the researchers want to use one or more factors as variables for another study, they need to create factor scores. Factor score creates a set of new variables that are estimates of the factors produced by factor or rotation. It can be examined by many methods such as regression estimates, the least squares criterion, Bartlett's method of minimizing the error variance, Anderson-Rubin's method of estimates with orthogonality constraints, simple summation of variables with high factor loadings and creation of principal component scales, etc.[28]

1.5.3 Strengths and limitations

Factor analysis strengths answer the question "is the data consistent with the definition of construct it is meant to be tapping?"

Limitations is when the factor solution cannot be interpreted, the computation results are seriously limit.[21]

1.5.4 Application:

Factor analysis application tries to

1 determine how many latent variables underlie a set of items

2 explain variation among many items (e.g. 25 items or variables) by using few new variables (factors or latent variables).

3 define the substantive content or meaning of the factors (latent variables) from the items that make up those factors.

1.5.5 Assumptions:

Bivariate normal distribution for each pair of variables, and observations should be independent. Variables are determined by common factors and unique factors. Unique factors are uncorrelated with each other and with the common factors.

1.5.6 Data:

Quantitative at the interval or ratio level

Categorical data are not suitable for factor analysis. However, the technique is applicable to dichotomous, on ordinal data if the appropriate correlation method is used with some special methods of estimation.

1.5.7 Software

LISREL is a known popularly software in factor analysis, the other common software is SPSS, SAS and R, etc.

1.5.8 Sample size

Although there is general agreement that large samples are imperative for stability of factor analytic results, there is no agreement as to what constitutes large.

"at least 200 subjects"; "a good rule is to have at least 10 times as many subjects as variables"; etc.[30]

1.5.9 Reliability

It is the proportion of variance of scale attributable to a common source, presumably true scores of latent variables.

1.5.10 Internal consistency

Homogeneity of the items within a scale

If items of a scale have a strong relationship to their latent variable, they will have a strong relationship to each other.

Cronbach's alpha is the most widely used reliability index.

Alpha = 1 - error variance (the proportion of total variance scale attributable to true scores of latent variables) with range from 0 to 1, based on covariance matrix or correlation matrix.

1.5.11 Examples of similar studies with factor analysis in group of symptoms and signs

For example, in a recent study of symptoms among subjects with unexplained chronic fatigue.[31] conducted dichotomous factor analysis of 21 chronic symptoms (items). Three factors (musculoskeletal, infection and cognition-mood-sleep) emerged. The symptoms with item loading higher than 0.35 were regarded as symptoms in the group, the three factor solution accounted for 74.4% of the item variance.

1.6 The cluster analysis

The cluster analysis, also called segmentation analysis or taxonomy analysis, is a rather loose collection of statistical methods that is used to assign cases to groups (clusters).[32] Group members share certain properties in common and it is hoped that the resultant classification will provide some insight into a research topic. The classification has the effect of reducing the dimensionality of a data table by clustering the number of cases.[33]

Most cluster analysis techniques are hierarchical, i.e. the resultant classification has an increasing number of nested classes. The result resembles a phylogenetic classification.

Others are non-hierarchical methods, for example k-means clustering. The non-hierarchical cluster analysis must be specified in advance the desired number of agglomerative seeds (cluster). Initial cluster centres are chosen in a first pass of the data, then each additional iteration groups observations based on nearest distance to the mean of the cluster. Cluster centres change at each pass. The process continues until cluster means do not shift more than a given cut-off value or the iteration limit is reached.

In conclusion, cluster analysis is an exploratory technique that it is used to "discover" underlying groups of individuals who are similar in their symptoms and signs. It will be used to examine symptoms and signs patterns in the populations of CLBP and identify subgroups of individuals.[34]

1.6.1 Cluster analysis CLBP symptoms and signs

The term "cluster" suggests the formation of an aggregate of symptoms that are related to each other in a logical or predictable way. Cluster analysis groups individuals with similar symptoms patterns. It could identify subgroups of individuals who have similar profile. So it is widely used to examine symptom patterns in other chronically ill populations.

The investigation of symptom clustering is in an early stage of testing empirically whether the characteristics defined can be observed in the TCM contexts. Identification of symptom clusters in TCM patients could yield important information for the assessment and management of symptoms. For example, the identification of key symptom clusters would allow for prioritization of symptoms for assessment, management and follow up. Understanding of key symptom clusters would also provide new avenues for interventions to minimize the impact of symptoms on health-related outcome.[35]

1.6.2 Strengths and limitations

	Strengths	Limitations
Hierarchical cluster	Can be clustered according to case or according to variable. Scale of variables can be interval, counts and binary	The analyst can choose to cluster by case or by variable. Used only for relatively small samples (< 250) Generates all possible cluster of sizes 1…k The optimum number of clusters is not well computerdefined and depends on the research

		purpose
K-means cluster (non-hierarchical)	Can be rapidly calculated even large simple size Much less computer-intensive and therefore sometimes preferred when datasets are very large (ex.>1,000)	The desired of number clusters must be specified in advance suitable for continuous variable only

1.6.3 Application:

Cluster analysis helps to identify homogeneous subgroup of cases in a population. It also helps to identify a set of groups which both minimize within-group variation.

In hierarchical clustering, every case is initially considered a cluster, and then, two cases with the lowest distance (or highest similarity) are combined into a cluster. The case with the lowest distance to either of the first two is considered next. If the third case is closer to a fourth case than it is to either of the first two, the third and fourth cases become the second two-case cluster; if not, the third case is added to the first cluster. The process is repeated, adding cases to existing clusters, creating new clusters, or combining clusters until all clusters are in one

cluster. This procedure of hierarchical cluster analysis uses either agglomerative or divisive clustering strategies.

In k-means clustering, this method differs from hierarchical clustering in many ways. In particular:

There is no hierarchy, the data are partitioned. The user will be presented only with the final cluster membership for each case. There is no role for the dendrogram in k-means clustering.

The user must supply the number of clusters (k) into which the data are to be grouped.

At the end of the analysis the data will be split between k clusters (where the user decides what value to assign to k).

1.6.4 Software

Common software supports to cluster analysis including R, SPSS and Stat, etc.

1.6.5 Current research

While symptom clusters are useful in creating diagnostic criteria for many diseases or syndromes, the processes that lead to symptom clusters are complicated.

Our research is using this technique to cluster CLBP patient into various subgroup, and interpret in the essential of TCM theory. In this project which is considered an exploratory phase, we will use

cluster analysis and factor analysis. The results of both analyses, however, will be compared to draw conclusion.

1.7 Background of the author and his home institute

It took five years for the author to graduate Bachelor degree of acupuncture and moxibustion from Guangzhou University of Chinese Medicine. The author has been working on acupuncture teaching and out-patients clinic work in Yunnan University of Traditional Chinese Medicine since 1996. He had graduated at Master-degree of Traditional Chinese Medicine.

His former research activities were related to the treatment of pain, menopausal syndrome and diabetes II using acupuncture and massage.

As an acupuncturist, the author has been facing with chronic low back pain patients in everyday. The hospital that he was working, Number 2 Affiliated Hospital for Yunnan University of TCM has a wide variety of CLBP patients. Since classification of CLBP patients has not been standardized, having opportunity to learn advance statistical techniques inspired him to coduct this thesis.

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Chapter 2

Manuscript I: Application of Delphi technique in identification of appropriate screening questions for chronic low back pain from Traditional Chinese Medicine experts' opinions

This manuscript was published in The Journal of Alternative and Complementary Medicine

TITLE PAGE

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Title Application of Delphi technique in identification of appropriate screening questions for chronic low back pain from Traditional Chinese Medicine experts' opinions

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1. Abstract

OBJECTIVE: The goal of the present study was to obtain a standard list of Traditional Chinese Medicine (TCM) symptoms and signs for screening chronic low back pain (CLBP) from a group of experts and to assess agreement and consistency among their opinions on the items of a questionnaire.

DESIGN, SETTINGS, AND SUBJECTS: The study design involved three rounds of modified Delphi technique, and it was carried out by 13 experts in orthopedics, massage, and acupuncture working in four hospitals affiliated with Yunnan University of Traditional Chinese Medicine, China.

OUTCOME MEASURES: The outcome was measured on the 5-score Likert-scale self-administered checklists.

RESULTS: A review of eight textbooks identified 12 pain characteristics, 11 associated factors, and 25 physical and tongue diagnostic expressions as important factors in the TCM diagnosis of cLBP. These 48 diagnostic characteristics were rated by 13 experts as "not important" to "very important" on a scale of 1-5. After three rounds of rating, 13 characteristics were eliminated from the list, with the final numbers for each group being 8, 11, and 16, respectively. Seven items based on Western medicine were also added by the experts. The intra-class correlation (ICC) coefficient for agreement among the experts was 0.2 at the end. Intra-rater, between rounds, consecutive pair-wise median kappa

values were 0.53 and 0.66. Analysis of variance using items appearing in all three rounds revealed significant effects of expert and group of symptoms and signs ($p < 0.001$) and nonsignificant differences among scores of the same expert in the three rounds ($p = 0.97$). Mean score of physical and tongue expressions were significantly ($p < 0.001$) lower than that of all other groups of symptoms and signs.

CONCLUSIONS: Modern TCM experts have de-emphasized the items on physical and tongue expressions and have adopted instead those from Western medicine. Intra-expert agreement across items was low, and each expert tended to stick to her/his original opinions.

Key words: chronic low back pain, traditional Chinese medicine, Delphi technique

2. Introduction:

Chronic low back pain (CLBP) manifests as pain, muscle tension, or stiffness of more than 12 weeks localized below the costal margin and above the inferior gluteal folds, with or without leg pain, and is not attributed to recognizable pathology.[1,2] In the United States acupuncture was reported to have been used by 11% of patients with back pain.[3] In the United Kingdom 35% of these patients used complementary and alternative medicine (CAM).[4] In Germany, it was estimated that a total of about 227,000 patients have CLBP as their primary indication for acupuncture.[5] With a lifetime LBP prevalence of 51-79% in the western industrial societies,[6] and the popularity of alternative medicine for this problem, Traditional Chinese Medicine (TCM) theory related to diagnosis of CLBP could be important for CAM practitioners.

The principle of making TCM diagnosis is based on pattern discrimination of symptoms and signs. A survey in US reported that among 50 acupuncturist respondents as many as 11 TCM patterns of diagnosis of CLBP were made in their practice.[7] Among 8 TCM textbooks reviewed by us, six described the same six patterns of LBP; the other two had their individual difference patterns. [8-15]

TCM practice is based on both theory and practical experience. It is not known how many and which parts of items appearing in the textbooks are actually accepted and practised by experts.

A checklist of symptoms and signs from the textbooks which is agreed upon by most of the experts would be useful as diagnostic inclusion/exclusion criteria in clinical practice and future research.

Delphi technique has been used widely in summarizing experts' opinions in all fields where consensus has not been reached. Over 900 research papers, retrievable from Medline reported the use of this technique within the past ten years in the human health field. These included its use in TCM problems.[16-18]

In brief, the process of Delphi technique includes 3 stages. Firstly, the opinions of a group of experts are sought based on a self-administered questionnaire which guarantees anonymity of respondents to eliminate the influence of peer pressure. Secondly, there is a feedback system to allow the respondents to compare their view against a statistical summary of the group's view. Finally, this process is repeated until opinions are stable.[19,20] While Delphi technique depends a lot on rating of importance of the items proposed by the research and the expert themselves, rather few studies explored deeply the nature of agreement within the same experts among different rounds and among different experts in each round. This information is important because it can assist the researcher to judge whether the opinions obtained from Delphi technique are really reliable.

The current research aimed to extract useful symptoms and signs of CLBP in TCM among a group of experts with the three-round Delphi technique. The primary objective was to construct a set of screening questions for CLBP patients. These symptoms and signs will be used to construct a set of screening questions for chronic low back pain patients in subsequent studies. In addition, a subsidiary objective was to examine agreement and consistency among the experts' opinions on the items of questions.

2.1 Materials and Methods

2.1.1 Explicit criteria development:

Firstly, an extensive literature review was performed to come up with symptoms and signs of CLPB potentially used in TCM. From eighteen TCM textbooks of internal Medicine, the word "Low back pain" was available in eight chapters. Altogether, there were forty-eight symptoms and signs identified, which could be categorized into three groups: pain characteristics (12 items), associated factors (11 items) such as weather, other physical and tongue expressions and pulse characteristics (25 items). A self-administered checklist questionnaire was then developed for expert rating. Each symptom and sign could be rated on a 5-score Likert-scale ("not important"=1, "slightly important"=2, "of medium importance"=3, "highly important"=4, "very important"=5).

In the process of expert selection, it was learned that approximately 95% of outpatients with CLBP are served by three

types of department, namely Orthopaedics, Massage and Acupuncture, in the four hospitals affiliated with Yunnan University of TCM, which are located in Kunming and Yunxi. From these institutes, 14 clinicians with over fifteen years clinical experience and holding the position of associate professor or full professor were invited as the experts. Thirteen of them participated.

Data collection was carried out during July - September, 2007. In the first round, the selected experts were provided with the aforementioned forty-eight items of the checklist. Within three weeks, the rated questionnaire was collected back together with suggestions for revision and addition of items. The returned items with a mean score less than two were deleted. For the second round, items receiving a score of 2 or more in the first round were re-circulated to the experts with disclosure of the first round mean score of each item. In addition, the revised and additional items were also listed for scoring and comments. The second round questionnaire was collected within three weeks after sending. The third round was conducted in a similar manner, and was followed by separate in-depth interviews of seven experts who agreed to give verbal opinions.

2.1.2 Statistical methods

Descriptive statistics on each item in each round were computed. Only the 36 items kept in all three rounds were used for agreement analysis. Inter-rater agreement was assessed among different experts on the same round using the two-way intra-class

correlation coefficient (ICC) as defined by the ratio of the inter-item variance to the sum of the inter-item variance, the inter-expert variance and the residual variance.[21] In addition, the level of agreement within same expert in different rounds was computed using linear weighted kappa statistic.[22] Effects of variation of round and expert on score were examined with analysis of variance (ANOVA). From the last round, mean and 95% confidence interval (CI) of scores of groups of symptoms and signs were compared. Statistical significance was set at $p < 0.05$. Data were computerized with the EpiData 3.1 and analyzed with R 2.6.1,[23] kappa analysis was computed with "Epicalc" package version 2.6.1.5,[24] and ICC with the package "Psy" version 0.7.[25] Strength of agreement using kappa was defined as: very good (0.81 -1.00), good (0.61 - 0.80), moderate (0.41 - 0.60), fair (0.21 - 0.40) and poor ($\leqslant$0.20).

3. Results

The rating experts consisted of ten males and three females. Five were full professors and eight were associate professors. Seven were orthopaedists; the others six were acupuncturists and massage specialists combined. They had an average age of 44.9 years (SD=7.3) and average working experience of 22.9 years (SD=7.0).

In return from the first round, ten composite items combining pulse and tongue were revised by six experts with pulse components removed (Table 1). Twelve other items had a mean score of less

than two and were removed. Fourteen new items including five meridian-related and nine other items which included symptoms and signs from modern medicine were added by six experts, resulting in fifty items in the second round. At the end of the second round, eight experts further suggested changing of meridian location into standard anatomy and raised the importance of modern imaging technology such as CT and MRI. In addition, tongue items were revised to be more specific. With these revisions, 43 items were obtained. During the third round, one item related to tongue was deleted as its mean score was less than 2. Six items related to tongue were finally revised. The final number of items coming out from the third round was forty-two. They are marked with double asterisks in the last column of Table 1. Thirty-six of these had been unchanged throughout the three rounds (marked by single asterisks on the second to last column) and were used in the analysis of agreement and ANOVA.

The numbers of items in each group over different rounds are summarized in Table 2. The group of physical and tongue expressions proposed initially was finally substantially reduced. For the group of modern medicine which had not been initially proposed, as many as seven items were added.

Table 3 summarizes inter-rater and within-rater agreement. The levels of inter-rater agreement as reflected in the ICC are generally low. The coefficients slightly increased in the 3rd round, suggesting more consensuses among the experts at the end.

Between-round intra-rater agreements as reflected by pair-wise kappa value were moderate in the first transit (1st vs. 2nd round) and good in the second transit (2nd vs. 3rd round).

Table 4 summarizes the effects of expert, group of symptoms and signs and round in the ANOVA model. Effects from variations among experts and among groups of symptoms and signs were highly significant ($p<0.001$), whereas that from variation across rounds was minimal ($p=0.97$). Thus, experts did not have high agreement among themselves and symptoms of different groups were not equally important. On the other hand, the opinions of the same expert on the same item were consistent among different rounds.

Table 5 compares means and 95% CI of score in the third round by group of symptoms and signs. Mean score of physical and tongue expression group was significantly lower than that of all other groups. There were no other significant differences.

4. Discussion:

This study constructed a set of screening questions for CLBP patients and demonstrated differences in how TCM texts and experts explain the importance of various symptoms and signs of CLBP. Physical and tongue expressions which were typical TCM in the textbook were considered the least important for CLBP by experts. In addition, diagnosis based on modern medicine often mentioned in TCM textbooks was well accepted by the experts. The rating experts' opinions, however, showed low agreement with each other

as shown by the low ICC of 0.2. Each tended to stick to his/her original opinion with little change toward consensus.

After a review of 16 TCM articles on differential diagnosis on LBP, Birch & Sherman reported that 11 of these books pointed to the etiology of cold/damp, 10 to blood stasis and 8 to kidney yang vacuity and kidney yin vacuity. Other etiologies were not consistently found in these articles.[26] Over 40 out of 50 acupuncturists who responded on the same issue in a survey by Sherman et al. rated that important symptoms and signs were: pain quality and location, aggravating and relieving factors, findings from palpation and history of pain onset.[7] Similar findings were observed in our data, although western-medicine-based items such as classification and position of pain on the lumbar disc were considered more important than points in the meridian. Moreover, pulse and tongue manifestations, which are a classic diagnostic approach of TCM, were rated as not much relevant to CLBP.

In the US, physician-licensed acupuncturists were reported to less commonly use various TCM measures to treat CLBP than their non-physician counterparts.[27] That our informants tended to adopt western medicine in diagnosis of CLBP may be explained by the general adaptation of TCM in China toward western medicine due to the need for modernization and standardization. [28] However, the items consistently considered as important were still associated factors to LBP, which is typical TCM.

Poor agreement among out experts in choosing important items to diagnose LBP is also consistent with findings in the US, where acupuncturists poorly agreed on diagnosis of the same set of LBP patients under a Latin-square independent assessment. [29] Poor agreement was also observed by 4 TCM therapists on 39 irritable bowel syndrome patients (kappa value was 0.32),[30] on 39 rheumatoid arthritis patients by 3 TCM US practitioners (kappa ranging from 0.23 to 0.30),[31] and on 37 patients with frequent headache by 3 US practitioners.[32] The difference between our study and the aforementioned studies was that ours was based on agreement on theory whereas the others were based on treatment of real patients. Perhaps, poor agreement on theory may lead to failure to agree in practice.

In 1996 , China carried out the Classification and Coding of Diseases in Traditional Chinese Medicine (TCM) , which has 1624 TCM names of diseases and syndromes. Out of these, 1027 came from a summary of 78,605 in-patients' medical records. None of these involved CLBP. More recently, in 2002 the state administration of TCM of the Chinese passed a regulation that in-patients' medical records must use the International Classification of Disease (ICD) code in addition to TCM diagnosis. However, these attempts have been confined to in-patient classification. CLBP is typically on ambulatory problem which has never been tackled.

5. Conclusion:

Decreasing role of TCM in explaining LBP and low agreement among experts' opinions on the importance of checklist items indicate the need to conduct further studies to solve these problems.

Finally, this study involved a relatively small number of experts. The findings that some of the TCM theory is playing a decreasingly important role in LBP diagnosis and that the level of agreement among the experts was low should be confirmed by further studies.

6. Acknowledgements:

The study was supported by a grant from Yunnan University of TCM Funds. We thank all participant experts for providing their opinions. This study is a part of the first author's thesis to fulfil the requirements for PhD in Epidemiology at Prince of Songkla University.

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Table 1 Mean score of symptoms and signs in three rounds

Items	1st round	2nd round	3rd round		
Pain characteristics					
cold-type pain	2.62±1.66	3.38±0.87	3.46±0.88	*	**
hot-type (burning) pain	2.54±1.81	3.46±0.78	3.46±0.78	*	**
distention pain	3.62±1.39	3.62±1.26	4±0.58	*	**
piercing pain	3.46±1.45	3.92±1.04	3.85±0.99	*	**
colic	1.77±1.09				
Tension pain	2.85±1.77	3.15±1.86	3.31±1.6	*	**
Cutting pain	1.92±1.44				
aching pain	3.46±1.71	3.69±0.95	3.85±0.99	*	**
Traction pain	3±1.91	3.38±1.8	4.15±0.9	*	**
vague pain	3.62±1.45	3.23±1.59	3.15±1.46	*	**
Swelling pain	2±1.35				
dull pain	1.46±1.45				
radiating pain		1.38±2.06			
Associated factors					
activity limited by feeling	3.38±1.71	3.54±1.33	3.77±0.93	*	**
Relieved by warmth	4.08±0.95	4.23±0.93	4.38±0.65	*	**
Worsened by warmth	3.62±1.26	3.08±1.71	2.85±1.68	*	**
Worsened by rain		2.62±1.85	3.54±0.88	*	**
Worsened by wind	3.23±1.64	3.23±1.24	3.54±1.45	*	**
lumbar fatigue requiring	4.15±0.99	4.15±0.99	4.15±0.99	*	**
Overwork strain	4.46±0.88	4.38±0.87	4±0.91	*	**
lumbar and flank stiffness	2.31±1.6	2.92±1.61	3.62±1.04	*	**
Worsened by emotion		1.46±1.66			
Feeling prick	2.69±1.8	2.23±2.01			
local tenderness	3.23±1.79	4.15±0.9	3.92±1.38	*	**
numb and pain	3±2	3.46±1.71	4.15±0.8	*	**
recurrent vague pain	3.54±1.81	3.62±1.5	4.08±0.86	*	**
Physical and tongue					

Items	1st round	2nd round	3rd round		
reduced amount and red urine	2.69±1.6	2.38±1.5	2.38±1.45	*	**
Constipation	2.62±1.71	2.92±1.38	2.69±1.55	*	**
Fever	2±1.58				
throat red and swelled	2.15±1.46	2.08±1.5			
dysphoria with feverish sensation in chest, palms	1.92±1.26				
Insomnia	2±1.47				
dry mouth	1.85±1.07				
dizziness	1.77±1.24				
thirst without desire to drink	2.31±1.6	2.15±1.52	2.31±1.55	*	**
cold and weak extremities	2.54±1.76	2.77±1.64	2.62±1.66	*	**
History of injury	4.69±0.63	4.15±1.34	4.46±0.88	*	**
Heavy head and dizzy	2.15±1.57	2.15±1.46	2.77±1.36	*	**
sputum	2±1.53				
pallor face	3±1.53	2.54±1.56	2.54±1.45	*	**
Discolour lip and nail	2.38±1.8	2.38±1.61	2.38±1.5	*	**
Du meridian		1±1.58			
the first left bladder meridian		2.92±1.98			
the second left bladder meridian		3.15±2.03			
the first right bladder meridian		3±2			
the second right bladder meridian		3±2.24			
white tongue and slow pulse (a)	2.15±1.52				
yellow tongue and string pulse (a)	1.92±1.38				
greasy tongue and floating pulse (a)	2.23±1.59				
yellow or red tongue and prickly (a)	2.15±1.46				
tongue coating thin and weak pulse (a)	1.85±1.32				

Items	1st round	2nd round	3rd round		
tongue greasy and deeply weak pulse (a)	2.08±1.44				
light red tongue and string pulse (a)	2.23±1.54				
ecchymosis on tongue (a)	3.15±1.86				
white tongue and slide pulse (a)	2.23±1.69				
red tongue and string thready pulse (a)	2.15±1.57				
White tongue (b)		2.46±1.39			
greasy tongue (b)		2.54±1.51			
yellow or red tongue(b)		2.15±1.52			
light red tongue(b)		2.15±1.52			
ecchymosis on tongue (b)		2.69±1.93			
white tongue (b)		2.15±1.52			
red tongue (b)		2.23±1.59			
tongue color red tongue (c)			2.54±1.45		**
tongue color white tongue (c)	2.15±1.52	2.46±1.39	2.69±1.55	*	**
tongue color purple tongue (c)			2.54±2.07		**
tongue coating color white tongue coating (c)			2.38±1.71		**
tongue coating color yellow tongue coating (c)			2.92±1.5		**
tongue coating color gray tongue coating (c)			1.69±1.44		
tongue coating quality thick tongue coating (c)			3.08±1.55		**
tongue coating quality thin tongue coating (c)			2.46±1.45		**
tongue coating quality greasy coating (c)	2.08±1.44	2.54±1.51	3.15±1.63	*	**
Symptoms and signs from modern medicine					
Worsened by lying down		3.31±1.65	3.77±0.83	*	**

Items	1st round	2nd round	3rd round		
Can walk for one kilometer?		3.31±2.1	4.23±0.6	*	**
Position of pain No. lumbar Disc.__ Side___ Distance ____cm			4.15±0.8	*	**
anteflexion limitation		3.54±1.33	3.92±0.64	*	**
extension limitation		3.62±1.33	4±0.71	*	**
left lateral bending		2.85±1.41	3.38±1.04	*	**
right lateral bending		2.92±1.38	3.38±1.04	*	**
Lifting leg test		2.92±2.14			

Abbreviations in order of appearance in the table (from left to right): "*" Items used in ANOVA in Table 4. "**" Items kept in the final stage. (a) Items related to tongue and pulse diagnosis, appeared only in the first round; (b) Items related to tongue diagnosis, revised in the second round; (c) Items related to tongue color, tongue coating color and tongue coating quality described in the third round

Table 2 Numbers of items remaining at the end of each round

Group	Initially proposed	Round 1	Round 2	Round 3
Pain characteristics	12	9	8	8
Associated factors	11	13	11	11
Physical and tongue expression	25	21	17	16
Symptoms and signs of modern medicine	0	7	7	7
Total	48	50	43	42

Table 3 Intra-class correlation coefficient (ICC) agreement among experts in each round and pair-wise between-round intra-expert kappa statistic

	1st round	2nd round	3rd round
ICC Agreement	0.129	0.120	0.200
Comparison pair-wise within same expert[a]	1st vs 2nd	2nd vs 3rd	
Median (IQR)	0.53 (0.35, 0.64)	0.66(0.55, 0.84)	

Abbreviations in order of appearance in the table (from left to right): [a] = pair-wise linearly weighted kappa statistic; IQR = inter-quartile range

Table 4 Analysis of variance (ANOVA) by expert, group of symptoms and round.

	Df	Sum Square	Mean Square	F value	Pr(>F)
Expert	12	287.52	23.96	22.75	<0.001
Group	3	89.69	29.90	28.39	<0.001
Round	2	0.06	0.03	0.02	0.97
Residuals	1269	1336.14	1.05		

Abbreviations in order of appearance in the table (from left to right): Df= degree of freedom

Table 5 Mean score and 95% CI of each group symptoms and signs in the third round

	Mean[a]	95%CI
Pain characteristics	3.71	(3.5, 3.9)
Associated factor	3.91	(3.7, 4.1)
Physical and tongue	3.02	(2.8, 3.3)
Modern medicine	3.81	(3.6, 4.0

[a] Values not having a superscript in common differ significantly at $P < 0.001$; CI = confidence interval

Chapter 3

Manuscript II: Factor Analysis on Symptoms and Signs of Chronic Low Back Pain Based on Traditional Chinese Medicine Theory

This manuscript has also been submitted in the Journal of Alternative and Complementary Medicine

TITLE PAGE

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Abstract

Objective: To use factor analysis to explore patterns of symptoms and signs from patients with chronic low back pain (CLBP) based on the traditional Chinese medicine (TCM) theory.

Design, settings, and subjects: A cross-sectional study was carried out among 513 patients with CLBP in four hospitals affiliated with Yunnan University of Traditional Chinese Medicine, China.

Outcome measures: 31 symptoms and signs on a 6-level self-report questionnaire.

Results: Four factors were extracted. They were eventually interpreted as (1) "qi and/or blood stagnation", which includes 8 items such as piercing pain; activity limited by feeling of local heaviness, lumbar and flank stiffness with bending limitation and purple tongue etc., (2) "cold/damp", which has 7 items for example cold/damp pain, pallid face and greasy coating, etc., (3) A part of "kidney deficiency", which includes 2 items - "dull pain and recurrent vague pain", (4) "warmth/heat", which is related to 3 items viz. yellow tongue coating. The four factors accounted for 12.7%, 8.2%, 8.2% and 7.8% of the total variance, respectively. There are 7 items with uniqueness over 0.8.

Conclusions: Four TCM major groups of pathophysiology could explain 37% of variance of 31 symptoms and signs of the CLBP patients. Thirteen items are not groupable.

Key words: factor analysis; symptoms and signs; chronic low back pain; traditional Chinese medicine

1. Introduction

Low back pain (LBP) is defined as pain localized between the 12th rib and the inferior gluteal folds, with or without leg pain. 90-95% cases are non-specific LBP, with no known underlying pathology. According to duration time, chronic LBP (CLBP) has duration of more than 3 months, or occurs episodically within a 6-month period. [1,2]

CLBP is a major health problem in modern society. Reported lifetime prevalence varies between 51%-79%. At any one time, 12%-30% of adults in the western industrialized societies would have CLBP. [3,4] In a national survey in England and Wales, 40% of the adult population reported having experienced back pain within the preceding 12 months. [5]

CLBP poses an economic burden to society, mainly in terms of the large number of work days lost (indirect costs) and direct repeated treatment tand diagnosis costs. In Australia, CLBP was estimated to incur 1025 million AUD of direct and 8149 AUD of indirect costs in 2001. These two figures in UK in 1998 were £1,632 million and £10,700 million, respectively. [6]

Complementary and alternative medicines (CAM) (including acupuncture and massage) are attributable to 2% of cost for CLBP care. [7,8] However, diagnosis of CLBP by TCM has not been fully standardized. There are many symptoms and signs required to be examined by the clinician. Yet the TCM theory behind CLBP has

never been quantitatively supported by data.[9] As the disease is an important health burden, there is a need to examine the underlying factors of this condition so that future TCM research on this disease could be carried out.

Factor analysis is a modern statistical method. It is used to examine the underlying factors that could explain the variation in items presented. The number of underlying factors is smaller than the number of items in the data. These factors identified can be used for further theory development.[10]

When certain symptoms and signs co-appear, they may indicate certain underlying pathology. For example, pain, heat, tenderness and swelling suggest inflammatory process. Items of symptoms and signs that tend to co-appear have a common underlying factor. A factor must be loaded with more than one item. In the other direction, an item can be loaded to more than one factor. Factors that share certain common items will be slightly correlated but ideally the correlation should be minimized. Items that are not loaded to any factor are said to have high uniqueness. In reality, there would be a mixture of factors and unique items of symptoms and signs of diseases. Factor analysis is done to identify these factors and unique items.

The objective of the present study was to identify underlying factors in TCM theory that can cover symptoms and signs of CLBP. The knowledge from this study can allow TCM practitioners to gain better insight into the theory that can explain CLBP.

1.1 Materials and Methods

This study was a cross-sectional study conducted at outpatient departments of 4 hospitals affiliated with Yunnan university of TCM. Three of them were in Kunming city and the other in Yuxi city. Subject inclusion criteria were: (1) suffering from low back pain for at least 3 months; (2) aged at least 18 years and less than 75 years; (3) being able speak Mandarin or local language. Exclusion criteria included: (1) history of back injury or surgery. (2) physical examination suggested organic diseases, such as having positive straight leg raising test (<60 degree), fever, etc.

A questionnaire was previously developed by a Delphi study using local experts,[11] which eventually contained 31 items assembled from textbooks and a group of experts' opinions. Each item was to be subjectively rated on a 6-choice Likert-scale from 0 = absent, 1 = 1-20% of the maximum, 2 = 21-40%… 6 = 81-100% maximum).

1.2 Statistical analysis

Descriptive statistics, including frequency, percentage, mean and standard deviation, were used to summarize characteristics of the subject.

Correlation matrix was computed among different items of the chronic low back pain symptoms and signs. This matrix was then subjected to further factor analysis. A scree plot of eigenvalues and parallel analysis were carried out to validate the results of

each other. For scree plot, the number of factors was chosen at the point where the eigenvalue was closest to unity. For parallel analysis, based on random rearrangement of the data set eigenvalues, factors were recomputed and the new eigenvalues plotted on the same graph as the scree plot. Cross point of lines from the scree plot and from the parallel analysis were also to need judge for the suitable number of factors.[12,13] To improve the fit, further rotation using the varimax technique was employed. The factors were interpreted based on TCM prior knowledge.[14-16] All statistics were carried out with R 2.9.1 for Windows.[17] All data are shown as mean ± SD. Data were input with the EpiData 3.1.[18] Demographic analysis was computed with "Epicalc" package version 2.9.1.7;[19] the parallel analysis and scree plot were calculated using the "nFactors" package version 2.2 .[20]

2. Results

Demographic characteristics

Table 6 summarizes characteristics of subjects under study. Five-hundred and thirteen subjects were interviewed. The mean age of the interviewed subjects was 49.1±11.2 years, and ranged from 18 to 79 years. They were 223 (43.5%) men and 290 (56.5%) women attending the four hospitals.

Factor analysis

Figure 1 displays relationship between numbers of factors (component) selected and the eigenvalue from scree plot and parallel analysis. The round dots are from actual value making a classical scree plot. The triangles are from randomly generated data from parallel analysis. The elbow of the scree plots and the crossing points between the line of the observed and the randomly generated data is at 4 factors.

Table 7 displays sum of squares (SS) according to the number of factors. Sum of square of the loading that crosses unity is located between the fourth and the fifth factors. The fifth factor additionally explains only less than three percent of variance. Therefore, it was decided that four factors should be optional. At this stage, the model explained 37% of the total variance.

Without rotation, all elements of the correlation matrix among four factors are practically zero. However, there were three items loaded on more than one factor. Varimax rotation with maximum likelihood method was used to recompute these loadings on multiple factors. The results are shown in Table 8. Only one item loaded on more than one factor. The rotated factors remained acceptably divergent. Reanalysis with correlation matrix showed that only one pair (factor 1 vs. factor 4) had a minor correlation coefficient of 0.2. Correlation coefficients between other pairs were less than 0.1.

The respective four factors accounted for 12.7%, 8.2%, 8.2% and 7.8% of the total variance. Factor 1 includes piercing pain,

activity limited by feeling of local heaviness, lumbar and flank stiffness with bending limitation and purple tongue etc. These could be interpreted as the domain of "qi and/or blood stagnation", which covers the domain concerning locations of pathology. Factor 2 "cold/damp" includes cold/damp pain, pallid face and greasy coating, which denotes arthritis problems. Factor 3 includes dull pain and recurrent vague pain. These could be interpreted as a part of "kidney deficiency", which concern non-localized systemic problems. Factor 4 includes yellow tongue coating and burning pain, which are related to "warmth/heat", reflecting inflammation problems.

There are 13 non-groupable items. Seven with uniqueness values above 0.8 included "distension pain", "tension pain", "numb and pain", "reduced amount and red urine", "constipation", "thirst without desire to drink" and "discolored lip and nail". Of these seven, "distension pain" and "numb and pain" had mean score of higher than 2.0 indicating that they are the most common unique symptoms and signs.

3. Discussion

Out of the 31 tested items of symptoms and signs in 513 patients with CLBP, four underlying factors were identified including "qi and/or blood stagnation", "cold/damp", "kidney deficiency" and "warmth/heat".

Thirteen items were not groupable. Five of these ungroupable items are with different pain characteristics, two have tongue manifestation and the rest are a mixture of various organ symptoms. Of these 13, "distension pain" and "numb and pain" are the most important due to their high uniqueness and mean score.

Qi and/or blood stagnation are well known causes of pain. The route of flow of qi passes through the region of the low back. This factor had local manifestation as demonstrated by patients being able to describe where the pain starts. Piercing pain is outstanding pain characterized by its direction. The factor is also elaborated by limitation of movement, local heaviness, lumbar and flank stiffness, local tenderness and overwork strain. Most items of this factor point to pathology at the lumbar region. An exception is purple tongue, which is a general expression of qi and/or blood stagnation and yellow tongue which expresses heat. [21]

The factor 1, therefore, arises from qi problem in TCM or localizable pathology in western medicine.

In TCM, there are specific tracks for each of the qi circulation. Qi stagnates can be relieved by manipulation of the obstruction points by methods of acupuncture, massage etc. In western medicine, the pathology causing this kind of pain can often be located by using imaging technology. These also could be relieved by manipulation such as lumbar traction, and occasionally surgery. Perhaps, purple tongue and yellow tongue are systemic consequences

of the pathology noticed only by TCM and ignored by western medicine.

Purple tongue and yellow tongue coating loaded to factor 1 and factor 4. We may interpret that factor 4 or heat is not completely separated from factor 1 or localized pathology. The former is additional or subsequent pathology of the latter. In western medicine, inflammation can follow local pathology and results in heat and pain, tenderness through the activation of pain fibre in neurological system and humeral components, such as inflammatory cytokines. So TCM "warmth and heat" and inflammatory process in western medicine constitute this factor 4.

While the first factor is local, the second or manifestation cold/damp is global. It is a result of general weakness, low flow of qi, aggravated by cold, damp and wet environment. The slow flow of qi results in collection of wet elements in the area, mostly around the joints. Both TCM and western medicine label this as typical arthritis. Unlike stagnation of qi with localized pathology, a damp joint pain aggravated by cold has neither any track nor localization but with generalized effects on multiple joints. In western medicine, low back pain can be a manifestation of systemic arthritis such as rheumatoid arthritis. Patients with such manifestation need further investigation on the cause of arthritis, which may include collagen diseases.[22]

The third factor is heavily loaded with dull pain and vague pain. This belongs to one of the big group of TCM pathology - kidney

deficiency. However, other symptoms related to kidney deficiency, i.e. lumbar fatigue requiring self massage; pallid face; cold and weak extremities are not well loaded in this factor. Thus, we consider this factor as only a part of, and not typical, kidney deficiency.

In western medicine, there are several possible causes of dull pain in the lower part the back such as those related to disease of ovary and uterus in women, prostate and urinary bladder problems in men. Problems of the vertebral column itself could also be manifested with dull back pain. Therefore, this factor is probably a secondary manifestation of other diseases.

The above four pathophysiology theories altogether are insufficient to explain CLBP nature. Five pain characteristics "aching pain", "traction pain', "distension pain", "tension pain" and "numb and pain" are unique. So were other constitutional symptoms and signs such as "heavy head and dizzy", "lumbar fatigue requiring self massage", "thirst without desire to drink". There may either be co-incidental problems or diseases of unknown nature that need further research.

Most previous TCM classifications of CLBP were based on experts' opinions. 23 Our study was based on data systematically collected from well defined patients and analyzed by modern statistics. With our relatively large sample size, the generalizability of the finding should not be a serious problem.

Factor analysis, employed in this study helped us to understand CLBP pathophysiology, but it has its own limitation. This statistical method needs continuous variables which must be graded. Categorical variable such as pulse characteristics could not be included. Further research is needed to improve the classification of this ill-defined problem.

4. Conclusion

From our data, four factors underly symptoms and signs for CLBP, i.e. "qi and/or blood stagnation", "cold/damp", "kidney deficiency" and "warmth/heat". However, almost two-thirds of the symptoms and signs are not explained by this TCM pathophysiology.

5. Acknowledgments

The study was supported by a grant from Yunnan University of TCM. It is a part of the first author's thesis in fulfilment of the requirements for Ph.D. in Epidemiology at Prince of Songkla University.

Disclosure Statement

No competing financial interests exist.

Table 6 Demographic characteristics of patients

Hospital			
	No.1	124	(24.2%)
	No.2	122	(23.8%)
	No.3	138	(26.9%)
	No.4	129	(25.1%)
Age			
	mean±SD	50.1±11.2	
Gender			
	Male	223	(43.5%)
	Female	290	(56.5%)
Ethnicity			
	Han	425	(84.7%)
	Hui	40	(8%)
	Yi	15	(3%)
	Dai	3	(0.6%)
	Bai	19	(3.8%)
Education			
	Illiteracy	10	(1.9%)
	Primary	67	(13.1%)
	Junior	89	(17.3%)
	Senior	167	(32.6%)
	University	180	(35.1%)
Occupation			
	Worker	111	(21.7%)
	Farmer	35	(6.8%)
	Civil servant	108	(21.1%)

	Army worker	21	(4.1%)
	Technician	183	(35.8%)
	Self-employed	53	(10.4%)
Smoking			
	No	376	(73.3%)
	Yes	137	(26.7%)
Drinking			
	No	331	(64.5%)
	Yes	182	(35.5%)
Weight			
	mean±SD	58.2±9.6 kg	
Height			
	mean±SD	161.8±6.8 cm	
Visual			
	mean±SD	6.5±1.4	

Table 7 Sum of squares of loading, proportion of variance and cumulative variances explained by the loading

	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6
SS loadings	4.36	2.78	2.18	1.80	0.86	0.62
Proportion Variance	0.14	0.09	0.07	0.06	0.03	0.02
Cumulative Variance	0.14	0.23	0.30	0.36	0.39	0.40

"SS" Sum of squares

Table 8 Mean and standard deviation and factor loading in every item

Items	Mean±SD	Factor1	Factor2	Factor3	Factor4	Uniquenesses
Piercing pain	2.13±1.9	**0.657**	-0.238	-0.240	0.342	0.337
Activity limited by feeling of local heaviness	2.46±1.49	**0.696**		-0.132	0.301	0.405
Lumbar and flank stiffness with	2.18±1.56	**0.691**			0.369	0.381
Purple tongue	0.76±1.0	**0.576**	-0.120	-0.232	**0.478**	0.372
Local tenderness	1.72±1.4	**0.530**		-0.155	0.291	0.607
History of injury	3.22±1.5	**0.509**	-0.156	-0.264		0.646
Overwork strain	4.05±1.1	**0.476**	-0.218	-0.150		0.701
Cold/damp pain	0.54±1.3	-0.196	**0.696**	0.106		0.463
Pallid face	0.36±0.8		**0.511**	0.102		0.726
Cold and weak extremities	0.55±1.1	-0.143	**0.506**	0.123		0.702
Greasy coating	0.37±0.6		**0.428**		0.335	0.701
Worsened by wind	0.87±1.2	-0.238	**0.411**	0.151		0.744
Relieved by warmth	1.99±1.5	-0.204	**0.408**	0.313	-0.407	0.529
Worsened by rain	1.1±1.31	-0.319	**0.403**	0.172		0.700
Dull pain	1.94±1.9	-0.329	0.203	**0.862**	-0.168	0.080
Recurrent vague pain	2.18±1.88	-0.476	0.147	**0.730**	-0.208	0.175
Yellow tongue coating	0.71±1.04	**0.458**	-0.155	-0.187	**0.520**	0.461
Burning pain	0.3±1.05			-0.182	**0.507**	0.708
Aching pain	2.56±1.7	-0.344	0.112	0.278	-0.401	0.631
Red tongue	1.37±1.2	0.356	-0.341	-0.279	0.383	0.532
Thick tongue coating	0.64±1.04	0.111	0.362		0.307	0.761
Traction pain	2.2±1.83	0.352	-0.248	-0.367		0.679
Heavy head and dizzy	1.68±1.32		0.379	0.371		0.709
Distension pain	2.99±1.4		0.144	0.286	-0.273	0.823
Tension pain	1.98±1.6	0.215				0.934
Numb and pain	2.12±1.4			0.118	-0.131	0.957

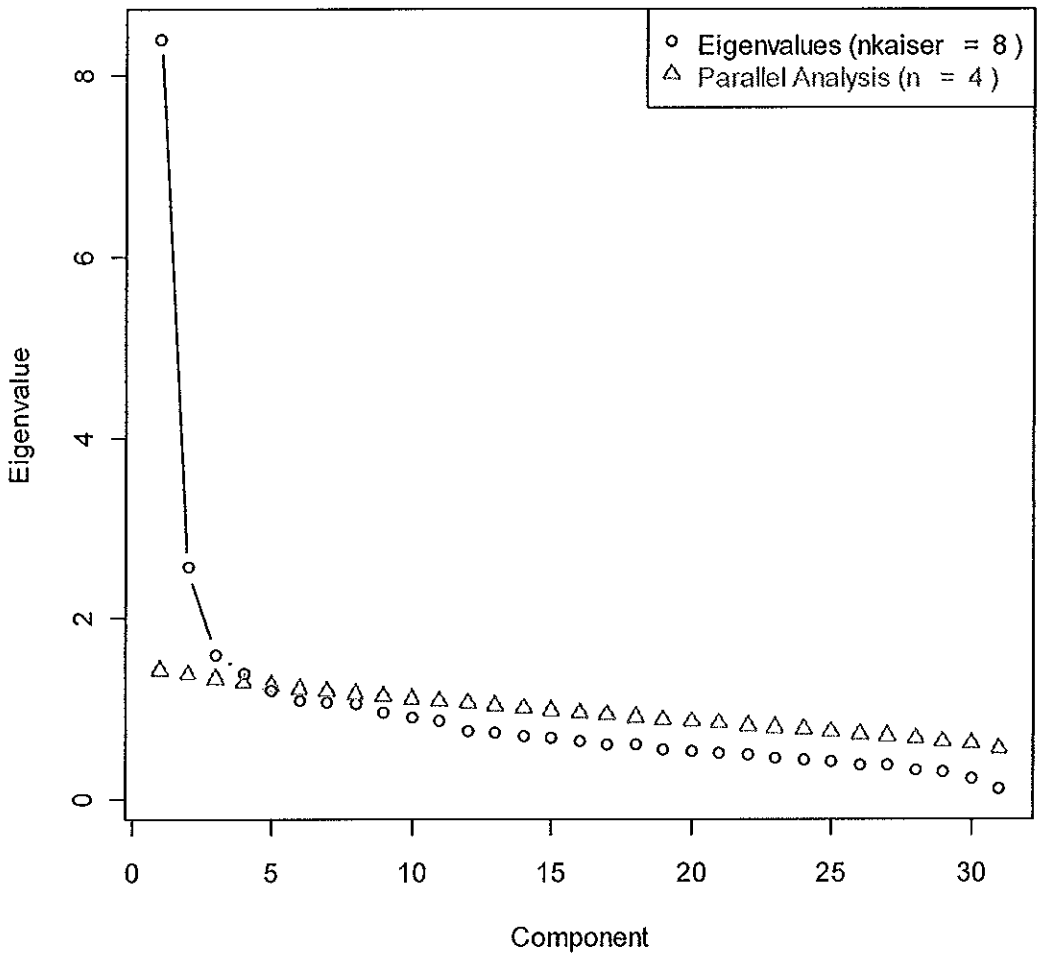
Reduced amount and red urine	0.27±0.73	0.105		-0.160	0.363	0.830
Lumbar fatigue requiring self	1.98±1.59	-0.435	0.176	0.376	-0.340	0.524
Constipation	1.11±1.1			0.113	0.326	0.879
Thirst without desire to drink	0.78±1.07		0.302	0.191	-0.104	0.857
Discolor lip and nail	0.02±0.22		0.107			0.980

Bold character number is factor loading higher than 0.4.

Table 9 Correlation matrix among factors after varimax rotation

	Factor1	Factor2	Factor3	Factor4
Factor1	1.00	-0.07	-0.07	0.20
Factor2	-0.07	1.00	0.06	0.01
Factor3	-0.07	0.06	1.00	-0.03
Factor4	0.20	0.01	-0.03	1.00

Figure 1 Scree test and parallel analysis



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Chapter 4

Cluster analysis for patients grouping

In contrast to the preceding two chapters this chapter is presented not as a manuscript but an integrated part of the thesis. The methodology and results are described followed by discussion of the findings.

1. Objective

To group the study CLBP patients into clusters based on their underlying pathophysiologic factors and to identify socio-demographic factors associated with the cluster.

2. Methodology

The data set used in chapter 3 was further analyzed using cluster analysis. The four main factor scores were used as a theoretical Euclidian location of symptoms and signs of the individuals. Virtual points were linked together based on their closest Euclidian distance and graphed in a hierarchical dendrogram. The number of clusters was then formulated from the dendrogram as well as k-means test. Each method was further analyzed for internal

validation. The final number of clusters was chosen based on the best internal validation results.

For each cluster, factor mean scores of each dimension were computed. The relationship between factor mean scores and the groups are displayed in Table 11. This enables readers to gain insight the influence of each factor in each cluster.

Finally, the clustering was cross-tabulated against socio-demographic variables to examine the association. Chi-squared test and Fisher's exact test were used and the results shown in Tables 12-21. Finally, multinomial logistic regression was used to adjust for confounding, the results of which are displayed in Table 22.

Note: the words "group" and "cluster" in this thesis, especially in this chapter, are used interchangeably.

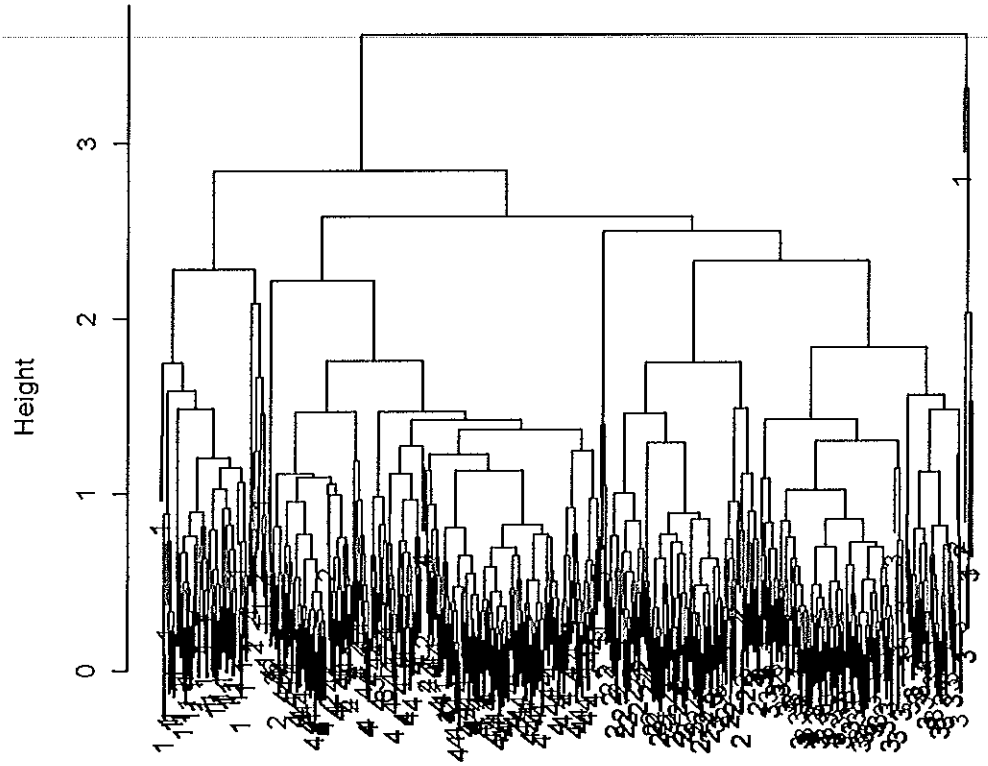

Figure 2: The ordination dendrogram tree

3. Results

3.1 Dendrogram

Figure 2 illustrates the dendrogram resulting from hierarchical cluster based on Euclidian distance. The vertical lines represent individual patients who are arranged so the persons having closest

levels of factor scores are next to each other. The branching was determining the grouping process.

Initially, from the graph, it is somewhat difficult to tell how many groups should there be. The numbers (1 to 4) at bottom of the graph came from k-means method of cluster analysis. From left to right, subjects are ordered as group 1, 4, 2 and 3, with minimal overlapping, suggesting consistency between hierarchical and k-means cluster analysis method. The order of group in this dendrogram, however, was imperfect because there have some overlapping. For example, a case of group 3, which should be on the left hand appeared on the furthest right-hand sild.

3.2 k-means analysis results

There were three methods of k-means cluster analysis employed: connectivity, Dunne Index and silhouette width. Their results are summarized in Table 10. Their scores are different due to different definitions. Connectivity and Dunn's Index methods suggest the existence of 2 clusters, whereas the silhouette width method suggested 4.

Table 10: The optimal scores in three methods using K-means

	Score	Method	Clusters
Connectivity	21.98	K-means	2
Dunn	0.08	K-means	2
Silhouette	0.36	K-means	4

3.3 Evaluation of validity of k

Evaluation of internal validity of each set of results is summarized in Figure 3. Connectivity score has a sharp rise at 2 to 3 clusters and continues to rise more gradually until 6 clusters, whereas Dunn score has a sharp drop at the same interval (2-3) and with another peak at 5 clusters. Silhouette scores have a distinct high value at 4 clusters. Out of all these three methods, we decided to choose 4 clusters suggested by Figure 3 (Silhouette width) since it fits best with the fact that there are four distinct factors.

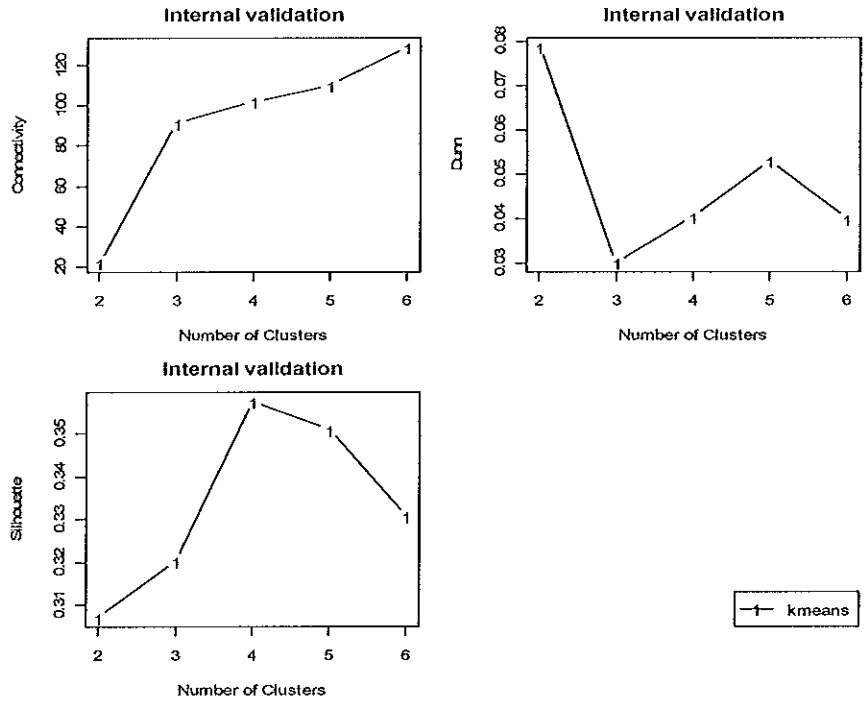

Figure 3: Three methods to evaluate number of clusters in k-means

Therefore, four clusters were finally selected as optimal clusters for further k-means clustering.

3.4 Cluster and underlying factors

The definitive groups generated by k-means clustering are cross-analysed with factor score in the Table 11. Cluster 1 comprised 73 patients with the highest mean score of 1.74 on factor 2 (cold/damp). Cluster 2 comprised 112 patients this cluster subjects having no positive factors. Cluster 3 was 142 patients: this pattern has two features of with mean 0.91 for factor 1 (qi and/or blood stagnation) and mean 0.76 for factor 4 (warmth/heat), this cluster mixed localizable pathology with inflammation problems. Cluster 4 consisted of 186 patients with mean score of 0.98 for factor 3 (kidney deficiency).

Table 11: Cluster means and number of individuals according to 4 factor scores

Factor	Characteristic	Cluster			
		1 (n=73)	2 (n=112)	3 (n=142)	4 (n=186)
1	"qi and/or blood stagnation"	-0.44	-0.40	**0.91**	-0.28
2	"cold/damp"	**1.74**	-0.36	-0.23	-0.29
3	a part of "kidney deficiency"	0.23	-1.04	-0.57	**0.98**
4	"warmth/heat"	-0.03	-0.64	**0.76**	-0.18

Bald word: mean scores are higher than 0.7

3.5 Cross-tabulations between clusters and other important variables

The frequency and percentage for each cluster and chi-square or Fisher's exact test by cluster are reported in Tables 12-21. Hospital, gender, age, education, occupation, food, smoking, drinking and BMI were factors significantly associated with group. However, the ethnicity and marriage situation had p values > 0.05.

To make it clearer, mosaic plots were used to elaborate the relationship between cluster and each variable.

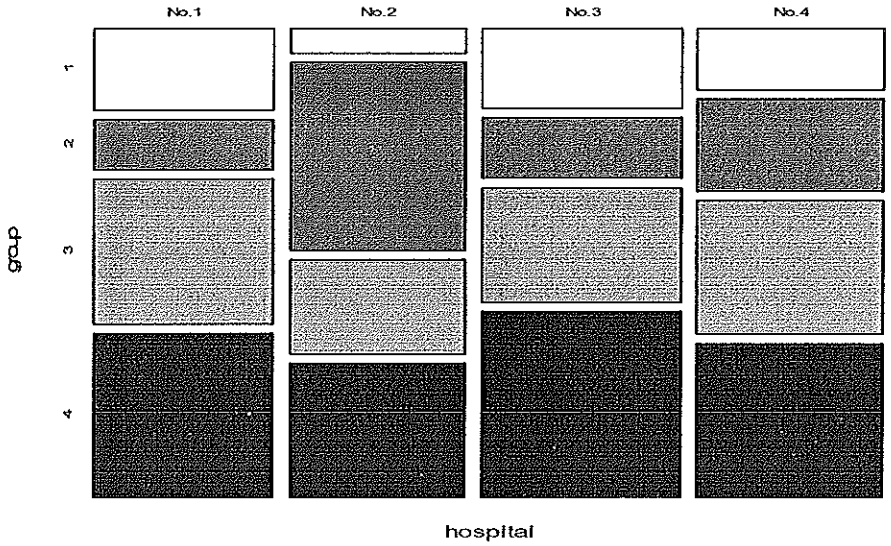

Figure 4: Distribution of group by hospital

Table 12: Distribution of cluster by hospital

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Hospital			Chisq. (9 df) = 49.96			< .001
General hospital No.1	23 (18.5)	14 (11.3)	41 (33.1)	46 (37.1)		
Community hospital No.2	7 (5.7)	52 (42.6)	26 (21.3)	37 (30.3)		
General hospital No.3	25 (18.1)	19 (13.8)	36 (26.1)	58 (42)		
General hospital No.4	18 (14)	27 (20.9)	39 (30.2)	45 (34.9)		

Group 2 was the largest faction (52/42.6%) in the No.2 hospital, but not in the other hospitals.

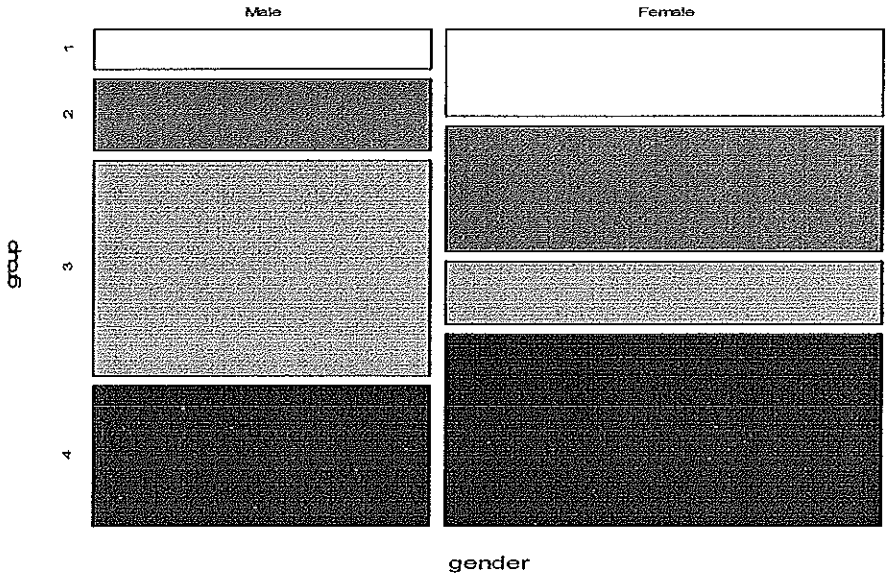

Figure 5: Distribution of group by gender

Table 13: Distribution of cluster by gender

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Gender			Chisq. (3 df)		= 69.89	<0.001
Male	19 (8.5)	34 (15.2)	103 (46.2)	67 (30)		
Female	54 (18.6)	78 (26.9)	39 (30.2)	119 (34.9)		

Figure 5 shown relationship between gender and group. Group 3 was the largest group 103(46.2%) among males, whereas group 4 was the largest group among females.

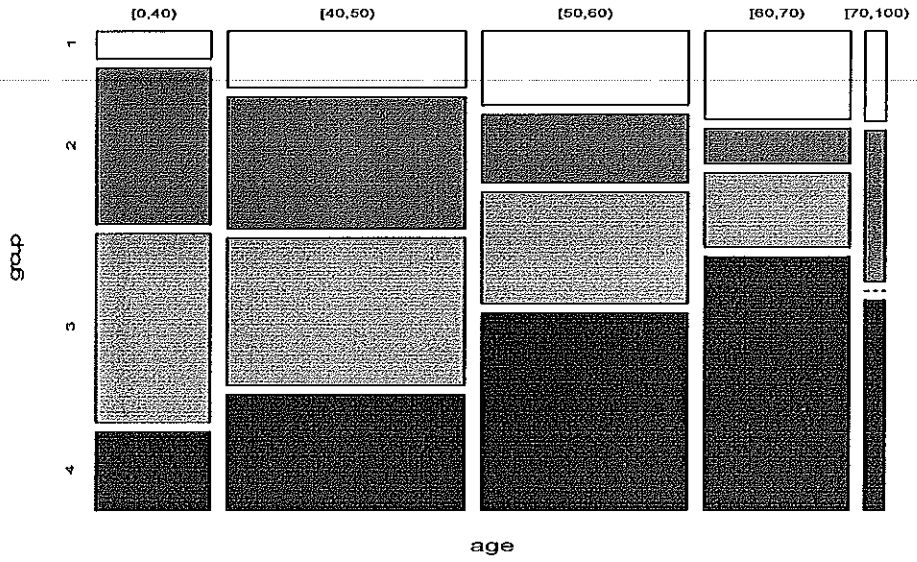

Figure 6: Distribution of group by age

Table 14: Distribution of cluster by age

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Age			Chisq. (12 df) = 74.61			<0.001
[0,40)	5 (6.2)	28 (34.6)	34 (42)	14 (17.3)		
[40,50)	21 (12.5)	49 (29.2)	55 (32.7)	43 (25.6)		
[50,60)	24 (16.4)	22 (15.1)	36 (24.7)	64 (43.8)		
[60,70)	20 (19.4)	8 (7.8)	17 (16.5)	58 (56.3)		
[70,100)	3 (20)	5 (33.3)	0 (0)	7 (46.7)		

Figure 6 shows that group 1 and 4 increased their percentage with increasing age whereas the opposite is true for group 2 and 3.

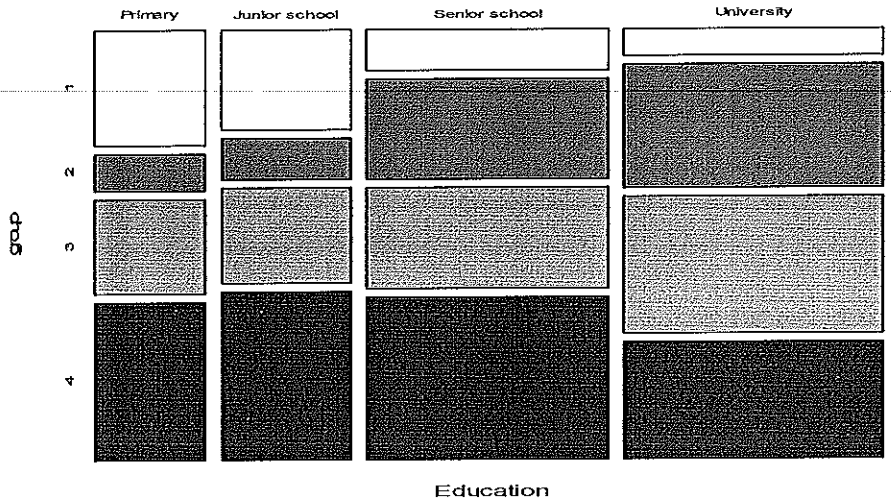

Figure 7: Distribution of group by education

Table 15: Distribution of clusters by education group

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Education			Chisq. (12 df) = 55.48			<0.001
Primary	22 (28.6)	7 (9.1)	18 (23.4)	30 (39)		
Junior school	22 (24.7)	9 (10.1)	21 (23.6)	37 (41.6)		
Senior school	17 (10.2)	41 (24.6)	42 (25.1)	67 (40.1)		
University	12 (6.7)	55 (30.6)	61 (33.9)	52 (28.9)		

For education, the group 2 and 3 had complement relationship against each other in a dose-response relationship fashion. In other words, group 1 reduced while group 2 increased with increasing level of education.

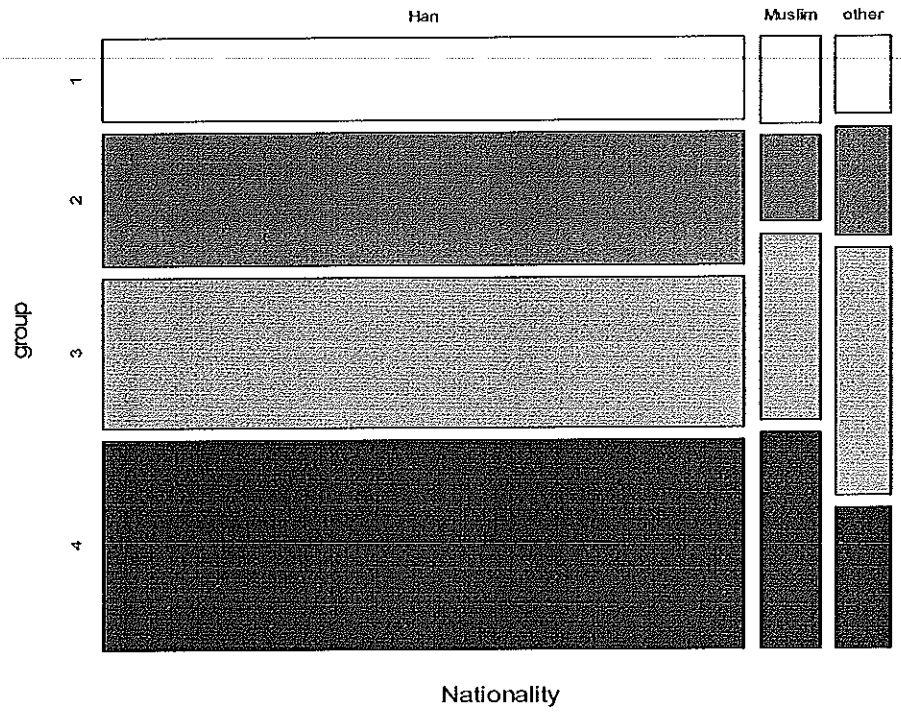

Figure 8: Distribution of group by nationality

Table 16: Distribution of clusters by ethnicity

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Ethnicity				Chisq. (6 df) =	6.65	0.355
Han	61 (14.4)	98 (23.1)	111 (26.1)	155 (36.5)		
Hui	6 (15)	6 (15)	13 (32.5)	15 (37.5)		
Other	5 (13.5)	7 (18.9)	16 (43.2)	9 (24.3)		

Distribution of ethnicities was not significant different in the different ethnicities.

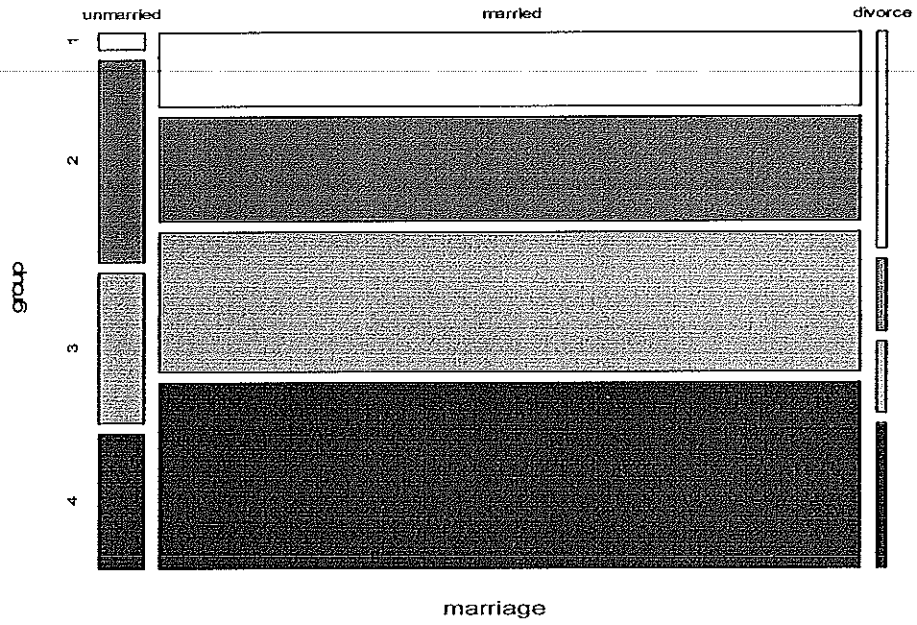

Figure 9: Distribution of group by marriage

Table 17: Distribution of cluster by marital status

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Marital status					Fisher's exact test	0.058
Unmarried	1 (3.3)	12 (40)	9 (30)	8 (26.7)		
Married	69 (14.5)	99 (20.8)	132 (27.7)	176 (37)		
Divorce	3 (42.9)	1 (14.3)	1 (14.3)	2 (28.6)		

Distribution of marital status was not significant different in different marital status.

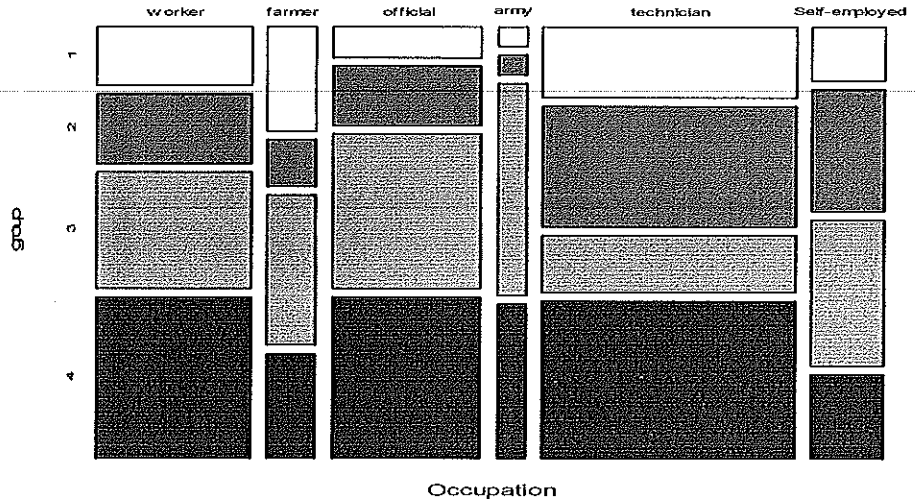

Figure 10: Distribution of group by occupation

Table 18: Distribution of cluster by occupation group

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Occupation			Chisq. (15 df) = 53.15			<0.001
Worker	16 (14.4)	19 (17.1)	32 (28.8)	44 (39.6)		
Farmer	9 (25.7)	4 (11.4)	13 (37.1)	9 (25.7)		
Official	8 (7.4)	16 (14.8)	41 (38)	43 (39.8)		
Army	1 (4.8)	1 (4.8)	11 (52.4)	8 (38.1)		
Technician	32 (17.5)	54 (29.5)	26 (14.2)	71 (38.8)		
Self-employed	7 (13.2)	16 (30.2)	19 (35.8)	11 (20.8)		

Occupation was significant variable effect by different cluster.

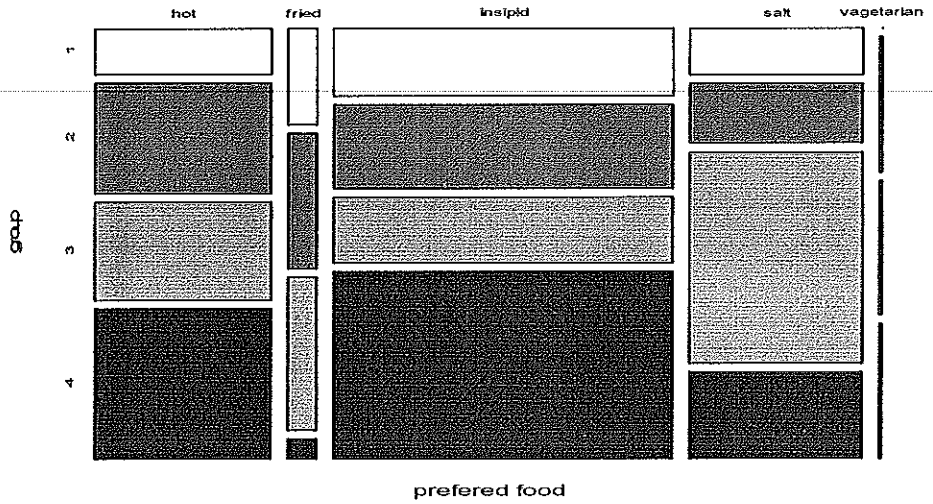

Figure 11: Distribution of group by prefered food

Table 19: Distribution of cluster by preferred food type group

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Preferred food type					Fisher's exact test	<0.001
Hot	14 (11.3)	34 (27.4)	30 (24.2)	46 (37.1)		
Fried	5 (23.8)	7 (33.3)	8 (38.1)	1 (4.8)		
Bland	40 (16.7)	50 (20.8)	39 (16.2)	111 (46.2)		
Salt	14 (11.5)	18 (14.8)	64 (52.5)	26 (21.3)		
Vegetarian	0 (0)	1 (33.3)	1 (33.3)	1 (33.3)		

Preferred food was significant variable effect by different cluster.

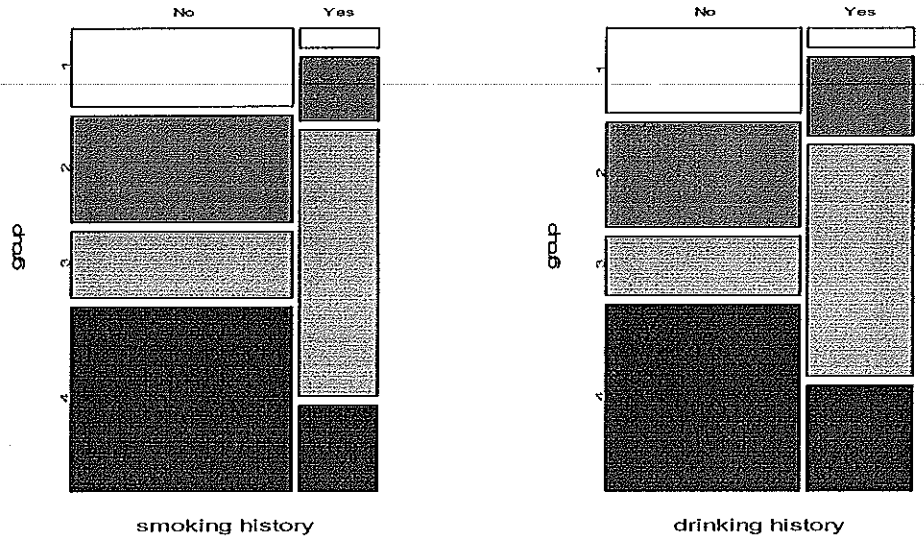

Figure 12 group by smoking & drinking

Table 20: Distribution of cluster by smoking and drinking

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
Smoking			Chisq. (3 df) = 107.73			<0.001
No	67 (17.8)	92 (24.5)	58 (15.4)	159 (42.3)		
Yes	6 (4.4)	20 (14.6)	84 (61.3)	27 (19.7)		
Drinking			Chisq. (3 df) = 99.17			<0.001
No	65 (19.6)	79 (23.9)	45 (13.6)	142 (42.9)		
Yes	8 (4.4)	33 (18.1)	97 (53.3)	44 (24.2)		

Among smokers and drinkers, group 3 was highest faction (61.3%) and (53.3%), compared with group 4 in the non smokers and non drinkers.

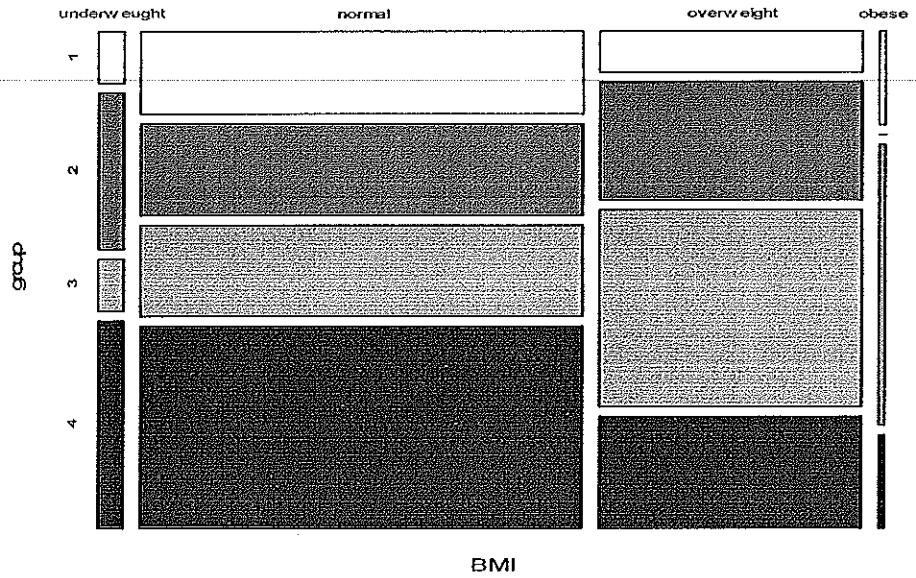

Figure 13: Distribution of group by BMI

Table 21: Distribution of cluster by BMI group

	Cluster					
	1 N=73	2 N=112	3 N=142	4 N=186	Test stat.	P value
BMI					Fisher's exact test	<0.001
Underweight	2 (11.1)	6 (33.3)	2 (11.1)	8 (44.4)		
Normal	54 (17.6)	60 (19.5)	60 (19.5)	133 (43.3)		
Overweight	16 (8.7)	46 (25.1)	77 (42.1)	44 (24)		
Obese	1 (20)	0 (0)	3 (60)	1 (20)		

Group 3 increased where group 4 decreased in proportion with increases BMI.

3.6 Multi-nominal logistic regression

Table 22 summarizes the results of multi-nominal logistic regression. It confirmed significant association between group and six variables (hospital, gender, age, education, smoking and drinking). Gender and drinking were not significantly associated with group in likelihood ratio test.

The effect of community hospital (Hospital No.2) was distinct. Using hospital as this reference patients in No.2 hospital were less likely to be in groups 1, 3 or 4, since their relative risk ratios (RRR) were consistently below 1. In other words, they were most likely to be in group 2, after adjustment for other factors. Similarly, females were more likely to be in group 3 than males.

Age effect was significant. Using youngest age group (0-40) as his reference, patients aged (50-70) were more likely to be in group 4 than group 2 with primary education as the reference, twice with high education were less likely to be in group 1 than in group 2.

Smoking was independently associated with group although 95% CI of RRR include 1 for all groups. Drinking, after adjustment for smoking other factors, was not an independent predictor of group.

Table 22: the ratios of relative risk (RRR) and likelihood ratio test (LR-test) in the multinomial logistic regression referred to cluster 2 (n=112)

		1	3	4	LR-test
		n=73	n=142	n=186	
Study variables	N	RRR (95%CI)	RRR (95%CI)	RRR (95%CI)	Pr(>Chisq)
Hospital					0.007 **
General Hospital No.1	124	1	1	1	
Community Hospital No.2	122	0.15*** (0.05,0.45)	0.32* (0.13,0.8)	0.3* (0.13,0.68)	
General Hospital No.3	138	1 (0.36,2.75)	1.05 (0.4,2.72)	1.19 (0.48,2.91)	
General Hospital No.4	129	0.39 (0.15,1.07)	0.51 (0.21,1.25)	0.64 (0.27,1.48)	
Gender					0.193
Male	223	1	1	1	
Female	290	0.66 (0.21,2.05)	0.32* (0.11,0.93)	0.69 (0.26,1.82)	
Age					< .001 ***
[0,40)	81	1	1	1	
[40,50)	168	0.94 (0.27,3.31)	0.56 (0.23,1.33)	0.99 (0.38,2.59)	
[50,60)	146	1.26 (0.33,4.86)	0.55 (0.2,1.53)	3.19* (1.13,8.96)	
[60,70)	103	2.04 (0.44,9.47)	0.53 (0.14,2.01)	6.12** (1.75,21.43)	
[70,100)	15	0.45 (0.06,3.45)	0 (0,Inf)	1.1 (0.23,5.33)	
Education					0.021 *
Primary	77	1	1	1	

		1	3	4	LR-test
		n=73	n=142	n=186	
Study variables	N	RRR (95%CI)	RRR (95%CI)	RRR (95%CI)	Pr(>Chisq)
Junior school	89	0.62 (0.17,2.21)	0.75 (0.2,2.91)	0.93 (0.28,3.12)	
Senior school	167	0.22* (0.07,0.72)	0.38 (0.12,1.24)	0.7 (0.24,1.99)	
University	180	0.11*** (0.03,0.39)	0.4 (0.12,1.4)	0.52 (0.17,1.61)	
Smoking					0.005**
No	376	1	1	1	
Yes	137	0.58 (0.12,2.77)	2.79 (0.95,8.15)	0.55 (0.18,1.63)	
Drinking					0.284
No	331	1	1	1	
Yes	182	0.29 (0.07,1.25)	0.96 (0.31,3.04)	0.79 (0.27,2.29)	

Significant codes: 0 '***' 0.001 '**' 0.01 '*'

Food preference, which was significant under univariate Chi-square test, was not an associated factor in multi-nominal regression. It was not included in the final model.

4. Discussion

This chapter used the cluster analysis to group the 513 patients with CLBP based on the factors identified in previous chapters.

Cluster analysis gave consistent results with factor analysis. There were four groups of patients who suffered from symptoms and signs of cold/damp, suffered from mixture of other symptoms and

signs, qi and/or blood stagnation combined with warmth/heat, and kidney deficiency.

The fact their patients in cluster 3 had high mean scores on both factor 1 (qi and/or blood stagnation) and factor 4 (warmth/heat) could be explained by the significant (although small) correlation between those two factors. Group 2 had no prominent factors. This is corresponding to the findings in the previous chapter that there are several items of symptoms and signs that are unique.

Hospital No.2 was different from other hospital in the fact that it had more patients with a mixture of non-groupable symptoms and signs. This difference is independent from other socio-economic status of the patients since these variables were adjusted for the final model.

The phenomenon that hospital No.2 had proportionally more non-groupable patients (group 2) could be explained by either different geographic catchment areas of other hospitals or by differences in self-referral pattern of the patients. Hospital No.2 is the only community hospital in this study. The nature of CLBP may be heterogeneous and milder, whereas other general hospitals were expected to serve patients with more specific groups of CLBP.

In TCM, female are more likely to suffer from kidney deficiency due to under expression of yang and male is more likely to get problem of qi/blood stagnation and warmth/heat due to over

expression yang. Crude analysis tended to support this theory, but this difference was not significant after multinomial regression. In Western Medicine, clinicians would believe that females are prone to CLBP due to weaker vertebral and muscle structure. The idea is not supported by our data, which, however, looked exclusively among CLBP patients without a control group.

The phenomenon of age could be explained by kidney deficiency. One study TCM study showed an association between the deficiency of kidney and bone mineral loss.

The phenomenon that the higher level education had proportionally more non-groupable patients could be explained by the self-referral pattern of the patients.

Smoking has been shown to be associated with LBP in several epidemiologic studies. Repeated microtrauma from chronic cough may result in leading to reduced blood flow to the discs and vertebral bodies leading to early degeneration, and decreased bone mineral density leading to vertebral body or end plate injury.

Drinking was similar to gender. It had significant the Chi-squared test but was not a significant in the LR test after multinomial logistic regression. Its impact was actually confounded by smoking.

Chapter 5

General Conclusion

This thesis has successfully identified the construct and underlying patterns of symptoms and signs based on checklist developed from traditional Chinese knowledge on chronic low back pain.

Three clusters were derived from these 4 factors (two of which were correlated) and one cluster that is miscellaneous. This cluster distribution is associated with age, and smoking which can be explained by TCM theory and hospital and education which may be due to self-referral pattern.

Based on our findings, we make the following recommendations.

Finding	Recommendation
Eight TCM textbooks identified different symptoms and signs	Textbooks should be standardized
Modern TCM experts have de-emphasized the items on physical	Need good measure and exact description of the physical and

and tongue expressions but our data showed that yellow tongue and red tongue are loaded in factor 1.	tongue characteristics. Importance of these characteristics should be reviewed
TCM experts have adopted Western Medicine approach. However our results show that TCM theory of pathophysiology also fits well with the data	Importance of TCM pathophysiology in practice should be further emphasized

Appendices

1. Appendix I: The first round questionnaire

Year Month Day

Items	Scores					If possible, please give some reasons
	1	2	3	4	5	
Pain characteristics						
Cold-type pain						
Heat (burning) pain						
Distention pain						
Piercing pain						
Colic						
Tension pain						
Cutting pain						
Aching pain						
Traction pain						
Vague pain						
Swelling pain						
Dull pain						
Associated factors						
Activity limited by feeling						

Items	Scores					If possible, please give some reasons
	1	2	3	4	5	
Relieved by warmth						
Worsened by warmth or raining weather						
Worsened by somber or wind						
Lumbar fatigue requiring						
Overwork strain						
Lumbar and flank stiffness, worsen by emotion						
Feeling prick						
Local tenderness						
Numb and pain						
Recurrent vague pain						
Physical symptoms						
Reduced amount and red						
Constipation						
Fever						
Throat red and swelled						
Dysphoria with feverish sensation in chest, palms and soles						
Insomnia						
Dry mouth						
Dizziness						
Thirst without desire to drink						

Items	Scores					If possible, please give some reasons
	1	2	3	4	5	
cold and weak extremities						
History of injury						
Heavy head and dizzy						
Sputum						
Pallor face						
Discolor lip and nail						
Tongue and pulse						
White tongue and slow pulse						
Yellow tongue and string pulse						
Greasy tongue and floating pulse						
Yellow or red tongue and prickly						
Tongue coating thin and weak pulse						
Tongue greasy and deeply weak pulse						
Light red tongue and string pulse						
ecchymosis on tongue						
White tongue and slide pulse						
red tongue and string thready pulse						
Added new symptoms and signs						

1=not important 2=slightly important 3=medium important 4=highly important 5=very important

2. Appendix II: The second round questionnaire

Year Month Day

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
Pain characteristics								
Cold-type pain								
Heat (burning) pain								
Distention pain								
Piercing pain								
Tension pain								
Aching pain								
Traction pain								
Vague pain								
Radiating pain								
Associated factors								
Activity limited by feeling								
Relieved by warmth								
Worsened by warmth								
Worsened by rain								
Worsened by wind								

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
Lumbar fatigue requiring								
Overwork strain								
Lumbar and flank stiffness								
Worsen by emotion								
Feeling prick								
Local tenderness								
Numb and pain								
Recurrent vague pain								
Physical symptoms								
Reduced amount and red								
Constipation								
Throat red and swelled								
Thirst without desire to drink								
cold and weak extremities								
History of injury								
Heavy head and dizzy								
Pallor face								
Discolor lip and nail								
Du meridian								
The first left bladder meridian								

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
The second left bladder meridian								
The first right bladder meridian								
The second right bladder meridian								
Tongue and pulse								
White tongue								
Greasy tongue								
Yellow or red tongue								
Light red tongue								
Ecchymosis on tongue								
Deep white tongue								
Red tongue								
Symptoms and signs from modern medicine								
Worsened by lying down								
Can walk for one kilometer?								
Anteflexion limitation								
Extension limitation								
Left lateral bending limitation								
Right lateral bending limitation								
Lifting leg test								
Added new symptoms and signs								

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	

1=not important 2=slightly important 3=medium important 4=highly important 5=very important

3. Appendix III: The third round questionnaire

Year Month Day

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
Pain characteristics								
Cold-type pain								
Heat (burning) pain								
Distention pain								
Piercing pain								
Tension pain								
Aching pain								
Traction pain								
Vague pain								
Associated factors								
Activity limited by feeling								
Relieved by warmth								
Worsened by warmth								
Worsened by rain								
Worsened by wind								

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
Lumbar fatigue requiring								
Overwork strain								
Lumbar and flank stiffness								
Feeling prick								
Local tenderness								
Numb and pain								
Recurrent vague pain								
Physical symptoms								
Reduced amount and red urine								
Constipation								
Thirst without desire to drink								
cold and weak extremities								
History of injury								
Heavy head and dizzy								
Pallor face								
Discolor lip and nail								
Tongue and pulse								
tongue color red tongue								
tongue color white tongue								
tongue color purple tongue								

Items	Mean score last round	Your score last round	Scores					If possible, please give some reasons
			1	2	3	4	5	
tongue coating color white tongue coating								
tongue coating color yellow tongue coating								
tongue coating color gray tongue coating								
tongue coating quality thick tongue coating								
tongue coating quality thin tongue coating								
tongue coating quality greasy coating								
Symptoms and signs from modern medicine								
Worsen by lying down								
Can walk for one kilometer?								
Position of pain No. lumbar Disc.__ Side___ Distance ____cm								
Anteflexion limitation								
Extension limitation								
Left lateral bending limitation								
Right lateral bending limitation								
Added new symptoms and signs								

1=not important 2=slightly important 3=medium important 4=highly important 5=very important

4. Appendix IV: Exclusion criteria

	Yes	No
Patient had low back pain less than 3 months		
Patient had no reason to reduce weight (> 5 kg during the three month)		
Patient had ever undergone spine surgery, fracture of back or nerve root		
Had morning pain and stiffness more than half hour		
Had low urology disease		
Had cancer, HIV or poliomyelitis		
Fever (> 38 degree)		
Co-treatment using steroid		
Physical examination	Yes	No
Raising straight leg test < 60 degree		
Abnormal FABER's test		
Abnormal Shober's test (measure 10cm, more than 5cm)		

Any positive symptom or sign will be reported to senior members of the research team for confirmation of exclusion.

5. Appendix V: Questionnaire to interview symptoms and signs of chronic low back pain based on TCM

ID Number	

ame		Gender	1 male 2 female	Date of birth	
hnicity	1 Han 2 Muslin 3 Yi 4 Dai 5 Bai 6 others ( )				
ducation	1 Illiteracy 2 Primary 3 Junior school 4 Senior school 5 University and above				
rriage	1 Unmarried 2 Married 3 Divorce 4 others ( )				
cupation	1 Worker 2 Farmer 3 Official 4 Arm 5 Technician 6 Self-employed				
rking place					
dress		Telephone number			
in symptoms					
story of medicine					
Behaviours	1 Preferred food: 1 Hot 2 fried 3 Insipid 4 Salt 5 Vegetaarian 2 Smoking: 1 yes 2 no 3 Drinking: 1 yes 2 no				
gh and weight	high cm	weight kg			

Symptoms and signs of chronic low back pain	
Pain characteristics	
Visual analogue scale	1 2 3 4 5 6 7 8 9 10
Cold-type pain	1 2 3 4 5
Heat (burning) pain	1 2 3 4 5
Distention pain	1 2 3 4 5
Piercing pain	1 2 3 4 5
Tension pain	1 2 3 4 5
Aching pain	1 2 3 4 5
Traction pain	1 2 3 4 5
Vague pain	1 2 3 4 5
Associated factors	
Activity limited by feeling	1 2 3 4 5
Relieved by warmth	1 2 3 4 5

Symptoms and signs of chronic low back pain	
Worsened by warmth	1 2 3 4 5
Worsened by rain	1 2 3 4 5
Worsened by wind	1 2 3 4 5
Lumbar fatigue requiring	1 2 3 4 5
Overwork strain	1 2 3 4 5
Lumbar and flank stiffness	1 2 3 4 5
Feeling prick	1 2 3 4 5
Local tenderness	1 2 3 4 5
Numb and pain	1 2 3 4 5
Recurrent vague pain	1 2 3 4 5
Physical symptoms	
Reduced amount and red urine	1 2 3 4 5
Constipation	1 2 3 4 5

Symptoms and signs of chronic low back pain	
Thirst without desire to drink	1 2 3 4 5
cold and weak extremities	1 2 3 4 5
History of injury	1 2 3 4 5
Heavy head and dizzy	1 2 3 4 5
Pallor face	1 2 3 4 5
Discolor lip and nail	1 2 3 4 5
Tongue and pulse	
Tongue color red tongue	1 2 3 4 5
Tongue color white tongue	1 2 3 4 5
Tongue color purple tongue	1 2 3 4 5
Tongue coating color White tongue coating	1 2 3 4 5
Tongue coating color Yellow tongue coating	1 2 3 4 5
Tongue coating color Gray tongue coating	1 2 3 4 5
Tongue coating quality Thick tongue coating	1 2 3 4 5

Symptoms and signs of chronic low back pain	
Tongue coating quality Thin tongue coating	1 2 3 4 5
Tongue coating quality Greasy coating	1 2 3 4 5
Symptoms and signs from modern medicine	
Worsen by lying down	1 2 3 4 5
Can walk for one kilometer? Claudication	1 2 3 4 5
Position of pain No. lumbar Disc.__ Side___ Distance ____cm	
Anteflexion limitation	1 2 3 4 5
Extension limitation	1 2 3 4 5
Left lateral bending limitation	1 2 3 4 5
Right lateral bending limitation	1 2 3 4 5
Others	
	1 2 3 4 5

Interviewer:

Year Month Day