Syndrome pattern (SP) is a core concept of Chinese medicine (CM) and is used to diagnose and treat patients based on an overall analysis of symptoms and signs. This study aimed to systematically review randomized controlled trials (RCTs) using the SP concept and to demonstrate how the SP concept could be applied to the design of parallel RCTs, considering a gold standard of clinical research. After conducting a brief systematic review by way of a PubMed search, we analyzed how the SP concept was applied to the design of a CM herbal medicine trial. We then formulated possible research questions, applied the SP concept to answer the research questions, and suggested possible RCT designs to be used for conducting future trials. Fourteen RCTs were included in our systematic review, and three key points of the SP concept were formulated for the design of parallel RCTs: the time point of SP diagnosis between before and after randomization; the relationship between the international classification of diseases (ICD) and SP for the inclusion of target population; and the proper diagnostic method of SP. In this study, we formulated three possible research questions and then suggested perspectives for five possible RCT models arrived at using SP concepts. Future trials applying SP concept to RCTs should overcome the shortcomings of past SP trials, moving CM forward from experience-based to evidence-based medicine.

KEYWORDS syndrome pattern, randomized controlled trial, traditional Chinese medicine, evidence-based medicine

Syndrome pattern (SP) is a core concept of Chinese medicine (CM) and is defined as the diagnosis of a patient's condition by comprehensive analysis of clinical information (symptoms and signs) obtained by the four main diagnostic CM procedures: observation, listening, asking about his/her condition, and pulse diagnosis. Several synonyms were used for syndrome differentiation, pattern identification, pattern differentiation, pattern diagnosis and CM patterns in relation to SP.

SP is a guideline for treating patients by CM practices such as herbal medicine or acupuncture following CM pattern classification. Paradoxically, patients diagnosed with the same disease by Western medicine (orthodox medicine) could be placed in different categories according to SP, and vice versa. Controversy arises regarding the classification of diseases. Current Western medicine adopted the international classification of diseases (ICD) which is currently on its 10th version. Hence, CM uses symptom classification in the system of subtypes of SP from an ancient era.

CM's history of experience-based medicine is more than 3,000 years old. However, in an era of evidence-based medicine, the SP of CM has encountered a challenge in proving its efficacy. It was reported that administration of herbal preparations matching the relevant SP that targets coronary heart disease resulted in an efficacy rate of 87% to 89%, whereas herbal preparations not matched with the SP resulted in an efficacy rate of only 60% to 65%.

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Because well-designed randomized controlled trials (RCTs) provide solid evidence, key resources of evidence-based medicine are trials from RCTs and systematic review of its' aggregate. (9) The aim of this research is to systematically review RCTs of herbal medicine in CM on the SP concept and to present a perspective of how the SP concept could be applied to the study design of parallel RCTs, considering a gold standard of clinical research.

METHODS

Study Process
Following a brief systematic review by way of a PubMed search, we analyzed RCTs from CM herbal medicine trials to observe how the SP concept was applied to parallel RCT design. Next, possible research questions were formulated using the SP concept to parallel RCT design. Despite the various possible research designs for applying the SP concept to RCT design, we focused on parallel RCT design. ICD was first considered as the diagnostic base; we then considered the SP concept in relation to the RCT design based on our systematic review. The SP application to the study design of RCTs was not applied to the treatment method. We then presented what be able to know and not be able to know about the selected RCTs and applied the SP concept for the conducting of future trials.

Data Sources and Searches
PubMed was searched up until July 26, 2012 for studies that applied SP to parallel RCT design to observe the use of SP to parallel RCTs in CM herbal medicine trials.

The search terms used were *(syndrome pattern OR syndrome differentiation OR pattern identification OR pattern differentiation OR pattern classification OR traditional Chinese medicine pattern OR traditional Chinese medicine syndrome) AND (traditional Chinese medicine)* and were limited by the term "randomized controlled trial" in human trials. Language was limited to English only.

Inclusion and Exclusion Criteria for Systematic Review
Following the search, all articles related to SP were selected and analyzed for the extraction of the relevant study design of RCTs by SP concept application.

Inclusion criteria for systematic review analysis included prospective parallel RCTs using the SP concept for any conditions in CM herbal medicine trials in an effort to prevent heterogeneity in acupuncture or moxibustion trials. Regardless of the types of control interventions used, we considered only parallel RCTs when comparing herbal medicine with other controls. All interventions using herbal medicine were included, and we did not consider the quality of the included RCTs.

Copies of relevant articles were obtained following the PubMed search. The data of the included RCTs were evaluated by two independent reviewers (Kim S and Cho YH) and the data were extracted according to pre-defined criteria, especially the inclusion method for the target disease (ICD vs. SP), SP type(s), SP evaluation method, and the time point for SP. Discrepancies were discussed and consensus among the authors was reached.

RESULTS

Study Description
One hundred and twenty-four publications were identified. After screening the abstracts, 15 potentially relevant studies were selected for further evaluation. After a detailed evaluation of the full text, 1 additional abstract was excluded because it was a crossover design. (10) In the end, 14 publications met our inclusion criteria (Figure 1). The key data of all the included RCTs are summarized in detail in Table 1.

Figure 1. Flow Chart of the Trial Selection Process

Among the included articles, RCT was first published on PubMed in 2003. (11) All of the RCTs were a 2 parallel-arm design. When target disease was included, 12 RCTs used inclusion criteria for ICD plus SP, (11,13-22,24) 1 RCTs adopted ICD-10 only, (23) and 1