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Syndrome Differentiation for Deficiency Syndromes in Traditional Chinese Medicine Based on Fuzzy Sets*

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A disease in traditional Chinese medicine is defined as a sequence of syndromes. The diagnosis of syndromes in traditional Chinese medicine is called syndrome differentiation. The construction of a syndrome differentiation system directly from clinical medical records using machine learning is still infeasible due to the lack of standardization of symptoms and syndromes in current clinical medical records. This article proposes a sophisticated approach to developing a syndrome differentiation system for 18 deficiency syndromes according to the knowledge of textbooks. This approach defines the syndrome differentiation problem as a membership problem of fuzzy sets. This approach designs a number of membership functions for fuzzy sets of syndromes based on a symptom grouping scheme and a symptom weighing scheme. Symptoms are grouped according to syndrome location, cause, and mechanism in the symptom grouping scheme. The symptom weighing scheme assigns exponentially decreasing weights to symptoms in each symptom group. An experimental evaluation based on a benchmark of 50 case reports shows that the proposed membership functions are very practical based on three differentiation metrics. This syndrome differentiation system can produce clinical medical records with standard symptoms and syndromes. In the future, these standard clinical medical records can be utilized to construct syndrome differentiation systems using machine learning.

Keywords: traditional Chinese medicine, syndrome differentiation, deficiency syndromes, fuzzy sets

1. INTRODUCTION

Technology has been applied extensively in western medicine to advance the diagnosis of diseases. On the contrary, technology is still rarely exploited in the diagnosis of diseases in traditional Chinese medicine (TCM). It would be promising to fulfill the appli-

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cation of technology to advance the diagnosis of diseases in TCM.

A disease usually transforms through a series of stages in TCM [5, 11, 37, 47, 70]. Each disease stage is defined as a syndrome in TCM. A syndrome can be a deficiency or excess syndrome. A deficiency syndrome is caused by the deficiency of one of the basic elements qi, blood, yin, and yang of organs. An excess syndrome is caused by external pathogenic factors or by accumulated pathologic products due to dysfunction of organs. A symptom is a subjective or objective indication or evidence of a disease. Each syndrome can be characterized by a set of symptoms.

The diagnosis of syndromes in TCM is called syndrome differentiation. The syndrome differentiation problem is a classification problem. Given the set of symptoms of a patient and a set of syndromes, determine which syndromes this patient suffers from. To develop a syndrome differentiation system, we need to solve two main issues. First, determine the set of symptoms a patient will indicate when this patient suffers from a syndrome. Second, determine the weight of each symptom used to evaluate whether the patient suffers from the syndrome.

There are two common approaches to solve these two issues. The first approach uses directly the knowledge of experts [4, 32, 35, 60]. There has been a large volume of knowledge of syndrome differentiation in TCM books and journals. Developers need to sort out and implement the knowledge manually using appropriate techniques. The second approach automatically infers and implements the knowledge of syndrome differentiation in TCM from a large volume of clinical medical records using machine learning techniques [14, 18, 20, 33, 41, 49, 53, 61-62, 66-68, 72].

These two approaches are complementary. The first approach provides a body of knowledge that is relatively valid, but it is hard to rapidly update the knowledge. The second approach can automatically learn and promptly update the knowledge. However, because there is a lack of standardization of symptoms and syndromes in most TCM clinical medical records, it is still infeasible to directly adopt the second approach in large scale at this time. In particular, TCM diseases have no standard classification until ICD-11 (International Classification of Diseases). ICD-11 was officially endorsed by WHO in 2019 [50]. Currently, ICD-10 is in use in Taiwan.

This article adopts the first approach to investigate the solutions to the syndrome differentiation problem. The knowledge of syndrome differentiation is based on 5 traditional Chinese medicine diagnostics books [5, 11, 37, 47, 70]. This article explores the classification approach based on fuzzy sets [1, 10, 65]. This article also uses the solutions to develop a syndrome differentiation system to aid the diagnosis of syndromes for practitioners. In the future, this system will be used to immensely produce standard clinical medical records with standard symptoms and syndromes. After that, we could apply the second approach to infer new knowledge from the collected standard clinical medical records and to automatically and continuously upgrade the system.

The rest of this article is organized as follows. We first review related work in Section 2. We then define the syndrome differentiation problem in TCM as a membership problem of fuzzy sets in Section 3. We next describe our syndrome differentiation system based on fuzzy sets in details in Section 4. We then illustrate an experiment to evaluate our syndrome differentiation system in Section 5. Finally, we give a conclusion in Section 6. The list of abbreviations used in this article is summarized in Table 1. The list of notations used in this article is summarized in Table 2.

Table 1. The list of abbreviations.

Abbreviations	Definitions
TCM	traditional Chinese medicine
CW	constantly-weighted
EW	exponentially-weighted
(CW/EW)N	(constantly-weighted/exponentially-weighted) naive
(CW/EW)G	(constantly-weighted/exponentially-weighted) grouping
(CW/EW)NG	(constantly-weighted/exponentially-weighted) nulled-grouping
(CW/EW)2G	(constantly-weighted/exponentially-weighted) 2-level-grouping
(CW/EW) N2G	(constantly-weighted/exponentially-weighted) nulled-2-level-grouping
BCD	baseline differentiation coefficient
ACSC	absolute clinical similarity coefficient
RCSC	relative clinical similarity coefficient

Table 2. The list of notations.

Notations	Definitions
U	the universal set of symptoms
$P(U)$	the power set of the universal set of symptoms
D	the set of syndromes
δ_d	the syndrome differentiation function for a syndrome d
δ_D	the syndrome differentiation function for a set of syndromes D
μ_d	the membership function of a fuzzy set for a syndrome d
(U,μ_d)	the fuzzy set for a syndrome d with the universe of discourse U and the membership function μ_d
S_d	the set of symptoms for a syndrome d
S	the set of symptoms of a patient
$\rho(n,\ m)$	the constantly-weighted ratio function of n over m
$\gamma(n,\ m)$	the exponentially-weighted ratio function of n over m
$S_{d,i}$	the set of symptoms for the ith group of a syndrome d
$u_{d,i}$	the membership function of a fuzzy set for the ith group of a syndrome d
$S_{d,i,j}$	the set of symptoms for the ith group and jth subgroup of a syndrome d
$u_{d,i,j}$	the membership function of a fuzzy set for the ith group and jth subgroup of a syndrome d
$\delta(d,\ x)$	the baseline differentiation between syndromes d and x
δ_d	the average of the baseline differentiation between d and all other syndromes in D
δ_D	the average of the baseline differentiation coefficients δ_d for all syndromes in D
$\sigma(X,\ Y)$	the Jaccard similarity coefficient of two sets X and Y
$S_\tau(S)$	the set of syndromes diagnosed by the system for the set of symptoms of a patient
$S_c(S)$	the set of syndromes diagnosed by a case report c for the set of symptoms of a patient
$\alpha_{c,\tau}$	the ACSC for a case report c and a threshold τ
$\alpha_{C,\tau}$	the ACSC for a benchmark C of case reports and a threshold τ
$S_r(S)$	the set of the first $\lvert S_C(S)\rvert$ ranked syndromes diagnosed by the system for the set of symptoms of a patient
β_c	the RCSC for a case report c
β_C	the RCSC for a benchmark C of case reports

2. RELATED WORK

To the best of our knowledge, there are three most related work with this research. All apply the classification approach based on fuzzy sets to solve the syndrome differentiation problem in TCM.

Yang *et al.* [60] proposed a two-stage syndrome differentiation approach and defined 24 fuzzy sets (U, μ_d) for 24 syndrome locations or causes d. The universe of discourse U of a fuzzy set is the universal set of symptoms. The membership function of a fuzzy set is defined as $\delta_d: U \rightarrow [0, 1]$. They used questionnaire to collect weights of symptoms for 22 common syndromes of heart diseases from 21 experts and used weights to define the membership functions. Given the set S of symptoms a patient suffers from, they computed the most similar syndrome location fuzzy sets and the most similar syndrome cause fuzzy sets in the first stage. They then inferred the diagnosed syndrome indirectly from the combination of these syndrome locations and syndrome causes in the second stage.

Chen *et al.* [4] also proposed a two-stage syndrome differentiation approach and defined 46 fuzzy sets (U, μ_d) for 46 syndrome locations, causes, characteristics, or conditions d. The universe of discourse U of a fuzzy set is the universal set of symptoms. The membership function of a fuzzy set is defined as $\delta_d: U \rightarrow [0, 1]$. The weights of symptoms for these fuzzy sets are determined from a large volume of electronic medical records. Given the set S of symptoms a patient suffers from, they computed the superposition of the membership degrees of each symptom in S for each fuzzy set to determine the diagnosed syndrome locations, causes, characteristics, and conditions in the first stage. They then inferred the diagnosed syndrome indirectly from the combination of these syndrome locations, causes, characteristics, and conditions in the second stage.

Long *et al.* [35] use semantic techniques based on ontologies to develop a prototypical system for the diagnosis of Psoriasis. This system uses the fuzzy pattern recognition for syndrome differentiation of basic syndromes and uses a case database and case-based reasoning for syndrome differentiation of final syndromes. The weights of symptoms in a fuzzy set for a basic syndrome are determined according as they are main symptoms or minor symptoms of the syndrome. The final syndromes for the patient are based on the similarity between the fuzzy vector obtained from the fuzzy sets for basic syndromes and the fuzzy vectors for the cases in the case database.

Lin *et al.* [32] presented a preliminary version of this article. That article proposed a one-stage syndrome differentiation approach and defined directly 18 fuzzy sets $(P(U), \mu_d)$ for 18 deficiency syndromes. The universe of discourse $P(U)$ of a fuzzy set is the power set of the universal set U of symptoms. The membership function of a fuzzy set is defined as $\delta_d: P(U) \rightarrow [0, 1]$. The membership function is designed based on grouping of symptoms according to syndrome locations, causes, and mechanisms, and exponentially decreasing weighing of symptoms.

One-stage syndrome differentiation approach has the following advantages. Since a syndrome usually consists of a syndrome location and a syndrome cause, there are symptoms that are common to the location, symptoms that are common to the cause, and symptoms that are neither common to the location nor common to the cause, but unique to the syndrome. These symptoms unique to the syndrome fuzzy set are difficult to determine if they should be included in a syndrome location fuzzy set or in a syndrome cause fuzzy set in a two-stage syndrome differentiation approach. In addition, the syndromes diagnosed in

the one-stage syndrome differentiation approach are usually more precise than the syndromes inferred from the combination of multiple syndrome locations and multiple syndrome causes diagnosed in the two-stage syndrome differentiation approach. For example, if syndrome locations A and B and syndrome causes X and Y are diagnosed, syndromes AX, AY, BX, BY can be inferred in the two-stage syndrome differentiation approach. However, with the appropriate handling of the symptoms unique to a syndrome, only one or two of the four syndromes may be diagnosed in the one-stage syndrome differentiation approach.

3. THE SYNDROME DIFFERENTIATION PROBLEM

This section defines the syndrome differentiation problem in TCM. The syndrome differentiation problem for a single syndrome could be defined as a decision problem. Given the set of symptoms of a patient, decide if this patient suffers from a specific syndrome?

Let D be the set of syndromes, U be the universal set of symptoms, and $P(U)$ be the power set of U. The solver of the syndrome differentiation problem for a syndrome $d \in D$ is a Boolean function δ_d: $P(U) \rightarrow \{true, false\}$. Given the set of symptoms $S \in P(U)$ of a patient, the syndrome differentiation function $\delta_d(S)$ for a syndrome d returns *true* if this patient suffers from the syndrome d; otherwise, it returns *false*.

The syndrome differentiation problem for multiple syndromes could be defined as a classification problem. Given a set of syndromes and the set of symptoms of a patient, classify which syndrome this patient suffers from?

The solver of the syndrome differentiation problem for a set of syndromes D is a function δ_D: $P(U) \rightarrow D$. Given the set of symptoms $S \in P(U)$ of a patient, the syndrome differentiation function $\delta_D(S)$ for a set of syndromes D returns the syndrome, which this patient suffers from.

4. SYNDROME DIFFERENTIATION BASED ON FUZZY SETS

The syndrome differentiation problem is inherently fuzzy. In many cases, it is difficult to give a definite solution to decide if a patient suffers from a specific syndrome. In addition, in many cases, a patient may suffer from more than one syndrome. Hence, it is more appropriate to define the syndrome differentiation problem as a membership problem of fuzzy sets. Given a set of syndromes and the set of symptoms of a patient, evaluate the degree to which this patient suffers from each syndrome.

Let $(P(U), \mu_d)$ be a fuzzy set for a syndrome $d \in D$ with the universe of discourse $P(U)$ and the membership function μ_d: $P(U) \rightarrow [0,1]$. Given the set of symptoms $S \in P(U)$ of a patient, the function $\mu_d(S)$ gives the membership degree of S in $(P(U), \mu_d)$. The syndrome differentiation problem could then be defined by a set F of fuzzy sets $(P(U), \mu_d)$ for all syndrome $d \in D$.

This section describes the approach to solving the syndrome differentiation problem based on fuzzy sets. It will give the details for the set D of syndromes, the universal set U of symptoms, and various potential membership functions μ_d for $d \in D$.

3.1 The Set of Syndromes

This article uses a scope of 18 deficiency syndromes as an example to demonstrate the efficacy of solving the syndrome differentiation problem based on fuzzy sets. These deficiency syndromes are collected by referring to five traditional Chinese medicine diagnostics textbooks [5, 11, 37, 47, 70]. Each syndrome implies a syndrome location and a syndrome cause. These 18 syndromes could be divided by the following five syndrome locations according to viscera: lung, heart, spleen, liver, and kidney, as listed in Table 3.

These 18 syndromes could also be divided by the following five syndrome causes: qi deficiency, blood deficiency, yin deficiency, yang deficiency, and essence deficiency, as listed in Table 4.

Table 3. Deficiency syndromes divided by syndrome locations.

Locations	Syndromes
Lung	lung qi deficiency, lung yin deficiency
Heart	heart qi deficiency, heart blood deficiency, heart yin deficiency, heart yang deficiency, heart yang collapse
Spleen	spleen qi deficiency, spleen qi fall, spleen blood control failing, spleen yang deficiency
Liver	liver blood deficiency, liver yin deficiency
Kidney	kidney essence deficiency, kidney failing to receive qi, kidney qi insecurity, kidney yin deficiency, kidney yang deficiency

Table 4. Deficiency syndromes divided by syndrome causes.

Causes	Syndromes
Qi deficiency	lung qi deficiency, heart qi deficiency, spleen qi deficiency, spleen qi fall, spleen blood control failing, kidney failing to receive qi, kidney qi insecurity
Blood deficiency	heart blood deficiency, liver blood deficiency
Yin deficiency	lung yin deficiency, heart yin deficiency, liver yin deficiency, kidney yin deficiency
Yang deficiency	heart yang deficiency, heart yang collapse, spleen yang deficiency, kidney yang deficiency
Essence deficiency	kidney essence deficiency

3.2 The Set of Symptoms

Each syndrome could be identified by a set of symptoms. The set of symptoms for each deficiency syndrome is also collected by referring to five traditional Chinese medicine diagnostics textbooks [5, 11, 37, 47, 70]. The symptoms of heart qi deficiency and heart yang deficiency syndromes are listed in Table 5 as examples.

Table 5. Symptoms of heart qi deficiency and heart yang deficiency syndromes.

Syndromes	Symptoms
Heart qi deficiency	spontaneous sweating, pale white complexion, palpitations, oppression in the chest, lack of strength, lassitude of spirit, shortness of breath, pale tongue, white fur, weak pulse
Heart yang deficiency	spontaneous sweating, pale white complexion, chest pain, heart pain, darkish complexion, palpitations, oppression in the chest, lassitude of spirit, shortness of breath, cold of the extremities, fear of cold, pale tongue, enlarged tongue, white fur, slippery fur, weak pulse, sunken pulse

Let D be the set of syndromes and S_d be the set of symptoms for a syndrome $d \in D$. Let the union of S_d for all syndrome $d \in D$ be the universal set U of symptoms. There is a total of 124 symptoms in U and the size of the power set $P(U)$ of U is 2^{124}.

3.3 A Naive Membership Function

This section gives a naive membership function of a fuzzy set for a syndrome. Let S be the set of symptoms of a patient and S_d be the set of symptoms for syndrome d. Then a naive membership function μ_d for syndrome d can be defined as a constantly-weighted (CW) ratio function

$$u_d(S) = \rho(|S \cap S_d|, |S_d|), \text{ for } S \in P(U), \tag{1}$$

where

$$\rho(n, m) = n/m. \tag{2}$$

Since the weights of symptoms in this naive membership function are equal, this membership function is called constantly-weighted naive (N) membership function, abbreviated as CWN.

3.4 Improving Membership Functions Based on Grouping of Symptoms

This section improves the membership function of a fuzzy set for a syndrome based on grouping of symptoms, namely, the division of the set of symptoms for a syndrome into multiple groups. Intuitively, if a patient suffers from a syndrome, he should have at least one symptom in almost every group of symptoms for this syndrome. We will perform symptom grouping based on syndrome location, cause, and mechanism.

3.4.1 Symptom grouping based on syndrome location and cause

The set S_d of symptoms for syndrome d contains the symptoms collected through four examinations: inspection, listening and smelling, inquiry, and palpation. In particular, tongue inspection in inspection and palpation contain abundant and unique symptoms. These symptoms should play significant roles in syndrome differentiation. In addition, since each syndrome implies a syndrome location and a syndrome cause, it is useful to identify the group of symptoms that are common to the set of syndromes with the same syndrome location, that are common to the set of syndromes with the same syndrome cause, and that are unique when the specific syndrome location and syndrome cause occur simultaneously. This subsection defines the membership function of a syndrome based on the division of the set of symptoms for a syndrome into five groups: palpation, tongue inspection, location, cause, and feature. Intuitively, if a patient suffers from a syndrome, he should have at least one symptom in almost every symptom group for this syndrome. The symptom groups for heart qi deficiency and heart yang deficiency syndromes are listed in Table 6 as examples.

The first group, called the palpation group, of symptoms consists of symptoms collected through palpation. As an example, the set of symptoms {weak pulse} is common to all qi deficiency and yang deficiency syndromes. The second group, called the tongue inspection group, of symptoms consists of symptoms collected through tongue inspection.

Table 6. Symptom groups of heart qi deficiency and heart yang deficiency syndromes.

Syndromes	Symptom Groups				
	Palpation	Tongue Inspection	Location	Cause	Feature
Heart qi deficiency	weak pulse	pale tongue, white fur	palpitations, oppression in the chest	lack of strength, lassitude of spirit, shortness of breath	spontaneous sweating, pale white complexion
Heart yang deficiency	weak pulse, sunken pulse	pale tongue, enlarged tongue, white fur, slippery fur	palpitations, oppression in the chest	lassitude of spirit, shortness of breath, cold of the extremities, fear of cold	spontaneous sweating, pale white complexion, chest pain, heart pain, darkish complexion

As an example, the set of symptoms {pale tongue, white fur} is common to all qi deficiency and yang deficiency syndromes.

The rest of the symptoms collected through inspection, listening and smelling, and inquiry are divided into the following three groups. The third group, called the location group, of symptoms consists of symptoms that are common to the set of syndromes with the same syndrome location. There are five syndrome locations, as shown in Table 3. Using the syndrome location, heart, as an example, the set of symptoms that are common to the five heart syndromes is {palpitations, oppression in the chest}.

The fourth group, called the cause group, of symptoms consists of symptoms that are common to the set of syndromes with the same syndrome cause. There are five syndrome causes, as shown in Table 4. Using the syndrome cause, qi deficiency, as an example, the set of symptoms that are common to the seven qi deficiency syndromes is {lassitude of spirit, lack of strength, shortness of breath}.

The fifth group, called the feature group, of symptoms consists of symptoms that are not in the previous two groups. These symptoms appear when the syndrome location and the syndrome cause occur simultaneously. Using the heart qi deficiency syndrome as an example, the set of symptoms in the feature group is {spontaneous sweating, pale white complexion}. These two symptoms are not common to the five heart syndromes and are not common to the seven qi deficiency syndromes, but are characteristic symptoms for heart qi deficiency syndrome.

In this way, a membership function u_d for syndrome d can be defined as a linearly weighted function as follows

$$u_d(S) = \sum_{i=1,5} w_i \times u_{d,i}(S), \text{ for } S \in P(U). \tag{3}$$

Here $u_{d,i}$ is the membership function for the group with the set $S_{d,i}$ of symptoms and can be defined as

$$u_{d,i}(S) = \rho(|S \cap S_{d,i}|, |S_{d,i}|), \text{ for } S \in P(U), \tag{4}$$

and w_i are weights for each group.

If a patient has no symptom in a group, then he loses the weight of that group. This can effectively differentiate irrelevant syndromes from relevant syndromes. Currently, w_i are assigned weights 0.1, 0.1, 0.3, 0.3, and 0.2 for the palpation, tongue inspection, location, cause, and feature groups, respectively, based on clinical experience of practitioners. Since the weights of symptoms in each group of the membership function defined by Eqs. (3) and (4) are equal, this membership function is called constantly-weighted grouping (G) membership function, abbreviated as CWG.

Each syndrome implies a syndrome location and a syndrome cause. For a patient with the set S of symptoms, if $u_{d,i}(S) = 0$ for both the location group and the feature group of d, then this patient should not suffer a syndrome relevant to the syndrome location of d. Similarly, if $u_{d,i}(S) = 0$ for both the cause group and the feature group of d, this patient should not suffer a syndrome relevant to the syndrome cause of d. This nulling of syndromes with small membership degrees helps us focus on more relevant syndromes. Therefore, a constantly-weighted nulled-grouping (NG) membership function, abbreviated as CWNG, u_d for syndrome d can be defined as

$$u_d(S) = \begin{cases} 0, & \text{if } (u_{d,3}(S) = 0 \wedge u_{d,5}(S) = 0) \vee (u_{d,4}(S) = 0 \wedge u_{d,5}(S) = 0); \\ \sum_{i=1,5} w_i \times u_{d,i}(s), & \text{otherwise.} \end{cases} \tag{5}$$

3.4.2 Symptom grouping based on syndrome mechanism

Some syndromes are closely related due to syndrome mechanism. For example, a yang deficiency syndrome is usually transformed from a qi deficiency syndrome if the qi deficiency syndrome is not properly treated. Many symptoms in the set of symptoms for the qi deficiency syndrome are also in the set of symptoms for the yang deficiency syndrome. Therefore, the symptoms unique to the yang deficiency syndrome should be the primary symptoms to identify the yang deficiency syndrome. The symptoms common to the qi deficiency syndrome should be the secondary symptoms to identify the yang deficiency syndrome. This subsection proposes a 2-level grouping to divide each group of symptoms further into two subgroups if the current syndrome is transformed from a closely related syndrome due to syndrome mechanism. The 2-level symptom groups for heart yang deficiency syndrome are listed in Table 7. The symptom groups for heart qi deficiency syndrome are not further divided. Except for the location group, the other four symptom groups of the heart yang deficiency syndrome are further divided into primary and secondary subgroups.

In this way, a membership function $u_{d,i}$ for symptom group i of syndrome d can be defined as

$$u_{d,i}(S) = \sum_{j=1,2} w_j \times u_{d,i,j}(S), \text{ for } S \in P(U). \tag{6}$$

Here $u_{d,i,j}$ are the membership functions for the primary or secondary subgroups with the set $S_{d,i,j}$ of symptoms and can be defined as

$$u_{d,i,j}(S) = \rho(|S \cap S_{d,i,j}|, |S_{d,i,j}|), \text{ for } S \in P(U), \tag{7}$$

and w_j are weights for each subgroup.

Table 7. 2-level symptom groups of heart yang deficiency syndrome.

Syndromes	Symptom Groups					
	Primary/ Secondary	Palpation	Tongue Inspection	Location	Cause	Feature
Heart qi deficiency		weak pulse	pale tongue, white fur	palpitations, oppression in the chest	lack of strength, lassitude of spirit, shortness of breath	spontaneous sweating, pale white complexion
Heart yang deficiency	Primary	sunken pulse	enlarged tongue, slippery fur	palpitations, oppression in the chest	cold of the extremities, fear of cold	chest pain, heart pain, darkish complexion
	Secondary	weak pulse	pale tongue, white fur		lassitude of spirit, shortness of breath	spontaneous sweating, pale white complexion

Currently, w_j are assigned weights 0.8 and 0.2 for the primary and secondary subgroups, respectively, based on clinical experience of practitioners. The membership function defined by Eqs. (3), (6) and (7) would be called the constantly-weighted 2-level-grouping (2G) membership function, abbreviated as CW2G. The membership function defined by Eqs. (5)-(7) would be called the constantly-weighted nulled-2-level-grouping (N2G) membership function, abbreviated as CW2NG.

3.5 Improving Membership Functions Based on Exponentially Decreasing Weighing of Symptoms

The set S_d of symptoms for a syndrome d usually contains the maximal number of characteristic symptoms for d. In practice, however, a patient often has only a small portion of S_d such that the membership degree usually tends to be too small. To enhance the practicability, we propose to assign exponentially decreasing weights to symptoms so that a small portion of the symptoms can still sufficiently manifest the syndrome. Let m be the size of S_d and n be the size of the intersection of S_d and the set of symptoms of a patient. An exponentially-weighted (EW) ratio function that assigns weights to symptoms according to a geometric series with a constant ratio of 1/2 can be defined as

$$\gamma(n,m)=\begin{cases}0, & \text{if } n=0;\\ \frac{1}{m}+\frac{m-1}{m}\times\sum_{i=1}^{n}(\frac{1}{2})^i, & \text{if } 0<n<m;\\ 1, & \text{if } n=m.\end{cases} \tag{8}$$

The comparison of the behavior of an exponentially-weighted membership function and the behavior of a constantly-weighted membership function is shown in Fig. 1. For a S_d of size 10, it needs 5 symptoms to achieve a membership degree of 0.50 for the constantly-weighted membership function, while it only needs 1 symptom to achieve a membership degree of 0.55 for the exponentially-weighted membership function. In practice, the exponentially-weighted membership function can effectively alleviate the issue that the membership degree usually tends to be too small.

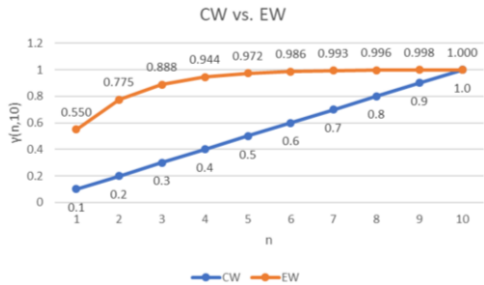

Fig. 1. Exponentially-weighted and constantly-weighted membership functions.

Then an exponentially-weighted naive (EWN) membership function could be defined as

$$u_d(S) = \gamma(|S \cap S_d|, |S_d|), \text{ for } S \in P(U). \tag{9}$$

An exponentially-weighted grouping (EWG) membership function could be defined as Eqs. (3) and (10)

$$u_{d,i}(S) = \gamma(|S \cap S_{d,i}|, |S_{d,i}|), \text{ for } S \in P(U). \tag{10}$$

An exponentially-weighted nulled-grouping (EWNG) membership function could be defined as Eqs. (5) and (10).

An exponentially-weighted 2-level-grouping (EW2G) membership function could be defined as Eqs. (3), (6) and (11).

$$u_{d,i,j}(S) = \gamma(|S \cap S_{d,i,j}|, |S_{d,i,j}|), \text{ for } S \in P(U) \tag{11}$$

An exponentially-weighted nulled-2-level-grouping (EWN2G) membership function could be defined by Eqs. (5), (6) and (11).

4. EXPERIMENTAL EVALUATION

This section uses 3 metrics to evaluate the differentiation capabilities of the 10 membership functions defined in Section 3.

4.1 Baseline Differentiation Coefficients

This section uses the baseline differentiation coefficients (BDC) to investigate the baseline differentiation among syndromes. In clinical cases, the differentiation among syndromes should be smaller than the baseline differentiation coefficients.

The baseline differentiation between syndromes d and x can be defined as

$$\delta(d, x) = u_d(S_d) - u_x(S_d) = 1 - u_x(S_d). \tag{12}$$

Note that $u_d(S_d) = 1$ for any syndrome d and $\delta(d, x)$ may be different from $\delta(x, d)$. The BDC δ_d for syndrome d is the average of the baseline differentiation between d and all

other syndromes in D and can be defined as

$$\delta_d = \frac{1}{|D|-1}\sum_{x\in D-\{d\}}\delta(d,x). \tag{13}$$

The BDC δ_D for the set D of syndromes is the average of the baseline differentiation coefficients δ_d for all syndromes in D and can be defined as

$$\delta_D = \frac{1}{|D|}\sum_{d\in D}\delta_d. \tag{14}$$

The BDC δ_D for the set D of syndromes for the 10 membership functions are shown in Fig. 2. For both constantly-weighted and exponentially-weighted membership functions, the grouping of symptoms can improve the BDC, and the nulling of syndromes with small membership degrees can further improve the BDC. Except that the EWN membership function is exceptionally small, the BDC for exponentially-weighted membership functions are only slightly smaller than that for constantly-weighted membership functions. This demonstrates that the grouping of symptoms can significantly alleviate the amplifying effects of the exponentially weighing of symptoms.

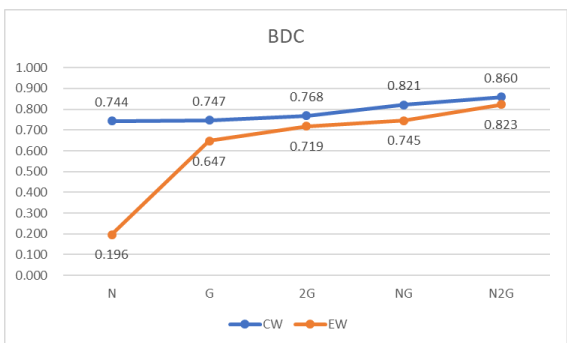

Fig 2. The BDC δ_D for the 10 membership functions.

We also investigate the BDC δ_d for all syndromes in D for the 5 constantly-weighted membership functions and the 5 exponentially-weighted membership functions as shown in Figs. 3 and 4, respectively. For each d, we rank δ_d from large BDC to small BDC. Fig. 3 depicts the ranks of δ_d for the five constantly-weighted membership functions. For example, δ_d for CWN, CWG, CW2G, CWNG, CWN2G in heart qi deficiency syndrome are 0.748, 0.709, 0.750, 0.810, and 0.843, respectively. Therefore, they are ranked as 4, 5, 3, 2, and 1, respectively. It shows that the ranks of δ_d for CWNG and CWN2G are consistently higher than that of CWN, CWG, and CW2G. It also shows that the ranks of δ_d between CWNG and CWN2G are mixed and the ranks of δ_d between CWN, CWG, and CW2G are mixed. Therefore, it is difficult to determine the best membership function among constantly-weighted membership functions. Fig. 4 depicts the ranks of δ_d for the five exponentially-weighted membership functions. It shows that the ranks of δ_d for EWN2G are consistently first, the ranks of δ_d for EWG is consistently fourth, and the ranks of δ_d for EWN is consistently fifth. It also shows that the ranks of δ_d between EWNG and EW2G are mixed and either second or third. Therefore, it is obvious that EWN2G is the best membership function among exponentially-weighted membership functions.

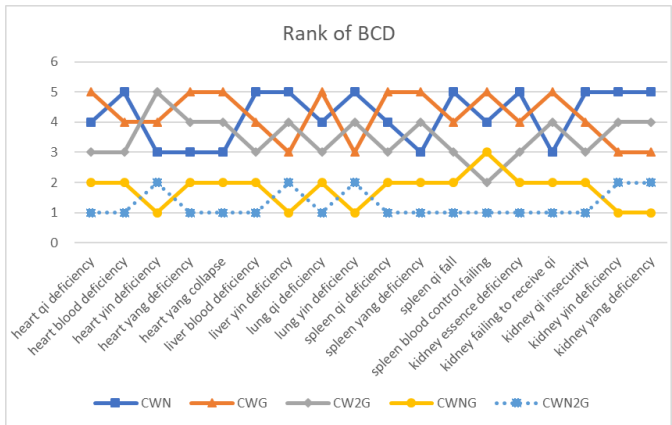

Fig 3. The rank of BDC δ_d for the 5 constantly-weighted membership functions.

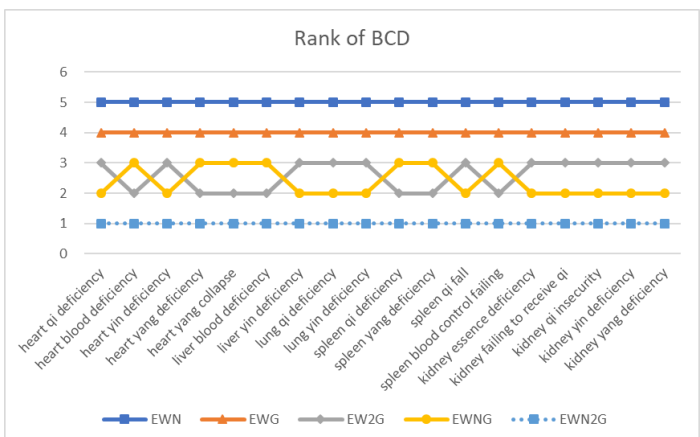

Fig. 4. The rank of BDC δ_d for the 5 exponentially-weighted membership functions.

4.2 Clinical Similarity Coefficients

This section uses two types of clinical similarity coefficients: absolute clinical similarity coefficients (ACSC) and relative clinical similarity coefficients (RCSC) to investigate the differentiation capability of the 10 membership functions for a benchmark of 50 clinical case reports collected from journals and books [2, 3, 6-9, 12, 13, 15-17, 21-31, 34, 36, 38-40, 42-46, 48, 51-52, 54-59, 63-64, 69, 71]. Each syndrome appears in at least one case report in the benchmark.

Since a patient usually suffers from more than one syndrome, we use Jaccard similarity coefficient [19] to evaluate the similarity between the sets of syndromes diagnosed by a case report and by the 10 membership functions. The Jaccard similarity coefficient $\sigma(X, Y)$ of two sets X and Y is defined as

$$\sigma(X,Y) = \frac{|X \cap Y|}{|X \cup Y|}. \tag{15}$$

4.2.1 Absolute clinical similarity coefficients

This section uses ACSC to evaluate the precision of the 10 membership functions with respective to a benchmark of case reports and a membership degree threshold.

Given the set S of symptoms of a patient and the set of membership functions u_d for all $d \in D$, the set $S_\tau(S)$ of syndromes diagnosed by this set of membership functions using threshold τ could be defined as

$$S_\tau(S) = \{d \mid u_d(S) > \tau, \text{ for all } d \in D\}. \tag{16}$$

Let $S_c(S)$ be the set of syndromes diagnosed by a case report c with the set S of symptoms. The ACSC $\alpha_{c,\tau}$ for a case report c and a threshold τ could be defined as

$$\alpha_{c,\tau} = \sigma(S_c(S), S_\tau(S)). \tag{17}$$

The ACSC $\alpha_{C,\tau}$ for a benchmark C of case reports and a threshold τ could be defined as

$$\alpha_{C,\tau} = \frac{1}{|C|} \sum_{c \in C} \alpha_{c,\tau}. \tag{18}$$

The ACSC for a benchmark evaluates the average ACSC over all case reports in the benchmark. For the benchmark of 50 clinical case reports, the ACSC for the 5 constantly-weighted membership functions and the 5 exponentially-weighted membership functions are depicted in Figs. 5 and 6, respectively. For example, $\alpha_{C,0.2}$ for CWN, CWG, CW2G, CWNG, CWN2G are 0.231, 0.227, 0.259, 0.246, and 0.303, respectively in Fig. 5.

From Figs. 2, 5 and 6, ACSC is consistently smaller than BDC. This is because BDC concerns the difference of membership degrees, while ACSC concerns the difference of syndrome sets. An ACSC $\alpha_{c,\tau} = 0.406$ is actually quite good because if $|S_c(S)| = 1$, then $\alpha_{c,\tau} = 0$ or 1. If $|S_c(S)| = 2$, then $\alpha_{c,\tau} = 0$, 0.33 or 1. If $|S_c(S)| = 3$, then $\alpha_{c,\tau} = 0$, 0.2, 0.5 or 1. For

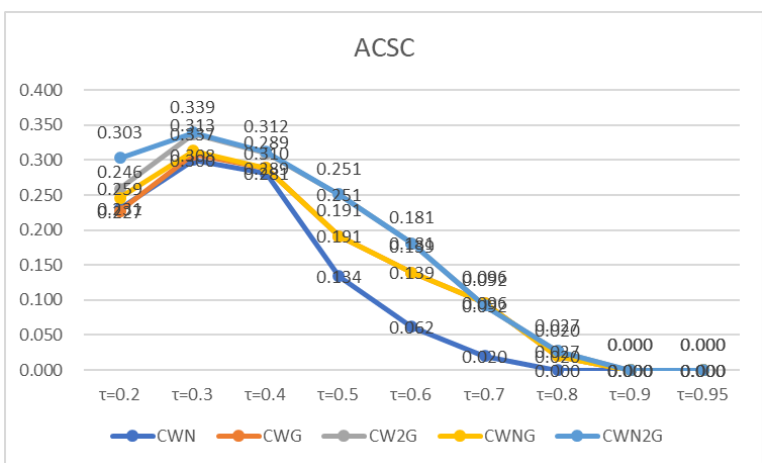

Fig. 5. The ACSC $\alpha_{C,\tau}$ for the 5 constantly-weighted membership functions.

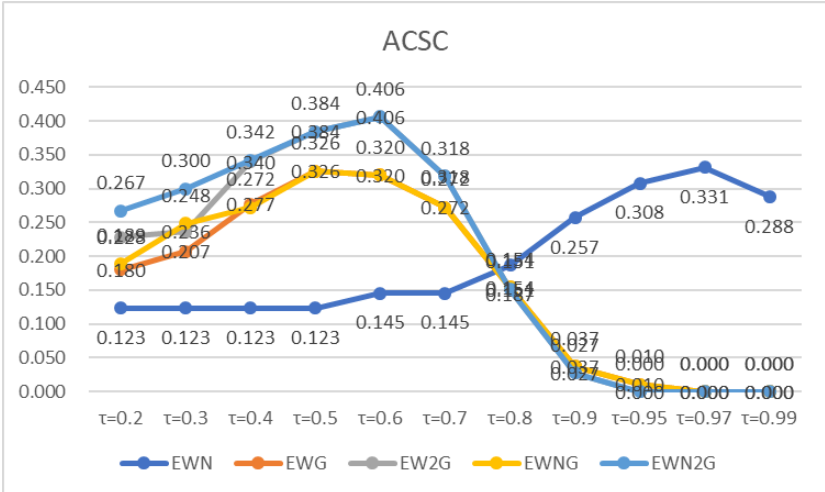

Fig. 6. The ACSC $\alpha_{C,\tau}$ for the 5 exponentially-weighted membership functions.

the EN2G membership function with $\alpha_{C,0.06} = 0.406$, there are 6 case reports with $\alpha_{C,\tau} = 1$. There are 10 case reports with $\alpha_{C,\tau} = 0$. Among them, 9 case reports have no syndrome with $u_d(S) > \tau$. The remained one case report has only one syndrome with $u_d(S) > \tau$. Therefore, in clinical case reports, since the sets of symptoms for patients are usually very small, the membership degrees are still very small even using the exponentially-weighted membership functions.

From Figs. 5 and 6, ACSC for the four grouping membership functions is consistently larger than that for the naive membership functions. This confirms that the grouping membership functions consistently improve the naive membership functions in clinical case reports. For ACSC, the effect of the nulled membership functions is ignorable. This is because the nulled membership functions have effect only in the lower division of the membership degrees. However, ACSC concerns only the upper division of the membership degrees. Therefore, the lines for CWG and CWNG are almost the same except for small τ. The same goes for CW2G and CWN2G, EWG and EWNG, and EW2G and EWN2G.

From Fig. 5, the optimal ACSC 0.339 occurs at $\tau = 0.3$ for the constantly-weighted membership functions. From Fig. 6, the optimal ACSC 0.406 occurs at $\tau = 0.6$ for the 4 exponentially-weighted grouping membership functions and the optimal ACSC 0.331 occurs at $\tau = 0.97$ for the exponentially-weighted naive membership function. This is because the membership degree for each exponentially-weighted membership function is consistently larger than its corresponding constantly-weighted membership function. In general, the threshold 0.3 is too small because it is easy to pass the threshold with a small number of symptoms. On the other hand, the threshold 0.97 is too large because it is difficult to pass the threshold even with a large number of symptoms. The threshold 0.6 is much more appropriate. It has enough space to spread patients suffering or not from a syndrome. It even has enough space to spread patients slightly, moderately, or seriously suffering from a syndrome. This result concludes that using both grouping scheme and exponentially decreasing weighing scheme provides a more appropriate optimal threshold at 0.6.

4.2.1 Relative clinical similarity coefficients

This section uses the size of the set $S_c(S)$ of syndromes identified by a case report to decide how many syndromes a patient suffers from and no membership degree threshold is used. Given the set S of symptoms of a patient, the set $S_c(S)$ of syndromes diagnosed by a case report c, and the set of membership functions u_d for all $d \in D$, the set $S_r(S)$ of syndromes the patient suffers from could be defined as

$$S_r(S) = \{d \mid rank(u_d(S)) \le |S_c(S)|, \text{ for all } d \in D\}. \tag{19}$$

The rank function ranks the membership degrees from large values to small values. The RCSC β_c for a case report c could be defined as

$$\beta_c = \sigma(S_c(S), S_r(S)). \tag{20}$$

The RCSC β_C for a benchmark C of case reports could be defined as

$$\beta_C = \frac{1}{|C|}\sum_{c \in C} \beta_c. \tag{21}$$

The RCSC for a benchmark evaluates the average RCSC over all case reports in the benchmark. For the benchmark of 50 clinical case reports, the RCSC for the 10 membership functions are depicted in Fig. 7.

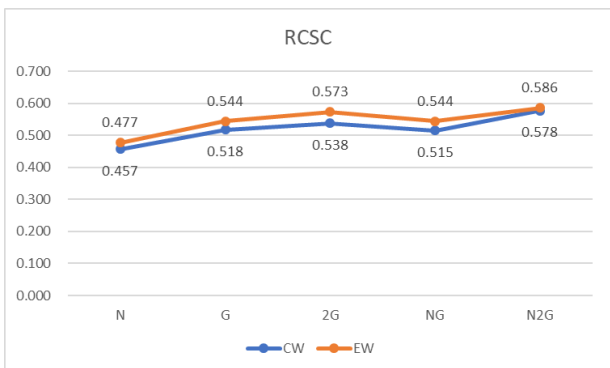

Fig. 7. The RCSC β_C for the 10 membership functions.

From Figs. 5, 6 and 7, RCSC is consistently larger than the corresponding ACSC. The largest RCSC is 0.586 which is pretty good. This implies that for the same number of diagnosed syndromes, the diagnosis of the proposed membership functions is very similar to the diagnosis of the clinical case reports. Although RCSC is useful for reference, ACSC should be a more appropriate metric for clinical evaluation. From Fig. 7, although RCSC for the exponentially-weighted membership functions is consistently larger than that for the constantly-weighted membership functions, the RCSC for the constantly-weighted membership functions is also pretty good. The largest RCSC for the constantly-weighted membership functions is 0.578. RCSC for the four grouping membership functions is consistently larger than that for the naive membership functions. This also confirms that the

grouping membership functions consistently improve the naive membership functions in clinical case reports.

5. CONCLUSIONS

This article investigates the syndrome differentiation problem for 18 deficiency syndromes. It applies the classification approach based on fuzzy sets to solve the syndrome differentiation problem. The syndrome differentiation problem is defined as the membership problem of fuzzy sets. It proposes a symptom grouping scheme to divide symptoms for each syndrome into five groups based on symptom location, cause, and mechanism. It also proposes a symptom weighing scheme to assign exponentially decreasing weights to symptoms in each symptom group. Applying these two schemes, it investigates 10 membership functions for fuzzy sets. An experiment shows promising results for this approach using three metrics: the baseline differentiation coefficients, the absolute clinical similarity coefficients, and relative clinical similarity coefficients. This experiment verifies that the membership functions using both symptom grouping scheme and symptom weighing scheme are very practical.

In the future, we will continue to investigate the efficacy of the above two schemes to excess syndromes. We will also extend the benchmark to a larger scale so that the benchmark can be used as a standard benchmark for future syndrome differentiation research.

In the future, this system could be used to immensely collect standard clinical medical records. After that, we could apply the machine learning approach to infer new knowledge from the collected standard clinical medical records and to upgrade the system automatically and continuously.

The ultimate goal of this research is to develop a practical clinical syndrome differentiation system. This syndrome differentiation system could be used in the clinical TCM diagnosis, the training of TCM practitioners, the support of an experimental environment for TCM research.

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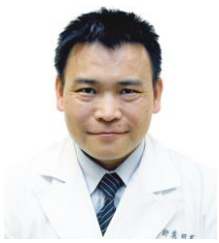

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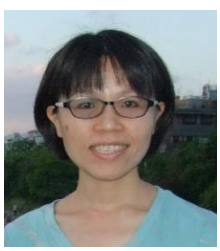

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