Symptom characteristics and prevalence of qi deficiency syndrome in people of varied health status and ages: A multicenter cross-sectional study

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**Abstract**

Objective: Aging caused by a deficiency syndrome can be found in ancient and modern traditional Chinese medicine literature. Qi deficiency syndrome (QDS) is a vital factor in the aging process. This study aimed to establish a full-scale trial to evaluate the prevalence, symptom severity, frequency, and distribution of QDS in different age groups and varying health status to elucidate the role of qi deficiency in the aging process and deterioration of health.

Methods: This cross-sectional study was conducted in four hospitals in China, and data from 1220 participants were included. The participants, aged between 20 and 79 years, completed questionnaires that recorded prevalence of QDS and severity or frequency of relevant symptoms, then were interviewed by investigators. We used frequency analysis and chi-squared tests to...
Introduction

China's older adult population, aged 65 years and above, has increased four times, from 25 million (4.1%) to 130 million (13.3%), over the past 60 years according to an official census. The United Nations estimated that there would be 438 million older adults in China by 2050, occupying one fifth of the world's older adult population. Although social health improvements benefit good health and longevity, the growing demand for health services for the aging population has become a great challenge to China despite having long been the world's most populous country.

Traditional Chinese medicine (TCM) aging theories have played a crucial role in health care, preventing disease, and promoting longevity in China. Based on a history of practice for more than 3000 years, TCM has developed unique theories of etiology and diagnosis. With increasing age, gradual and inevitable alterations occur in response to internal functional decline of the organs, meridians, deficiencies of qi and blood, and yin and yang.

Evidence supporting the qi theory can be found in ancient and modern TCM literature dating back to the Han dynasty (200s CE). For thousands of years, TCM has described qi as one of the three essentials of the body’s entire physiological function. Qi deficiency syndrome (QDS) and its symptoms are very popular in middle aged or older adult populations. In TCM theory, there is a close relationship between qi deficiency and common external symptoms of aging: a core aging theory is known as aging caused by qi deficiency.

Modern studies have explored the mechanism of qi deficiency, the roles of nerves, immunity, and the endocrine system in QDS. The characteristics of blood rheology of QDS have been partly revealed by past studies. Metabolomics-based studies have expanded the vision of demonstrating the mechanism of TCM syndromes including QDS.

Epidemiologic studies have shown a correlation between QDS and aging. Compared with young and middle-aged adults, older adults have a higher prevalence of QDS, especially women. In males, the prevalence decreases markedly after 60 years of age. The conditions of health, sub-health (sub-optimal health), chronic diseases, and geriatrics have attracted great attention in China, and they have been clearly defined by TCM medical professionals. QDS is also one of the most common syndromes in the sub-healthy population and it is complicated by other complex syndromes in individuals. In addition, past studies have shown a close relationship between QDS and typical chronic-diseases or geriatrics, including hypertension, coronary heart diseases, stroke, type 2 diabetes and their common complications.

Despite progress in gaining a better understanding of QDS as related to aging, there are a number of limitations in existing epidemiologic studies on QDS. First, few studies are multi-centered or include large samples. Second, some of the studies lack robust quality control and adequate statistical analyses. Third, most of the previous studies have only focused on qi deficiency constitution instead of QDS itself. In addition, none of the studies describe QDS-related changes in terms of prevalence, symptom severity, frequency, and distribution. Finally, none of the studies compare the prevalence and symptom characteristics in healthy, sub-healthy, and chronic-disease populations of different ages.

The key objectives of our study were to establish a full-scale trial to evaluate the prevalence, symptom severity, frequency, and distribution of QDS in different age groups (healthy, sub-healthy, and chronic disease) to elucidate the role of spleen deficiency in the aging process and deterioration of health status in detail.

Methods

Study design and participants

This was a cross-sectional study conducted between April 2009 and October 2012, using a participant survey to collect...
data. Outpatients, inpatients, and individuals who visited various hospitals for annual physical examinations were recruited using simple random sampling from medical centers in Beijing and Xiamen. The hospitals in Beijing and Xiamen include Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, Peking Union Medical College Hospital Affiliated to Chinese Academy of Medical Sciences, Beijing Hospital Affiliated to the National Health and Family Planning Commission of China, and Xiamen Traditional Chinese Medicine Hospital. All participants signed consent forms and the numbers of participants were evenly distributed across all four seasons.

Diagnostic criteria

Based on the Guideline for Traditional Chinese Medicine Deficiency Syndrome Differentiation issued by the China Association of Integrative Medicine, participants were identified as having QDS if they manifested at least three of the five following signs and symptoms: fatigue, shortness of breath or no desire to talk, spontaneous sweating, swollen tongue with teeth marks on side, and deficient and weak pulse (weak, soft, slippery).

Diagnostic criteria of chronic disease were specialty-based. Diagnoses were made after detailed evaluation, including medical history, physical examination, and diagnostic testing.

Diagnostic criteria of sub-health were based on the Chinese Medicine Clinical Guidelines on Sub-health published by the China Association of Chinese Medicine. After physical examination and appropriate diagnostic testing, patients were diagnosed as sub-healthy when they presented with somatic symptoms (fatigue, sleep disorders), psychological symptoms (depression, anxiety, irritability, fear, decline in short-term memory, lack of concentration), or symptoms of social adaptation (lack of interpersonal communication, interpersonal tension) that had a duration of at least 3 months.

Participants who did not meet the criteria of sub-health, chronic disease or any acute disease were diagnosed as healthy.

Inclusion and exclusion criteria

Inclusion criteria: 20–79 years of age; meeting diagnostic criteria of being healthy, sub-healthy, or having chronic disease; willing and able to respond truthfully to investigator queries after completing the clinical observation questionnaires; signed informed consent.

Participants were excluded at screening if they did not meet the requirements or any of the above diagnostic criteria such as being unwilling or unable to complete questionnaires, having mental disorders, or being unwilling to sign the consent form.

Questionnaire content and administration

As a health study based on a survey of participants, a clinical observation questionnaire was designed with the following contents: demographic information such as name, gender, age; disease information such as chief complaint, present and past medical history; and sub-health-related information including physical, psychological, and social adaptation symptoms. In addition, the questionnaire contained data on TCM symptoms. Syndrome differentiation, including tongue examination and pulse reading, was performed by TCM physicians according to deficiency syndrome differentiation guidelines. A list of degree-definition of severity and frequency of symptoms was attached to each questionnaire for investigators and participants to refer to.

Each participant was interviewed by at least two resident TCM physicians. Two or more senior physicians supervised each interview session to ensure quality control. Questionnaires were provided to participants after they were enrolled in the study. Investigators at each medical center received training on standard operating procedures before the study began.

Statistical analysis

Comparative analysis of prevalence of QDS in different age groups and health status groups was conducted using frequency analysis and chi-squared tests, and expressed with composition ratios. Comparative analysis of quantitative scores of the severity and frequency of symptoms was conducted using a rank-sum test. A probability of $P < .05$ was considered statistically significant. Regression analysis of correlation of QDS occurrence and potential factors including age, health status, and symptoms was performed using non-conditional binary logistic stepwise regression of numerical variables. The significance level for introducing and removing variables was 0.05 and 0.10, respectively. All statistical analyses in this study were performed using SPSS software (version 17.0, SPSS Inc. Chicago, IL).

Results

Characteristics of participants

A total of 1315 questionnaires were delivered and 1248 (94.90% response rate) were completed and returned. A total of 1220 (97.76%) forms were deemed eligible for the study after eliminating questionnaires with incomplete information. There were 593 males and 627 females, a gender ratio of 0.946. In the age range there were 446 participants aged 20 to 39, 414 aged 40 to 59, and 360 aged 60 to 79. In the health status identification, 321 participants were identified as healthy, 654 sub-healthy, and 245 chronic diseases.

Prevalence of QDS in the same health status at different ages

In each health status group, QDS prevalence varied by age (Table 1, Fig. 1).

QDS prevalence in the sub-healthy group showed a significant rising trend with increasing age. Comparisons between the 20–39 and the 60–79 age groups, and between the 40–59 and 60–79 age groups were both statistically significant ($P < .001$ and $P = .001$, respectively). However, QDS prevalence in the sub-healthy participants did not
appear significantly different between the 20–39 and 40–59 age groups ($P > .05$).

In the chronic disease group, QDS prevalence did not demonstrate a similar tendency to that in the sub-health group as age increased. However, such prevalence in participants aged 60–79 was even lower than that in the 20–39 and 40–59 age groups ($P = .022$ and $P = .001$, respectively).

In the healthy group, comparisons of QDS prevalence between 20–39, 40–59 and 60–79 year-old participants were not significantly different ($P > .05$, respectively), which showed a stable trend. QDS prevalence in the sub-healthy and chronic disease participants also did not appear significantly different between the 20–39 and 40–59 age groups ($P > .05$).

### Prevalence of QDS in varied health status within the same age group

Prevalence of QDS in the same age group showed a significant rising trend, generally, when physical condition worsened (Table 2, Fig. 2).

In the 20–39 and 40–59 age groups, QDS prevalence in participants with chronic disease was significantly different compared with the healthy and sub-healthy individuals ($P < .001$, respectively).

In the 60–79 age groups, comparisons of QDS prevalence between the healthy and sub-healthy groups, and between the healthy and chronic disease groups showed statistically significant differences ($P < .001$ for both analyses).

QDS prevalence in the 60–79 age group did not show significant difference between the sub-healthy and chronic disease groups ($P > .05$). Prevalence in the 20–39 and 40–59 age groups also did not show significant difference between the healthy and sub-healthy groups ($P > .05$).

### Severity and frequency of QDS-related symptoms

Degree definitions of severity and frequency of the five qi-deficiency symptoms (fatigue, shortness of breath or no desire to talk, spontaneous sweating, swollen tongue with teeth marks on side, deficient and weak pulse) were attached to the questionnaire for participants and investigators to refer to. The following scores were assigned for symptom severity: asymptomatic = 0; mild = 1; moderate = 2; severe = 3. Symptom frequency was assigned in the following scores: never = 0; occasional = 1; intermittent = 2; often = 3.

QDS symptom severity and frequency at different ages
Symptom severity and frequency scores were not significantly different between the three age groups ($P > .05$) (Tables 3 and 4, Fig. 3).

QDS symptom severity and frequency in relation to health status
Symptom severity scores in the sub-healthy group were higher than those in the healthy group ($P = .006$). Symptoms were more severe in the chronic disease group than in the sub-healthy ($P < .048$). Comparisons of symptom frequency scores among healthy and sub-healthy or chronic disease groups were statistically significant ($P = .049$ and $P = .012$, respectively), indicating that QDS-related symptoms presented more severely and frequently when health status worsened (Tables 5 and 6, Fig. 4).

### Prevalence of QDS and potential factors

Unconditional binary logistic stepwise regression of numerical variables evaluated the correlation of QDS prevalence and other potential related factors including age, health status, and symptoms. The significance levels of

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### Table 1  Age and prevalence of QDS.

<table>
<thead>
<tr>
<th>Health status</th>
<th>Total number</th>
<th>QDS number (%)</th>
<th>Age group, QDS number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health</td>
<td>321</td>
<td>37 (11.5)</td>
<td>20–39 y (12.8) 40–59 y (8.7) 60–79 y (10.2)</td>
</tr>
<tr>
<td>Sub-health</td>
<td>654</td>
<td>171 (26.2)</td>
<td>46 (18.3) 65 (25.2) 60 (41.7)</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>245</td>
<td>141 (57.6)</td>
<td>30 (66.7) 47 (73.4) 64 (47.1)</td>
</tr>
</tbody>
</table>

### Table 2  Health status and prevalence of QDS.

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Total number</th>
<th>QDS number (%)</th>
<th>Groups by health status, QDS number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–39</td>
<td>446</td>
<td>95 (21.3) 19 (12.8) 46 (18.3) 30 (66.7)</td>
<td></td>
</tr>
<tr>
<td>40–59</td>
<td>414</td>
<td>120 (29.0) 8 (8.7) 65 (25.2) 47 (73.4)</td>
<td></td>
</tr>
<tr>
<td>60–79</td>
<td>360</td>
<td>134 (37.2) 10 (12.5) 60 (41.7) 64 (47.1)</td>
<td></td>
</tr>
</tbody>
</table>

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**Fig. 1** Trend in QDS prevalence with increasing age.

**Fig. 2** Trend in QDS prevalence with deterioration of health.
Table 3  QDS symptom severity scores at different ages.

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>20–39</td>
<td>151</td>
</tr>
<tr>
<td>40–59</td>
<td>112</td>
</tr>
<tr>
<td>60–79</td>
<td>107</td>
</tr>
<tr>
<td>Total</td>
<td>370</td>
</tr>
</tbody>
</table>

Table 4  QDS symptom frequency scores at different ages.

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>20–39</td>
<td>312</td>
</tr>
<tr>
<td>40–59</td>
<td>258</td>
</tr>
<tr>
<td>60–79</td>
<td>201</td>
</tr>
<tr>
<td>Total</td>
<td>771</td>
</tr>
</tbody>
</table>

Fig. 3  Trends in severity and frequency of QDS symptoms with increasing age.

Fig. 4  Trends in severity and frequency of QDS symptoms with deteriorating health.

Table 5  QDS symptom severity scores in varied health status.

<table>
<thead>
<tr>
<th>Age group (y)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Health</td>
<td>153</td>
</tr>
<tr>
<td>Sub-health</td>
<td>162</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>55</td>
</tr>
<tr>
<td>Total</td>
<td>370</td>
</tr>
</tbody>
</table>

Table 6  QDS symptom frequency scores in varied health status.

<table>
<thead>
<tr>
<th>Group</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Health</td>
<td>248</td>
</tr>
<tr>
<td>Sub-health</td>
<td>419</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>104</td>
</tr>
<tr>
<td>Total</td>
<td>771</td>
</tr>
</tbody>
</table>

Symptom characteristics and prevalence of qi deficiency syndrome 177
entered and removed variables were 0.05 and 0.10, respectively.

Independent variables were: \( \chi^1 \) gender, \( \chi^2 \) age, \( \chi^3 \) health status, \( \chi^4 \) fatigue, \( \chi^5 \) shortness of breath or no desire to talk, \( \chi^6 \) spontaneous sweating, \( \chi^7 \) swollen tongue with teeth marks on side, \( \chi^8 \) deficient and weak pulse.

Dependent variable \( y \) represented whether or not participants met QDS diagnostic criteria. The logistic regression equation was:

\[
y = -5.448 + 0.462y^1 + 0.844y^4 + 2.308y^5 + 1.365y^6 + 1.959y^7 + 2.492y^8
\]

Results showed that health status, fatigue, shortness of breath or no desire to talk, spontaneous sweating, swollen tongue with teeth marks on side, deficient and weak pulse contributed to the prevalence of QDS (\( P < .05 \)) and for which OR > 1. Gender and age did not affect the prevalence of QDS (\( P > .05 \)).

### QDS symptoms in relation to health status and different ages

Prevalence of QDS symptoms exhibited dramatic trends with increasing age. Among healthy individuals, prevalence of both fatigue and spontaneous sweating increased in the age groups of 20–39 and 40–59, but declined in the age groups of 60–79. A deficient and weak pulse rose sharply between 40–59 and 60–79 years of age, but this symptom remained stable between ages 20–39 and 40–59. The prevalence of shortness of breath or no desire to talk and swollen tongue with teeth marks on side, dropped dramatically in middle age, while the former then remained steady and the latter increased markedly in the 60–79 age group (Table 7, Fig. 5).

In the sub-healthy group, prevalence of fatigue, spontaneous sweating and deficient and weak pulse rose slowly with increasing age. Shortness of breath or no desire to talk and swollen tongue with teeth marks on side slowed markedly between 20–39 and 40–59 years of age, while both of them accelerated significantly between 40–59 and 60–79 years of age (Table 7, Fig. 6).

Persons with chronic diseases, prevalence of fatigue, spontaneous sweating and deficient and weak pulse showed an increase between 20–39 and 40–59 years of age, followed by a decline in the 60–79 age group. Prevalence of swollen tongue with teeth marks on side remained steady, while that of shortness of breath or no desire to talk decreased markedly as health status worsened (Table 7, Fig. 8).

Prevalence of QDS symptoms manifested certain trends as health status deteriorated. Among the 20–39 age group, prevalence of swollen tongue with teeth marks on side, shortness of breath or no desire to talk and deficient and weak pulse showed a decline or slight increase between healthy and sub-healthy persons, then, followed a sharp increase in the chronic disease group. Prevalence of fatigue and spontaneous sweating increased steadily as health status worsened (Table 7, Fig. 8).

In the 40–59 age group, prevalence of all QDS symptoms was markedly higher with increasing age. Prevalence of fatigue in healthy and sub-healthy persons was almost

<table>
<thead>
<tr>
<th>Table 7</th>
<th>Prevalence of QDS symptoms in relation to health status and age.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health status group</td>
<td>Age group (n)</td>
</tr>
<tr>
<td>Health</td>
<td>20–39</td>
</tr>
<tr>
<td></td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td>60–79</td>
</tr>
<tr>
<td>Sub-health</td>
<td>20–39</td>
</tr>
<tr>
<td></td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td>60–79</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>20–39</td>
</tr>
<tr>
<td></td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td>60–79</td>
</tr>
</tbody>
</table>
twice that of shortness of breath or no desire to talk, swollen tongue with teeth marks on side and deficient and weak pulse. Prevalence of spontaneous sweating increased less precipitously than other symptoms among healthy and sub-healthy individuals (Table 7, Fig. 9).

In the 60–79 age group, prevalence of spontaneous sweating, swollen tongue with teeth marks on side, deficient and weak pulse respectively rose slowly. Prevalence of fatigue and shortness of breath or no desire to talk increased slowly between healthy and sub-healthy individuals, then declined dramatically in sub-healthy and chronic disease persons (Table 7, Fig. 10).

Generally speaking, prevalence of QDS-related symptoms increased when physical conditions worsened from healthy to sub-healthy or with increasing age between youth and middle age. In all the six health status and age groups, fatigue had the highest prevalence of all QDS symptoms (Table 7, Figs. 5–10).

**Feature-selection based internal correlations of QDS-related symptoms**

With association rules based on feature selection analysis, internal correlations of QDS-related symptoms were found. The levels of relevance between the different symptoms are presented as lines of different widths in the visual image (Fig. 11). Several symptoms related to deficiency of *qi*, kidney, lung, stomach, yin and yang have formed tight-knit groups (lines in red) in QDS populations, and may contribute to the occurrence of QDS, including persistent cough with white sputum, sexual dysfunction or infertility, shortness of breath or wheezing, edema of face or feet, rapid thin pulse, afternoon fever, abdominal pain relieved by pressing, abdominal pain relieved by eating, loose stools and clear copious urine.

**Discussion**

From the perspective of modern medicine, aging is associated with a wide range of human chronic diseases, including diabetes, cardiovascular, neurodegenerative diseases and even cancer. The field of modern aging research has progressed rapidly over the past decades. Several physiological and environmental interventions have been shown to influence the rate of aging in organisms ranging from yeast to mammals. The biologic aging mechanism is complicated and may arise from various and serious causes, including deterioration or destruction of the cells in organs through mutations and infections, aging by failure to eliminate harmful waste products, poisoning or radiation damage from external sources.

The aim of this study was to determine how the syndrome of *qi* deficiency in Chinese medicine manifests during human aging and deteriorating health. We observed QDS symptoms in people in different age groups and of varied health status. The present findings indicate the value of taking TCM QDS-based interventions into account in anti-aging health promotion and chronic disease prevention strategies.

Our results demonstrated that as sub-healthy people aged, QDS prevalence rose significantly. QDS prevalence in the chronic disease group did not demonstrate such an association with increasing age. By the time this group reached late adulthood, they exhibited an even lower QDS prevalence than the young and middle aged individuals.
the healthy group, QDS prevalence showed a stable trend with increasing age.

There was a very close relationship between QDS and health status. QDS prevalence in the same age group showed a significant rising tendency when physical condition worsened in general. However, in the 20–39 and 40–59 age groups, QDS prevalence increased slightly as they became sub-healthy, which was followed by a dramatic increase when they developed chronic disease. In the 60–79 age group, QDS prevalence remained stable between the sub-healthy and chronic disease statuses, and there was a significant decrease between the healthy and sub-healthy or chronic disease statuses.

As for the young and middle-aged people in the chronic disease group, the QDS prevalence tripled of those in the healthy and sub-healthy groups, respectively. Interestingly, QDS prevalence in the chronic disease group dropped sharply in the older adults compared with a huge increase of such prevalence in the sub-healthy individuals of the same age, equaling half of that in people with chronic disease. These results suggest that qi deficiency has less impact on chronic diseases with increasing age, compared with healthy and sub-healthy individuals of the same age.

Qi deficiency may play a crucial role in young and middle-aged chronic disease pathogenesis and in old-age sub-healthy pathogenesis. Middle age may be the turning point of the effects of QDS in people with sub-health and chronic disease. Explanations for these phenomena may be that the etiology and pathogenesis of aging as health declines from a state of sub-health to chronic disease is much more complicated than predicted in middle-aged and older adults. Aside from qi deficiency as a directly related factor in deterioration of health status, other factors may play roles in these processes, especially in late adulthood.

Symptom severity and frequency scores of QDS showed a rising trend with deteriorating health status, while such a tendency did not accompany increasing age. Thus, it appeared that health status, fatigue, shortness of breath or no desire to talk, spontaneous sweating, swollen tongue with teeth marks on side, and deficient and weak pulse were important contributing factors to QDS. However, age did not affect the prevalence of QDS, which is not the common expectation.

Distribution of QDS symptoms in certain health statuses and age stages also showed dramatic irregularities. As physical condition worsened from health to sub-health or age increased from youth to middle age, prevalence of QDS symptoms showed a rising trend generally. Fatigue has become the most common symptom of all health statuses and ages in QDS individuals, the result of which emphasizes the importance of this symptom as a typical QDS wake-up call by a certain degree of universality.

The concept of sub-health has received attention by both health professionals and the general public in China, primarily because it is based on TCM theory. (TCM continues to be an essential component in the Chinese health care system.) With an overall estimate that more than 60% of QDS prevalence in China occurs with increasing age, there is concern that if the warning signs and symptoms of sub-health are not recognized and treated, critical public health and social problems may arise. A consequence of untreated sub-health leads to chronic diseases, including heart disease, stroke, cancer, chronic respiratory diseases and diabetes, which, as the leading causes of mortality, represent 63% of all deaths worldwide. There has been a gradual increase in the incidence of chronic diseases with a mortality rate of more than 85% of all deaths in China annually. Furthermore, 91.7% of Chinese seniors, 60 years and older, are affected by chronic diseases and 55% have more than three concomitant persistent conditions.

Long thought to be an inexorable road toward decline and diseases, aging is in fact remarkably plastic in TCM deficiency syndrome distributions including qi, spleen and kidney. Our former research clearly revealed the wide distribution of both SDS (spleen deficiency syndrome) and KDS (kidney deficiency syndrome) in persons of three varied
health status (health, sub-health and chronic disease).\textsuperscript{50,51} Interestingly, this study also demonstrated the existence of relatively similar distributions for QDS and its syndrome-related symptoms. The result of this implies that qi deficiency became a less common constitution compared with other deficiency syndromes existing in healthy or young individuals in previous studies. QDS may finally result in deficiency syndrome-associated sub-health and chronic diseases, and be involved in the mechanism of aging. Such plasticity could be harnessed to approach age-related sub-health and chronic diseases from a novel perspective.

Relevant studies indicate that QDS is a pathophysiological basis of sub-health, chronic diseases, and aging\textsuperscript{24–37} which is accompanied by other complex syndromes.\textsuperscript{29–31} Although most of these studies have stated the relationship between QDS prevalence, age, and general health status, some limitations in study design may impact the reliability of their results. This large-scale study has attempted to overcome these disadvantages, allowing us to find compelling evidence of the role of spleen deficiency in the aging process and deterioration of health status. Our work has revealed that the role of qi deficiency in the aging process may not be as important as previous studies have predicted. Also, gender does not relate to the prevalence of QDS, which differs from the notion in past studies that QDS prevalence may partly depend on gender.\textsuperscript{21–25}

Based on feature selection, our preliminary studies have also tested and proven the internal relationships of deficiency syndrome-related symptoms in SDS and KDS individuals, which are far more complex than expected.\textsuperscript{50,51} The association rules based on the study of QDS also show that several symptoms related to deficiency of qi, kidney, lung, stomach, yin and yang have formed existing tight-knit groups in the QDS population and may contribute to the occurrence of QDS (Fig. 11). More modern computational solutions can be applied to excavating core rules of QDS on the basis of the ancient Chinese philosophic concept of holism objectively and systematically, including decision trees, association rules, artificial neural nets and complex system entropy clustering analysis algorithms.

There are, however, several limitations in this study. Selection bias may exist because the data extracted from urban hospitals in Beijing and Xiamen may not be representative of the rest of China where the prevalence of QDS and distribution of symptom severity and frequency may vary from those in eastern urban areas. Prospective cohort studies with longer follow-up times would be needed; longitudinal studies may provide stronger evidence for the role of QDS in spontaneous, long-term aging and health status-related processes.

Conclusions

This study appears to support the TCM concept that QDS is an important mechanism of sub-health and chronic diseases, while not contributing to problems related to aging. It may play a crucial role in young and middle-aged chronic disease pathogenesis and in old-aged sub-health pathogenesis. Early recognition of the warning signs and symptoms of QDS may lead to promotion of healthy living as well as early intervention and even prevention strategies for sub-health and chronic diseases.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

YZ and XD conceived the study, and participated in its design and coordination. XD directed the study process and optimization. YZ, LZ and YL designed the questionnaire, FSL and ZQZ trained investigators at each medical center on standard operating procedures of this study. XZ, LZ, SYD and JL performed the statistical analysis. YZ, YL and XD wrote the manuscript with contributions from all other authors. All authors carried out the clinical investigation and approved the final manuscript.

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