



A JAPANESE FIVE-CONSTITUTION MODEL: VALIDATION AND CHARACTERIZATION USING THE CONSTITUTION IN CHINESE MEDICINE QUESTIONNAIRE - JAPANESE VERSION

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ABSTRACT – Objective: The 60-item Constitution in Chinese Medicine Questionnaire (CCMQ), based on a traditional nine-constitution framework, has been widely used in China for health assessments. However, its length poses a practical barrier to its widespread clinical use. A previous study in Japan suggested that a five-constitution model was more optimal for the Japanese population and subsequently developed a simplified 18-item questionnaire. This study aimed to validate the structure of this five-constitution model and establish the standalone diagnostic accuracy of the 18-item questionnaire.

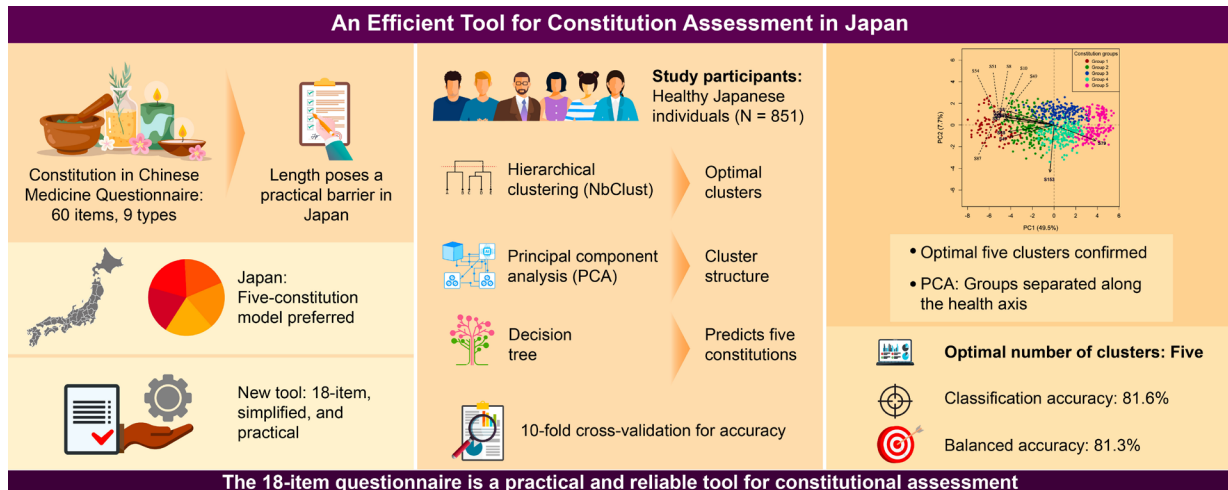
Materials and Methods: This was a secondary analysis of a cross-sectional dataset comprising 851 healthy Japanese participants who completed the 60-item CCMQ. We first used hierarchical clustering (the NbClust package) on the 18-item data to determine the optimal number of clusters. We then used principal component analysis (PCA) to analyze the structure of the clusters. Finally, a decision-tree model was developed to classify participants based on the 18 items, and its performance was evaluated using 10-fold cross-validation.

Results: Clustering analysis of the 18-item data confirmed that five was the optimal number of clusters. PCA revealed that the five groups were clearly separated along a primary “health axis”. The decision-tree model, using only 18 items, successfully classified participants into five constitution types (a structure validated on the 18-item data itself), with an overall accuracy of 81.6% and a balanced accuracy of 81.3%.

Conclusions: The 18-item simplified questionnaire is a valid and reliable instrument for constitutional assessment in Japan. This concise tool effectively retains the structural and predictive information of the original 60-item version, offering a practical solution for large-scale research and personalized health management in clinical settings.

KEYWORDS: Machine learning, Personalized medicine, Mibyo, Diagnostic accuracy, Taishitsu.





Graphical Abstract. A simplified 18-item questionnaire, using machine learning, validates a five-constitution model for the Japanese population with 81.6% accuracy.

INTRODUCTION

Personalized preventive medicine is a critical objective in contemporary healthcare that aims to tailor interventions based on individual susceptibility¹. In line with this approach, the concept of “constitution” (*Taishitsu*), originating from Traditional Chinese Medicine (TCM), is gaining attention as a framework for understanding inherent individual differences in health status and disease risk. An extensive body of research, including a review of over 1,600 studies, has demonstrated significant associations between specific constitution types and various diseases². Scholars have suggested that these traditional classifications may correlate with objective biological markers, thereby strengthening their scientific relevance³. Reflecting its international acceptance as a standard tool, the Constitution in Chinese Medicine Questionnaire (CCMQ) has been systematically translated and validated for diverse populations, including Japanese, Korean, Vietnamese, and various Chinese-speaking communities⁴⁻⁸. However, although comprehensive, the original 60-item CCMQ imposes a considerable burden on both patients and practitioners in clinical settings and large-scale epidemiological studies. Moreover, the number of items can be a practical barrier to their widespread adoption. Furthermore, the standard CCMQ framework, developed primarily for the Chinese population, may not fully capture the unique constitutional characteristics of Japanese people. Therefore, developing and validating more concise instruments that retain the core evaluative properties of the original CCMQ are essential to advance research and facilitate clinical applications in this field.

In Japan, a notable advancement was made by Sato et al⁹, who analyzed data from 851 individuals using the 60-item Japanese version of the CCMQ

(CCMQ-J)⁹. Their cluster analysis suggested that a five-constitution model, rather than the traditional nine-constitution model, was optimal for this population. Subsequently, a simplified 18-item questionnaire was developed from a much larger item pool using a machine learning approach specifically designed to predict the five constitution types¹⁰. This methodology – first identifying an optimal population-specific constitution structure and then developing a tool for it – contrasts with other efforts to shorten the CCMQ. Alternative approaches typically focus on reducing the number of items while retaining the original nine-constitution framework^{11,12}. While this represents a significant step towards a more practical assessment tool, a comprehensive validation of this new framework is still needed. Specifically, the reproducibility of the five-constitution model requires independent confirmation. Moreover, the predictive accuracy of the 18-item questionnaire as a standalone tool has not been quantitatively evaluated, nor have the defining characteristics of each of the five constitutions been fully elucidated. Addressing these gaps is crucial for confirming the robustness of the model and establishing an 18-item questionnaire as a reliable, independent assessment tool.

Therefore, the present study was designed to comprehensively validate this new framework. Our primary objective was to assess the standalone performance of the 18-item questionnaire, first, by confirming its ability to produce a robust five-constitution structure that is conceptually aligned with the original, and second, by evaluating the predictive performance within this 18-item-derived classification. We hypothesized that this 18-item scale would be accurate and informative. To test this, we conducted a multifaceted structural analysis using principal com-

ponent analysis (PCA) to assess group separation, response pattern histograms to detail group profiles, and dendrograms to examine inter-item relationships. We then constructed a decision-tree model¹³ to evaluate predictive performance.

MATERIALS AND METHODS

Study design and reporting guidelines

This diagnostic accuracy study aimed to validate a prediction model using data from a previously published cross-sectional survey⁹. This report was prepared according to the Transparent Reporting of a Multivariate Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) statement¹⁴.

Source of data and participants

This study used a dataset from a large-scale cross-sectional survey previously described by Sato et al⁹. The original data were collected from the Japanese population *via* a crowdsourcing service. The participants were healthy Japanese men and women aged 20-85 years who provided informed consent online prior to participation. The

final dataset for the present analysis comprised 851 participants (350 men and 501 women) who provided complete responses to the 60-item Japanese version of the Constitution in Chinese Medicine Questionnaire (CCMQ-J).

Outcome variable (gold standard)

The outcome variable for this study was a five-constitution classification that served as the gold standard for validating our predictive model. This classification is conceptually based on the five-group framework established by Sato et al⁹, who used the full 60-item dataset. To validate the 18-item questionnaire as a standalone tool, we first performed hierarchical clustering on the 18-item data from all 851 participants. This analysis confirmed that a stable five-cluster solution was also optimal for the reduced dataset, conceptually aligning with the original findings. This classification, derived directly from the 18-item data, served as the operational gold standard for the subsequent training and validation of the decision-tree model. The specific counts for each of the five groups in this operational gold standard are shown as the “Actual” totals in the confusion matrix (Table I).

Table I. Confusion matrix and performance metrics of the decision-tree model.

	Predicted				
	Group 1: Severe Psychosomatic Distress Type	Group 2: Mild Psychosomatic Distress Type	Group 3: Transitional Type	Group 4: Pre-Healthy Type	Group 5: Healthy Type
Actual					
Group 1: Severe Psychosomatic Distress Type	65	16	1	2	0
Group 2: Mild Psychosomatic Distress Type	11	136	21	16	0
Group 3: Transitional Type	0	2	163	3	12
Group 4: Pre-Healthy Type	0	19	15	184	12
Group 5: Healthy Type	0	0	9	18	146

Performance metrics:

- Overall Accuracy (Recognition Rate): 81.6%
- Balanced Accuracy: 81.3%

Predictor variables (the 18-item questionnaire)

The predictor variables for the model were 18 items from a simplified constitution questionnaire¹⁰. These items consisted of multilevel ordinal scales tailored to each question's content (e.g., frequency or state) and one binary variable for sex. The exact wording of all 18 items and their corresponding response scales are presented in [Supplementary Table 1](#) for full transparency. These categorical responses served as input features for the analysis.

Statistical Analysis

Reproducibility and structural analysis of the five constitution types

To determine the optimal number of constitution types that emerged *de novo* from the 18-item simplified questionnaire, we conducted a hierarchical clustering analysis. Hierarchical clustering is an exploratory data analysis method used to identify natural groupings (clusters) within a dataset without making prior assumptions about the number of groups¹⁵. We used this approach to objectively assess the number of distinct constitutional types supported by the 18-item data. Using the NbClust package in R (Ward's method, Euclidean distance), a wide range of validation indices were calculated to identify the most plausible number of clusters in the reduced dataset¹⁶. The five groups were supported by the D-index¹⁷ and the Hubert Statistic¹⁸. The average number of participants per group was 170.2 (standard deviation: 49.3).

Following confirmation of the five-group structure, we conducted several further analyses, as described below, on the 18-item data to elucidate the characteristics of the groups and structure of the items. PCA was performed to visualize the separation of the five constitution types in a lower-dimensional space and interpret the meaning of the principal components by examining the factor loadings. PCA is a technique used to reduce the complexity of a dataset with many variables (in this case, 18 questions) into a few key underlying dimensions, or "principal components"¹⁹. This allowed us to visualize the overall relationship among the five groups and identify the main axis that differentiates them. To understand the specific response patterns for each constitution type, histograms of each of the 18 items were generated and stratified into five groups. Histograms are a basic graphical tool used to display the distribution of data, which, in this context, allowed for a direct visual comparison of how each group responded to a specific question. Finally, to explore the interrelationships among the questionnaire items, a separate hierarchical cluster-

ing analysis was conducted, and the resulting structure was visualized as a dendrogram. A dendrogram is a tree-like diagram illustrating the arrangement of clusters produced by hierarchical clustering. We used this to understand which questions were the most similar to each other, thereby revealing the thematic structure of the questionnaire.

Development and validation of the predictive model

A decision-tree model was developed to classify the five constitution types using only 18-item questionnaire responses. A decision tree is a machine-learning algorithm that creates a flowchart-like model to classify individuals based on a series of questions²⁰. We chose this model primarily because of its high interpretability, as the resulting classification rules are easy to visualize and understand. The model was constructed using the rpart package in the R statistical environment. For model training, the "information" criterion was used as the splitting rule, and model complexity was controlled by setting the complexity parameter (cp) to 0.005 and the maximum tree depth to 20. To ensure the robustness and generalizability of the model, its performance was evaluated using a 10-fold cross-validation procedure. Cross-validation is a standard technique used to assess how the results of a statistical analysis can be generalized to an independent dataset²¹. The 10-fold method involves repeatedly training the model on 90% of the data and testing it on the remaining 10%, which helps ensure that the reported accuracy of the model is reliable and not simply a result of overfitting the original dataset.

Model performance evaluation

The classification performance of the final decision-tree model was assessed using a confusion matrix, which cross-tabulated the model's predicted constitution types against the gold standard classifications. From this matrix, two primary performance metrics were calculated: (1) overall accuracy (also referred to as the recognition rate), defined as the proportion of all correctly classified participants, and (2) balanced accuracy, defined as the arithmetic mean of the accuracies (recall) for each of the five constitution types.

Ethical considerations

This study is a secondary analysis of a fully anonymized dataset provided by the authors of the original study⁹. The original study was conduct-

ed in accordance with the Declaration of Helsinki and approved by the Ethics Committees of Nara Institute of Science and Technology and Suntory Global Innovation Center Limited (approved on 19 February 2018). All participants in the original study provided informed consent before participating in this survey.

RESULTS

Establishing the operational gold standard: structural analysis of the 18-item data

The structural analysis first confirmed that the 18-item data could reproduce a stable five-group structure, consistent with the conceptual framework of the gold standard. This was established through hierarchical clustering prior to the development of the predictive model. According to the simple majority rule of all indices, a two-cluster solution was most frequently proposed (10 of 26 indices), suggesting a primary division between “healthy” and “unhealthy” states (Supplementary Table II). However, the two-cluster solution was deemed too simplistic to capture the nuanced spectrum of constitutional

types. Graphical methods provided additional insights; the second difference plot for the D-index showed a notable secondary peak at five clusters, in addition to the highest peak at three clusters (Figure 1). Considering the theoretical background of the five-constitution model proposed by Sato et al⁹ from the original 60-item data and the support for a five-cluster solution from key indices, such as the Duda and PseudoT2 statistics (Supplementary Table II), we determined that five was the most statistically plausible and clinically meaningful number of clusters for subsequent analyses.

Structural characteristics of the five constitutions and items

A PCA was performed on the 18-item questionnaire to visualize the relationships among the five constitution types. The distribution of the participants (scores) and contribution of the 10 most discriminating items (loadings) are shown in a single biplot (Figure 2). The first two principal components (PC1 and PC2) explained 49.5% and 7.7% of the total variance, respectively. These five groups were separated along the first principal compo-

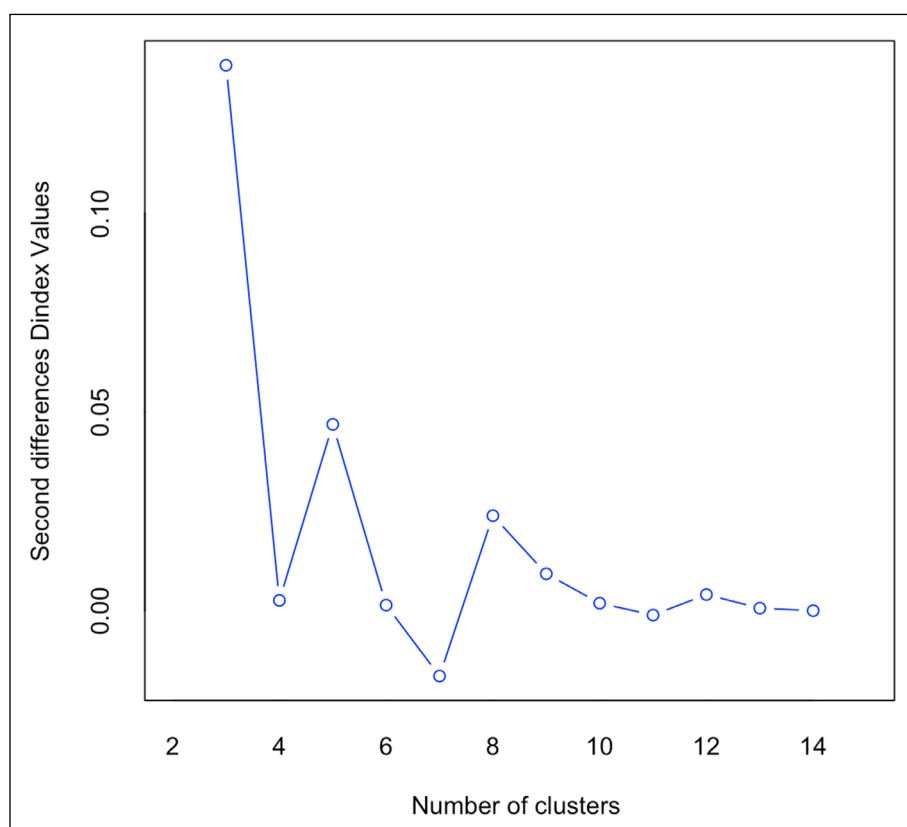


Figure 1. Determination of the optimal number of clusters using the D-index. The plot displays the second difference in the D-index against the number of clusters (k) tested. The optimal number of clusters was indicated by a significant peak. The plot shows the highest peak at k=3 and a notable secondary peak at k=5, supporting the selection of a five-cluster solution based on the majority rule of multiple indices.

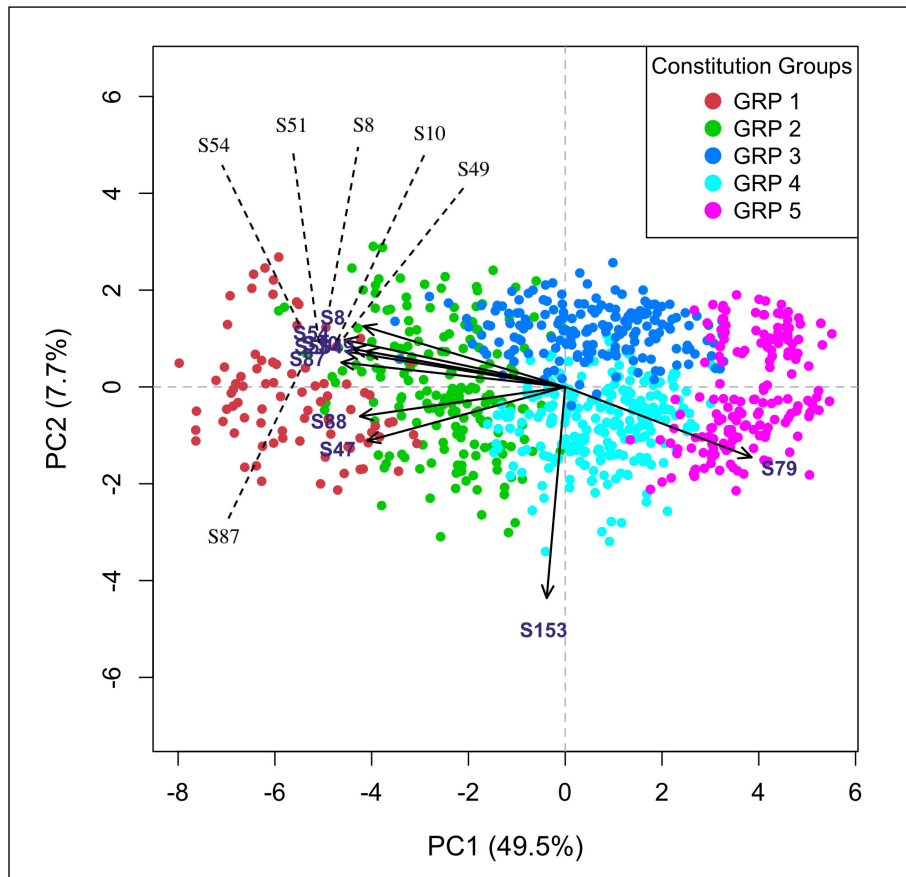


Figure 2. Principal component analysis (PCA) biplot of the 18-item questionnaire data. The biplot displays the results of a PCA on 851 participants, with the first two principal components explaining 49.5% (PC1, horizontal axis) and 7.7% (PC2, vertical axis) of the total variance, respectively. The points (scores) represent the participants, clearly color-coded by their assigned constitution type (GRP 1-5), demonstrating their separation along the PC1 “health axis.” The arrows (loadings) represent the contribution of the 10 most discriminating items (e.g., S54, S79) to the principal components. This single plot streamlines the visualization by showing both the grouping of participants and the influence of key variables simultaneously. GRP: Group; PCA: Principal Component Analysis.

ment (PC1). The groups were ordered along PC1 from Group 1 on the far negative side to Group 5 on the positive side, indicating that PC1 (explaining 49.5% of the variance) represents the primary dimension differentiating the constitution types. As shown using the loading arrows in the biplot, most questionnaire items had negative loadings on PC1, whereas S79 had a strong positive loading. This opposing pattern suggests that PC1 can be interpreted as a general “health axis,” where a higher PC1 score reflects better health status.

To further characterize the five constitution types, the distribution of responses for each of the 18 questionnaire items was visualized using histograms stratified by group. These histograms reveal clear differences in response patterns among the groups for numerous items, providing qualitative support for their distinct profiles. Figure 3 shows representative examples for items S54 (Gloomy Mood), S80 (Fatigue), and S79 (Energetic State). The complete set of histograms for all 18 items is available in [Supplementary Figure 1](#).

A detailed analysis of the response distributions for each item revealed the following distinct psychosomatic profiles for the five constitutional types.

Group 1: Severe psychosomatic distress type. This group had the most severe adverse conditions across the board. Responses to the vitality indicator S79 (Energetic State) were almost exclusively “Never.” Conversely, for items concerning mental distress, such as S88 (Irritability) and S90 (Fearfulness), responses were strongly skewed towards “always.” This profile suggests a state of chronic mental stress combined with a severe depletion of physical and mental energy.

Group 2: Mild psychosomatic distress. This group represented a transitional phase towards more definite adverse health. While less severe than in Group 1, responses to items concerning physical fatigue, such as S80 (Fatigue) and S46 (Exhaustion), were centered on “sometimes” and “often,” indicating a noticeable level of physical exhaustion.

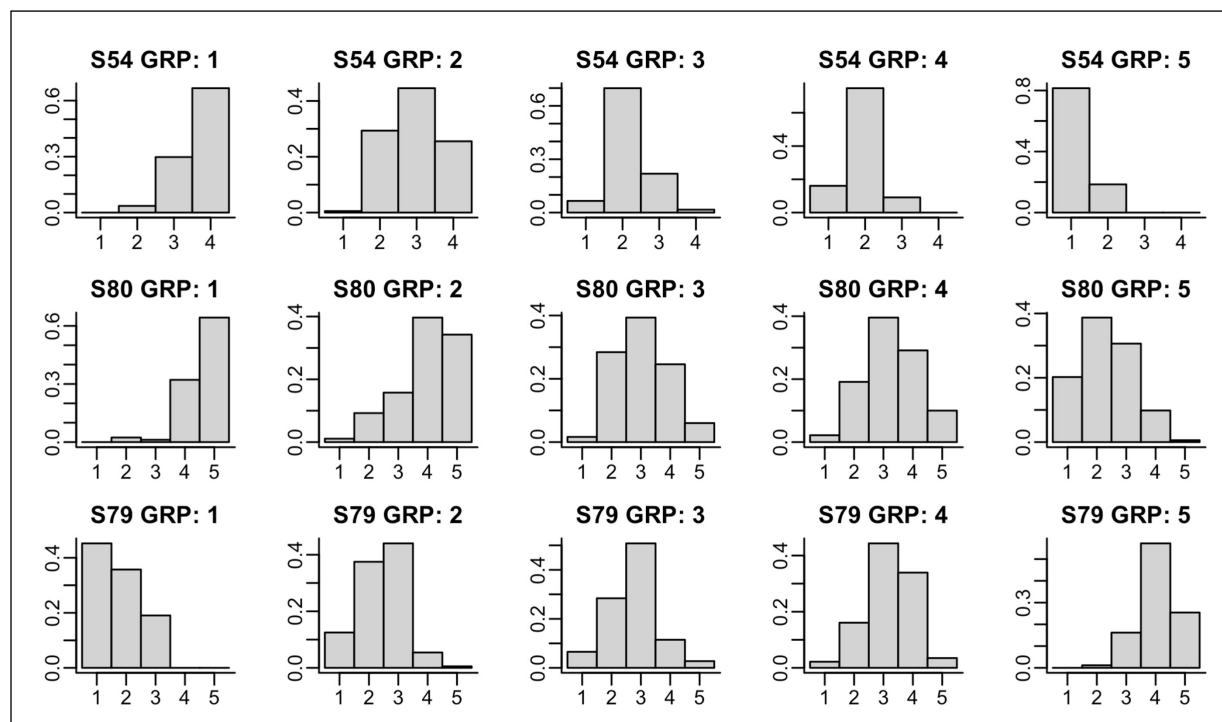


Figure 3. Representative response distributions for key questionnaire items stratified by constitution type. The histograms show the response distributions for the three representative items: S54 (Gloomy Mood), S80 (Fatigue), and S79 (Energetic State). The plots illustrate the distinct response patterns that characterize each of the five groups (Group 1-5). GRP: Group.

Group 3: Transitional type. Positioned between the unhealthy and healthy groups, the healthy group was observed to have a higher proportion of men than women. A majority of this group responded “Good” to S182 (Health Status), suggesting a generally positive self-assessment of their health.

Group 4: Pre-healthy type. This group demonstrated a clearer state of health than Group 3. This distinction was evident in several items: their self-assessment of health (S182) peaked at “Good”; their responses to S79 (Energetic State) were shifted more towards “often”; and their responses to S90 (Fearfulness) were more concentrated at “Never,” indicating higher vitality and mental stability.

Group 5: Healthy type. This group represented the optimal health state. For S54 (Gloomy Mood), the most critical predictor in the decision tree, nearly all responses were “Almost never.” Furthermore, scores for the vitality indicator S79 (Energetic State) were concentrated at “often” and “always,” reflecting a robust state of physical and mental well-being.

Finally, a hierarchical cluster analysis of the 18 items was conducted to explore their inter-relationships. The resulting dendrogram ([Supplementary Figure 2](#)) revealed that the items were grouped into four distinct and thematically coherent clusters, which we labeled as follows:

Cluster 1: Physical fatigue. This cluster comprised three items directly related to physical exhaustion: S80 (Fatigue), S46 (Exhaustion), and S47

(Weariness). The strong correlation among these items highlights the importance of physical fatigue as a core dimension of constitution.

Cluster 2: Mental distress. This was the largest cluster and was further divided into two distinct subgroups, suggesting that mental symptoms were composed of multiple facets.

Sub-group 2a (General Mental State): This included items reflecting general modulations of one’s mental state, such as S7 (Nervousness), S182 (Health Status), S93 (Sighing), and S53 (Concentration).

Sub-group 2b (Mood and Affect): This included items related to psychological distress, such as depressive mood and anxiety, including S8 (Hopelessness), S54 (Gloomy Mood), S49 (Insecurity), and S88 (Irritability).

Cluster 3: Vitality. This cluster consisted of a single positively worded item, S79 (Energetic State). Its distinct position, separate from the symptom-focused clusters, suggests that it serves as a unique and important indicator of positive health within the constitutional assessment.

Cluster 4: Objective and physical characteristics. This cluster comprises S119 (Complexion) and S153 (Sex). Their low correlations with other symptom-based items indicated that they functioned as independent variables.

This overall structure demonstrates that the 18 items are not redundant but effectively capture several distinct and interpretable dimensions of a person’s constitution.

Predictive model performance

The decision-tree model effectively classified five constitution types using an 18-item questionnaire. The final model structure (Figure 4) identified key questions that were highly effective in discriminating among groups, with S54 (Gloomy Mood) serving as the primary splitting factor for the entire dataset. The detailed classification results are presented in the confusion matrix in Table I. The model achieved an overall accuracy (recognition rate) of 81.6%. The balanced accuracy, which accounted for the differences in the number of participants in each group, was 81.3%.

As shown in the confusion matrix, the model correctly classified a high proportion of participants for most constitutional types. The main sources of misclassification were observed among the intermediate groups, particularly between the mild psychosomatic distress and transitional types.

DISCUSSION

This study demonstrated that a five-constitution model is a robust and appropriate framework for classifying health status in the Japanese population, as this structure was successfully identified

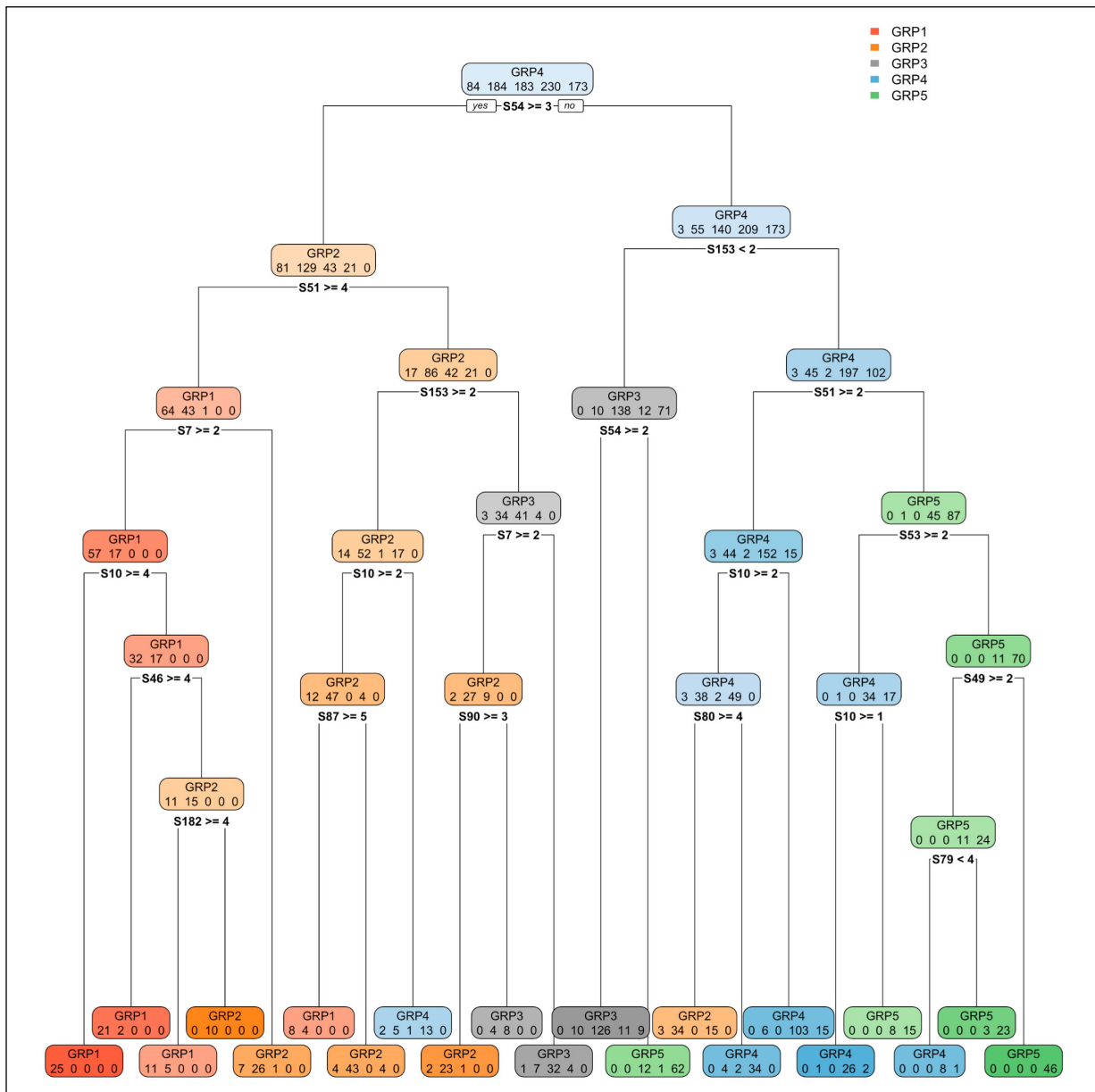


Figure 4. Visualization of the final decision-tree model. This figure shows the decision tree used to classify participants into one of five constitution types based on the 18-item questionnaire. The nodes show the splitting criteria (questions), and the terminal leaves indicate the final classification. The numbers on the leaves represent the number of participants classified into groups at each node. GRP: Group.

from a simplified 18-item questionnaire. Furthermore, we established that this concise 18-item instrument serves as a valid stand-alone tool capable of classifying individuals into one of the five constitution types with high accuracy (81.6%). These findings address the critical need for a validated and practical assessment tool for constitution types, confirming that a substantially shorter questionnaire can effectively retain the essential structural and predictive information of a much longer and more comprehensive instrument.

A key finding of this study was the confirmation that the data from the simplified 18-item questionnaire inherently supported a five-constitution model, a structure that aligns with the initial findings from the full 60-item instrument⁹. While the original study first proposed this five-group framework, our analysis provides stronger evidence of its structural validity. This is particularly significant given that the five clinically interpretable health profiles, ranging from healthy to severely distressed, emerged *de novo* from a much smaller, curated set of questions. This finding emphasizes the potential of population-specific models, as the original Japanese validation of the CCMQ focused on a standard nine-constitution framework⁴. Establishing a robust and representative classification framework is critical, as recent studies have demonstrated significant associations between TCM constitutions and tangible health factors, including lifestyle behaviors²² and depression²³. Therefore, our validation of the five-constitution model provides a solid foundation for future research in Japanese constitutional medicine.

Our data-driven characterization of the five groups provides an empirically grounded interpretation of the labels originally proposed by Sato et al⁹ based on TCM theory. This correspondence is most direct at the extremes of the health spectrum. The “Healthy Type” (Group 5) aligns perfectly with the “Balanced type” in TCM theory, showing high scores on vitality (S79) and low scores on all negative symptoms. Conversely, the “Severe Psychosomatic Distress Type” (Group 1) is a clear empirical representation of the “Mixed Yang-Deficiency and Qi-Stagnation type”; our findings show this group is defined by a near-total lack of vitality (S79), a key feature of Yang-Deficiency, combined with the highest levels of anxiety and mood disturbance (S88, S90), which are hallmarks of Qi-Stagnation. The intermediate groups also show logical correspondence: the “Mild Psychosomatic Distress Type” (Group 2) fits the description of a “Borderline” state, while the “Transitional Type” (Group 3) profile of lower vitality and neutral health assessment is consistent with a mild “Yang-Deficiency” state. While the “Pre-Healthy Type” (Group 4) corresponds to the original

“Qi-Stagnation” group, our 18-item data characterizes it as a state of relatively good mental stability, suggesting our data-driven labels provide a more precise profile for this specific, concise tool. Therefore, our descriptive labels serve not to replace the original concepts, but to provide a more accessible and clinically transparent definition of what these constitutional types represent in the Japanese population.

Beyond confirming the underlying five-group structure, this study established the standalone validity of an 18-item questionnaire as a practical diagnostic tool. The performance of our decision-tree model was particularly noteworthy, achieving an overall accuracy of 81.6%¹³. This is a significant finding compared to other efforts to shorten the standard nine-constitution CCMQ¹². Our approach, which reevaluates the optimal population-specific structure before building a predictive tool, achieved a high level of accuracy while being tailored to the target population. Although objective diagnostic methods using biomarkers are an important area of research²⁴, accessible and validated questionnaire-based tools remain indispensable for large-scale health screening. An accurate and concise instrument is crucial for applying constitutional theory to practical health maintenance and disease prevention, which are the primary goals of both TCM and its Japanese adaptation, *Kampo*^{25,26}. Therefore, the high predictive performance of the 18-item questionnaire establishes it as a reliable and practical instrument for constitutional assessment in Japan.

While these results are promising, it is important to acknowledge the limitations of this study. First, it was a secondary analysis of a dataset recruited *via* crowdsourcing. As the data do not derive from a probabilistic sample, the cohort may not be fully representative of the general population. Therefore, the results should be interpreted as descriptions of observed patterns in the available sample, and claims of generalizability must be made with caution. Second, the conceptual framework for our gold standard is based on a longer questionnaire rather than on objective clinical diagnoses or biomarkers.

Despite these limitations, validation of this concise and accurate 18-item questionnaire has significant practical implications, potentially bridging traditional constitutional assessments with modern evidence-based health management. A key application lies in personalized preventive medicine. Given that specific TCM constituents are associated with lifestyle factors^{27,28}, our simplified tool can provide more efficient and targeted health guidance. For example, the distinct profile of severe psychosomatic distress suggests that individuals classified in this group may warrant targeted screening for

depression and anxiety disorders. Furthermore, the identification of intermediate groups, such as the mild psychosomatic distress and transitional types, could enable early preventive interventions before individuals progress to a more severe state of ill health (*Mibyō*). The tool can also help identify individuals who may benefit from specific interventions, including Kampo medicines, for age-related conditions (e.g., frailty and sarcopenia)²⁹. In an aging population, the questionnaire could serve as a valuable initial screening instrument because certain constitutions have been linked to neuro-cognitive function in the elderly³⁰. Ultimately, by making constitutional assessments more accessible, this tool can empower both clinicians and individuals. Beyond clinical screening, it provides a simple method for individuals to self-monitor their condition daily, fostering awareness and proactive management for prevention, which are the primary goals of modern health management¹².

CONCLUSIONS

In conclusion, this study provides a comprehensive validation of a five-constitution framework in the Japanese population, defining five distinct, clinically relevant constitution types and establishing a practical stand-alone tool for their assessment. Future research should focus on validating this 18-item tool in diverse clinical populations and using objective physiological markers. Specifically, clarifying the subtle distinctions between the transitional and pre-healthy types warrants further investigation. Longitudinal studies are required to determine whether these constitutional types can predict future health outcomes. Despite these limitations, this study offers a validated, accessible, and population-specific instrument that facilitates new opportunities for large-scale research and application of personalized preventive medicine.

CONFLICT OF INTEREST

Hideyuki Arie, Yumi Nakamura and Norihito Murayama are employed by Suntory Global Innovation Center Limited. The remaining authors declare that they have no conflict of interest to disclose.

AUTHORS' CONTRIBUTIONS

Shintaro Yokoyama: conceptualization, visualization, writing – original draft.

Hideyuki Arie: conceptualization, investigation, project administration, data curation, writing – review and editing.

Yumi Nakamura: conceptualization, investigation, funding acquisition, project administration, data curation, writing – review and editing.

Norihito Murayama: investigation, project administration, writing – review and editing.

Koichi Murashita: writing – review and editing.

Tatsuya Mikami: writing – review and editing.

Nobutaka Suzuki: conceptualization, writing – review and editing.

Shigehiko Kanaya: conceptualization, methodology, formal analysis, visualization, supervision, data curation, writing – review and editing.

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DATA AVAILABILITY

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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