A quality-of-life system to evaluate children with leukemia in China

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Abstract  
The scale for assessing the quality of life (QOL) of children with leukemia of different ages is vacant in China. Items for developing a QOL scale were selected through a literature review, interviews with 58 parents and children with leukemia by Delphi method, which involved pediatric oncologists, psychologists, and pediatricians. The initial items were formulated through 2 rounds of the Delphi method and statistical analyses. The formulated scale was pre-tested for reliability and validity. A method was adopted to weight the importance of items within the evaluation index system. The final scale includes 5 dimensions. There are 10 secondary items for age 2 to 4 years, 12 secondary items for all other age groups, and 29, 46, 52, and 50 tertiary items for the age groups 2 to 4 years, 5 to 7 years, 8 to 12 years, and 13 to 18 years, respectively. The authority coefficient for experts was 0.75, with Kendall’s W coefficient $P < .01$, for both rounds. The entire Cronbach alpha was $>0.9$, and the content validity $>0.75$. The weights of the first-grade items are: 0.201, 0.203, 0.198, 0.201, and 0.198. This quality-of-life scale for children with leukemia in China has demonstrated reliability and validity, while a further validity assessment is required.  

Abbreviations: CVI = content validity, QOL = quality of life.  

Keywords: Delphi method, pediatric leukemia, quality of life scale

1. Introduction

Leukemia is a malignant disease of abnormal hematopoietic tissue that seriously threatens the life and health of children.\cite{3,2} Childhood leukemia is mostly acute lymphocytic or acute myeloid leukemia; chronic types are rare. Leukemia is the most common cancer in children, and is characterized by high malignancy. Survival rates have increased over the last 30 years, but relapse is frequent.\cite{3}  
Chemotherapy is the main treatment of childhood leukemia; only a few high-risk patients need radiotherapy or hematopoietic stem cell transplantation.\cite{4,5} Chemotherapy generally involves combinations of multiple drugs and courses of treatment. Without timely intervention, the leukemia patient’s condition may deteriorate, with anemia, infection, disseminated intravascular coagulation, sepsis, intracranial hemorrhage, and other serious complications affecting prognosis.\cite{6}

Children with leukemia and their parents also face unusual challenges that affect their quality of life (QOL) and psychological health.\cite{7-10} An assessment of patients’ QOL may indicate factors that require improvement to restore physical and mental health.  
Assessment scales are typically used to evaluate patients’ QOL, both in China and abroad. Experts outside of China have developed QOL assessment scales for children. The most commonly used is the Children’s Quality of Life Assessment Scale System (PedsQLTM), developed by Dr. James W. Varni of the United States.\cite{8} The PedsQLTM includes generic core scales and modules. Although the PedsQLTM\cite{8} has been widely used for evaluating the QOL of children with malignant tumor, the items of the scale reflect the economic, cultural, and other features of the country of origin, and in a different culture direct translation of the original scale will compromise the measurement results.\cite{11}  
China’s economic level is low and the medical security system is currently not perfect. The vast majority of families are unable to pay high medical costs, and children with leukemia often do not receive timely and regular treatment. In addition, parents of other countries are more likely to attribute scientific explanations for the causes of illness, and not to personal error or divine judgment. Chinese parents are also likely to encourage their ill children to perform as normally as possible, but are more likely to blame themselves for the child’s illness, attributing it to neglect of care. They often pamper their children, which encourages dependence, timidity, and bad habits such as picky eating.\cite{12}  

Consideration of children’s QOL began late in China, and there has been little study of the QOL of children with malignant tumor. Only Tao Chang (Zhejiang Medicine University, China) has independently researched the QOL scale in children with malignant solid tumors in long-term survivors.\cite{13}  
Leukemia is a non-solid tumor and therefore differs from solid tumors by diagnosis, clinical manifestation, and treatment. Therefore, we developed a systematic scale to evaluate the QOL of Chinese children with leukemia that is appropriate for different ages. The scale involves 2 rounds of the Delphi method.
2. Methods

2.1. Study design

To determine the content of the scale through literature analysis and with consideration for parents in China with children affected by leukemia, a consensus was reached via the Delphi method. This involved recruiting a panel of experts and parents of children with leukemia to answer questions pertaining to areas of concern.

2.2. Delphi method

2.2.1. Selection of item pool. The literature review. We searched PubMed, Ovid, MEDLINE, CNKI, VIP, and Wan Fang database to find the literature for nearly 10 years. Search terms included the following: QOL, leukemia, child or pediatric, and different ages. Studies have shown that the main factors affecting QOL in China are regional and cultural environment, social support, availability of professional medical information and support, family support.[5,12] All of these factors provided a theoretical basis for assessing the QOL of children with leukemia at different ages in China.

2.2.1.2. In-depth interview. We interviewed 58 parents of children with leukemia from the local Hospital, whose disease duration was more than 2 years, using a semi-structured interview and purposive sampling. Among the study population, there are 41 parents and 17 children with leukemia (Table 1).

Table 1

| The basic information of interviewees. | n (%) |
|--------------------------------------|-------|
| Children with leukemia               | 17 (29.3) |
| Gender                               |       |
| Male                                 | 9 (52.9) |
| Female                               | 8 (47.0) |
| Age, y                               |       |
| 8–12                                 | 10 (58.8) |
| 13–18                                | 7 (41.2) |
| Treatment phase                      |       |
| On therapy                           | 98 (43.8) |
| Recent                               | 87 (38.8) |
| Long after                           | 39 (17.4) |
| Parents                              | 41 (70.7) |
| Age, y                               |       |
| 20–30                                | 23 (56.1) |
| 30–40                                | 25 (61.0) |
| 40–50                                | 10 (24.4) |
| Diploma                              |       |
| Associate                            | 20 (48.8) |
| Senior school                        | 29 (70.7) |
| Junior school                        | 9 (21.9) |
| Occupation                           |       |
| Management                           | 14 (24.1) |
| Operations                           | 15 (25.9) |
| Agricultural                         | 11 (19.0) |
| Service                              | 9 (15.5) |
| Business                             | 9 (15.5) |
| Income/mo, Yuan                      |       |
| >8000                                | 6 (10.3) |
| 5000–8000                            | 10 (17.2) |
| 3000–5000                            | 10 (17.2) |
| <3000                                | 32 (55.1) |

The interview data were analyzed by the method of cosmos,[14] and Colaizzi’s method of phenomenological analysis.[15] The method of cosmos refers to methodological triangulation, which combines both quantitative (questionnaire) and qualitative (semi-structured interview) methods.

The results of the in-depth interview can be seen at Supplementary material, http://links.lww.com/MD/C436

2.3. Consultation questionnaire

We adapted the PedsQL4.0 and PedsQL3.0 cancer module developed by Dr. Varni[8,16,17] to form the first round of inquiry questionnaire (Table 2). This combines the group discussion, literature review, and semi-structured interviews. The World Health Organization (WHO) QOL research group proposed 6 dimensions for a children’s quality-of-life assessment.[18] The consultation questionnaire included three parts: instruction of the consultation questionnaire, including the concept of QOL, purpose of research, and significance; the demographics of the experts, the degree of familiarity, and the basis for judging; and the items of the QOL assessment for children with leukemia. Each index is expressed in declarative sentences and space was allowed for comments or advice. The Likert-type scale was applied to screen the items, which were reverse-scored and linearly transformed from a 1 to 5 point scale as follows: 5, very important; 4, important; 3, generally important; 2, not important; and 1, very unimportant.

2.4. Selecting experts and inquiry

A number of experts that is appropriate is 15 to 50.[19] In this study, we selected the experts by the scale and feasibility of the research.

Inclusion criteria of experts: a college degree higher than associate with at least 8 years of experience in pediatric oncology, children psychology, or rehabilitation. In this study, the convenience sampling method was adopted to select the experts, combined with the universality, representativeness, and authority of the experts.

A total number of experts were 30, who came from various regions across China in 11 hospitals. The questionnaire was sent to the experts using mail or on-site distribution.

2.5. Reliability and validity test

Cronbach’s alpha was used to test the internal consistency in this study. Cronbach’s alpha is the most commonly used indicator of internal reliable consistency, which can be used to evaluate the consistency of each index. The higher the reliability, the more stable the results.[20] It is generally considered that Cronbach’s α ≥ 0.9 indicates very good results. We choose 224 children with leukemia to fill out the questionnaire, from the local Hospital (Table 3). The purpose was to investigate the reliability and
Table 3
Basic information of validation object.

| Gender | Male | 136 (60.7) |
|--------|------|------------|
| Female | 88   | 39.3       |
| Age, y | 2–4  | 64 (28.6)  |
|        | 5–7  | 64 (28.6)  |
|        | 8–12 | 58 (25.9)  |
|        | 13–18| 38 (17.0)  |
| Disease duration, y | <2 | 170 (75.8) |
|        | 2–5 | 43 (19.2)  |
|        | >5  | 11 (4.9)   |
| Leukemia type | Acute lymphoblastic | 158 (70.5) |
|        | Acute myeloid | 25 (11.2)  |
|        | Chronic lymphocytic | 13 (5.8)  |
|        | Chronic myeloid | 18 (8.0)  |
| Treatment phase | On therapy | 92 (41.1)  |
|        | Recent | 70 (31.3)  |
|        | Long after | 62 (27.7) |
| Leukemia risk | Low | 104 (46.4) |
|        | Moderate | 88 (39.3)  |
|        | High | 32 (14.3)  |

validity of the questionnaire, the relevancy of the content, language, patient comprehension, and consistency.

The content validity (CVI) test was used to test validity, which was calculated as the experts agreed with the items. The CVI reflects whether the results are valid, and usually combine logical and statistical analyses to reduce the error caused by subjective judgment. We sent the CVI to 6 experts, with an introduction to explain the concepts, purpose, and significance.[21]

2.6. Weight construction

There are many ways to assign weight to items, including proportioning, or through analytic hierarchy or cumulative methods. In this study, we chose the proportioning method, based on the expert score of the second round of the Delphi method. The weight was determined as the ratio of the average score of the experts for the items, and the sum of the averages of the higher-level items.[21] The experts' scoring of the second round of the Delphi served as the basis to construct the weights of the indicators.

The flowchart of the study design, process is shown in Figure 1.

2.7. Data processing

After recovering the questionnaires, we entered the data into Excel with a double check. For missing answers and mistakes, the researchers asked the experts to refill or confirm by telephone. If clarification was not received, these ambiguous or incorrect questionnaires were removed to ensure the integrity and validity of the questionnaire. The research uses descriptive statistics, and the data were analyzed with SPSS 19.0 software (America). We also calculated the positive coefficient, coordination coefficient, authority coefficient of experts, and Kendall’s W coefficient.

The boundary value method was used to screen items.[23,24] We calculated the arithmetic mean of index (Mj), out rate (Kj), standard deviation, and coefficient of variation (CV). We ultimately screened the index by the boundary values of the Mj, Kj, and CV. The principle of screening consisted of the following: If the 3 values of the items are in line with the standard, retention or deletion was decided by group discussion based on comprehensive, scientific validity, or feasibility. If the 3 values of the items did not meet the standard, then the items were deleted. The consultation ended when the expert opinions converged.

2.8. Ethics statement

This study was approved by the IRB of Children’s Hospital of Chongqing Medical University.

3. Results

3.1. Basic information concerning experts

The demographic information describing our experts is shown in the Table 4. Most of experts had more than 20 years’ experience and worked as educators. Twelve experts were from the southwestern region of China.

3.2. Positive coefficient and authority coefficient of experts

The recovery rate of the 2 rounds was 100%. The authority, harmony, and determination coefficients were 0.76, 0.62, and 0.89, respectively. The first round included 15 experts who wrote recommendations on the questionnaire, and 5 experts contributed further detailed and constructive comments. One expert provided advice via a telephone conversation. During the second round, 2 experts wrote recommendations on the questionnaire, and 1 expert gave detailed comments. The harmony coefficient of experts was excellent for analysis (P < .01; Table 5).

3.3. Results of two rounds of consultation

According to the boundary value method and experts’ suggestions, the first round required that 37 items be deleted, 7 items added, 18 items modified, and 36 items merged. In the modified version, there were 5 primary items. For children ages 2 to 4 years, there were 10 secondary items and 12 secondary items for all the other ages. There were 35, 49, 54, and 56 tertiary items for the age groups 2 to 4 years, 5 to 7 years, 8 to 12 years, and 13 to 18 years, respectively.

After the second round of consultations, 8, 4, and 1 item were deleted, modified, and merged, respectively. Eventually, the scale including 5 primary items, with 10 secondary items for aged 2 to 4 years, and 12 secondary items for all the other age groups. In the final versions, there were 29, 46, 52, and 50 tertiary items for the age groups 2 to 4 years, 5 to 7 years, 8 to 12 years, and 13 to 18 years, respectively. The results for the 2 to 4 years age group are shown in the Table 6. The results of the scales are shown only for the 2 to 4 years age group.

3.4. Reliability and validity

In the study, for the whole scale, Cronbach’s α was >0.9. In addition, the sentences seemed easy to understand, and most of the testers required only 10 to 15 minutes to complete the questionnaire. In addition, the CVI was >0.75, which suggests good CVI.[25]

3.5. Weights of the evaluation index system

We used the proportional method to construct the weights. The results for the 2 to 4 years age groups are shown in Table 7. The results show that psychological concerns was highest in primary items, and as secondary items, the top 4 were emotional response,
self-evaluation, and interpersonal relationship and environment of the home. These also suggested that more attention should be paid to the mental health of the family and social support of children with leukemia.

3.6. Limitations

As in other similar studies, this may suffer from some subjective judgments due to the Delphi method. In addition, neglecting a few people’s opinions may lead to a deviation in the prediction results. However, harmonious and positive communication between researchers and experts may avoid these problems to some extent. Third, the verification of the scale was based on one single area with a small sample size, which might have limited the representativeness of the results. We plan to conduct a modified study with greater statistical power, involving more than one center and a large sample, to verify these results concerning the quality of survival of children with leukemia.
4. Discussion

The experts in this study comprised undergraduates and above (86.67%), working for more than 15 years (63.66%), and senior titles (53.33%), and this guarantees the reliability of the research. In the two rounds of consultation, the authority coefficient was > 0.75, showing a high degree of expert authority and credible results. The questionnaire recovery rate was 100%. Of the experts, 56.67% offered suggestions in the first round of expert consultation, indicating that they thought highly of this research. In the second round, 6.67% added suggestions, which indicated consensus. After two rounds of expert consultation, Kendall’s W coefficient was P < .01 by the χ² test. Therefore, the results of this study are reliable.

In consideration of the characteristics of physical and psychological development of children with leukemia in China, modifications were made in the PedsQL4.0 and PedsQL3.0 cancer module. This was then formatted as a quality-of-life system scale for children with leukemia of different ages in China. There are 5 first indicators in the field of physiology, psychology and emotion, social communication, environment, and school/role identity. There are 9 secondary items for 2 to 4 years, and 12 for all other age groups; and 29, 46, 52, and 50 tertiary items for the age groups 2 to 4 years, 5 to 7 years, 8 to 12 years, and 13 to 18 years, respectively. For example, for children aged 2 to 4 years, we deleted the items “learning ability” and “self-image” due to their lack of understanding of these concepts. We also modified items such as “do not want to eat,” “too tired to go outside and play,” and other items. The understanding and expressive abilities of children aged 5 to 7 years allowed the addition of the items “don’t know what to do when troubled” and “satisfied with appearance and size.” The understanding and analytical abilities of children aged 8 to 12 years are relatively mature, and items that were added included “other students and my friends talk about me,” “I feel lonely,” and “I perform chores with difficulty.” Adolescents aged 13 to 18 years are psychologically more mature, and items such as “feel inferior” and “feel I am a burden to the family” are applicable.

China’s culture and lifestyle and children’s character traits meant that some items on the PedsQLTM could be deleted: “It is difficult to explain my condition to others”; “I feel embarrassed when others look at my body”; “It is difficult to do homework”; and “It is difficult to complete the math homework.” Other items were added because children with leukemia may be withdrawn, introverted, or asocial: “It is difficult to play with other children”; and “I like to stay at home.” In addition, taking into account that the economic development of China is not balanced and the medical support policy is not perfect, we added the item “medical insurance has played a big role in reducing the financial burden”. Because of the lack of medical personnel and health education, we added "medical staff or other institutions often provide you with information regarding disease." With respect to the parenting style in China, we added the items "parents understand and respect your ideas"; "parents often communicate with you"; and "parents can give you help in time," which included reverse wording to ensure the quality of the questionnaire by avoiding random answers or social expectations.

Reliability mainly reflects the accuracy, stability, and consistency of the scale, when the reliability coefficient of the total scale is >0.8. Cronbach’s α of the total scale is >0.9, which shows that the scale has good internal consistency. In addition, the validity was 0.85 to 0.95 in the present study. It is generally believed that the research content is consistent with the research purpose if the content validity is >0.75. Therefore, the QOL of children with leukemia at different ages in China has high reliability and validity.

Furthermore, the assigned weights of this study was conducted by using the Delphi and proportional methods, and the top three weights are physiological, psychological, and environmental, which are the factors of most concern relevant to the QOL of children with leukemia in China, and can provide the basis for planning individualized treatment and intervention measures.

5. Conclusions

The study concerned the content of a children’s QOL assessment conducted by the WHO QOL group and based on Dr. Varni’s PedsQLTM, based on a literature review,
Table 6
Rounds of expert consultation for the 2 to 4 years age group.

| Primary items | Secondary items | Tertiary items | Mj   | Kj   | SD  | CV  |
|---------------|----------------|----------------|------|------|-----|-----|
|               |                | R1  | R2  | R1  | R2  | R1  | R2  | R1  | R2  | R1  | R2  | R1  | R2  |
| Physiological | Activity ability | R1  | 4.033 | 3.9  | 0.467 | 0.4  | 1.159 | 1.269 | 0.287 | 0.325 |
|               |                | R2  | 3.6  | 3.933 | 0.267 | 0.367 | 1.276 | 1.112 | 0.354 | 0.283 |
|               |                | R1  | 3.9  | 3.833 | 0.333 | 0.4  | 1.125 | 1.206 | 0.288 | 0.315 |
|               |                | R2  | 3.867 | 3.967 | 0.367 | 0.533 | 1.137 | 1.326 | 0.294 | 0.334 |
|               |                | R1  | 3.967 | 3.933 | 0.333 | 0.3  | 0.964 | 0.980 | 0.243 | 0.249 |
|               |                | R2  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
| Somatic       | function       | 2   | 3.933 | 3.833 | 0.267 | 0.367 | 1.223 | 1.278 | 0.340 | 0.356 |
|               |                | 3   | 4.077 | 3.8  | 0.467 | 0.4  | 1.081 | 1.215 | 0.266 | 0.330 |
|               |                | 4   | 3.967 | 3.967 | 0.333 | 0.3  | 0.964 | 0.980 | 0.243 | 0.249 |
|               |                | 5   | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 6   | 3.967 | 3.867 | 0.333 | 0.3  | 0.964 | 0.980 | 0.243 | 0.249 |
|               |                | 7   | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 8   | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 9   | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 10  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 11  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 12  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 13  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 14  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 15  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 16  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 17  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 18  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 19  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 20  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 21  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 22  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 23  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 24  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 25  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 26  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 27  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 28  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 29  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 30  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 31  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 32  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 33  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 34  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |
|               |                | 35  | 4    | 4.066 | 0.433 | 0.467 | 1.017 | 1.048 | 0.254 | 0.258 |

R1 = round 1, R2 = round 2.
† New item added.
‡ and † have merged into one.
interviews, group discussion, and the Delphi method. It took into account factors specific to children with leukemia in China, combining the economic, cultural background, living habits, and physiological and psychological characteristics of the different age groups. This scale warrants further testing in a multi-center study. Such testing would improve the scale’s scientific value and effectiveness for evaluating the QOL of children with leukemia.

These scales can serve as a reference for the evaluation of the QOL related to leukemia in China and abroad. They also provide the basis for the development of individualized treatment, nursing, rehabilitation programs, and interventions, to improve the QOL of children with leukemia. We hope that this scale will be promoted globally, due to the differences in culture, living habits, family education, and other aspects among Chinese people worldwide.

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### Table 7

The weight of the indexes for the 2 to 4 years age group.

|       | Mj | Secondary wt | Combined wt |
|-------|----|--------------|-------------|
| **A** |    |              |             |
| Physiological |    |              |             |
| As Activity ability | 4.933 | —           | 0.201 |
| As Activity ability | 4.867 | 0.333       | 0.067 |
| As Activity ability | 3.000 | 0.498       | 0.033 |
| As Activity ability | 3.933 | 0.502       | 0.034 |
| Ab Somatic function | 4.867 | 0.333       | 0.067 |
| Ab Somatic function | 3.833 | 0.243       | 0.016 |
| Ab Somatic function | 3.967 | 0.251       | 0.017 |
| Ab Somatic function | 3.933 | 0.249       | 0.017 |
| Ab Somatic function | 4.067 | 0.257       | 0.017 |
| Ac Symptoms and side effects | 4.900 | 0.335       | 0.067 |
| Ac Symptoms and side effects | 3.567 | 0.236       | 0.016 |
| Ac Symptoms and side effects | 3.800 | 0.251       | 0.017 |
| Ac Symptoms and side effects | 3.500 | 0.231       | 0.016 |
| Ac Symptoms and side effects | 4.267 | 0.282       | 0.019 |
| **B** |    |              |             |
| Psychological | 5.000 | —           | 0.203 |
| Ba Emotion response | 4.900 | 0.504       | 0.102 |
| Ba Emotion response | 3.000 | 0.496       | 0.051 |
| Ba Emotion response | 3.967 | 0.504       | 0.052 |
| Bb Self-evaluation | 4.830 | 0.497       | 0.101 |
| Bb Self-evaluation | 3.500 | 0.296       | 0.030 |
| Bb Self-evaluation | 4.167 | 0.355       | 0.036 |
| Bb Self-evaluation | 4.067 | 0.347       | 0.035 |
| **C** |    |              |             |
| Social | 4.867 | —           | 0.198 |
| Ca Interpersonal relationship | 4.833 | 0.505       | 0.101 |
| Ca Interpersonal relationship | 3.870 | 0.245       | 0.024 |
| Ca Interpersonal relationship | 4.370 | 0.277       | 0.028 |
| Ca Interpersonal relationship | 4.170 | 0.264       | 0.026 |
| Ca Interpersonal relationship | 3.400 | 0.215       | 0.022 |
| **D** |    |              |             |
| Environment | 4.933 | —           | 0.201 |
| Da Home | 4.900 | 0.504       | 0.101 |
| Da Home | 4.567 | 0.205       | 0.021 |
| Da Home | 4.200 | 0.188       | 0.019 |
| Da Home | 4.467 | 0.200       | 0.020 |
| Da Home | 4.533 | 0.203       | 0.021 |
| Da Home | 4.567 | 0.205       | 0.021 |
| Db Social | 4.833 | 0.497       | 0.090 |
| Db Social | 4.433 | 0.334       | 0.033 |
| Db Social | 4.433 | 0.334       | 0.033 |
| Db Social | 4.400 | 0.332       | 0.033 |
| **E** |    |              |             |
| School/role | 4.867 | —           | 0.198 |
| Ea Independence | 4.733 | 0.495       | 0.098 |
| Ea Independence | 3.867 | 0.500       | 0.049 |
| Ea Independence | 3.877 | 0.500       | 0.049 |
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