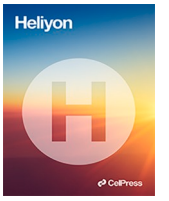
Heliyon 10 (2024) e34724

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

# Validation of the Chinese orthostatic discriminant and Severity Scale (ODSS) for detection of orthostatic intolerance syndrome

Weiting Tang [a,1], Hui Gu [b,1], Bin Chen [a], Sheng Hu [a], Wenjie Fan [d], Yong You [a,c,*]

[a] Department of Neurology, Affiliated 2nd Hospital of Hainan Medical University, Haikou, 570100, China
[b] Department of Neurology, First People's Hospital of Changde City, Changde, 415003, China
[c] International Center for Aging and Cancer (ICAC), Hainan Medical University, Haikou, 570100, China
[d] Department of Pathology, The First Affiliated Hospital of Nanhua University, Hengyang, 421001, China

ARTICLE INFO

*Keywords:*
Orthostatic intolerance
Autonomic reflex screen
Orthostatic discriminant and severity scale
Supine-to-stand test
Valsalva maneuver
Transcranial Doppler

ABSTRACT

*Background:* Orthostatic intolerance (OI) is the inability to tolerate orthostatic stress during any postural change. The etiology of OI varies, and methods to obtain a specific diagnosis and plan appropriate treatment are important. The tools available within the Chinese context to swiftly identify orthostatic intolerance syndrome (OIS) are currently limited.
*Methods:* Patients with OI symptoms were included in this study and categorized into two groups based on the results of the supine-to-stand test. Those with abnormal test results were assigned to the OIS group, while those with normal test results were placed in the non-OIS group. We evaluated the internal consistency and predictive value of the Chinese Orthostatic Discriminant and Severity Scale (ODSS) by comparing patients' scores with their physiological measurements collected during orthostatic stress tests and the results of other available questionnaires, including the orthostatic Symptom Questionnaire and Orthostatic Grading Scale (OGS).
*Results:* Patients with OIS scored significantly higher on all three questionnaires and showed significant differences in autonomic responses during orthostatic stress tests compared with non-OIS patients. Receiver operating characteristic curve analysis showed that the orthostatic score from the ODSS had moderate predictive value for the supine test (area under the curve [AUC] = 0.754). Further subgroup analysis revealed that the orthostatic score from the ODSS had uniquely high specificity and sensitivity for identifying patients with orthostatic hypotension with abnormal cerebral blood flow (OH–U, AUC = 0.919).
*Conclusions:* We conclude that the Chinese version of the ODSS has sufficient reliability and validity to distinguish patients with OIS and could possibly be used as a diagnostic tool for OH–U patients. Thus, the Chinese ODSS offers a beneficial screening tool for quickly assessing whether patients have OIS that requires further clinical assessment.

## 1. Introduction

Orthostatic intolerance (OI) is a broad term describing the inability to tolerate orthostatic stress during any postural change, for

* Corresponding author. International Center for Aging and Cancer (ICAC), Hainan Medical University, Yehai Avenue No. 368, Longhua District, Haikou City, Hainan Province, Haikou, 570100, China.
*E-mail address:* youyong@hainmc.edu.cn (Y. You).
[1] These authors have contributed equally to this work and share first authorship.

https://doi.org/10.1016/j.heliyon.2024.e34724
Received 11 June 2023; Received in revised form 12 July 2024; Accepted 15 July 2024
Available online 18 July 2024

example, from a supine to upright position [1,2]. During a postural change, a natural dip in blood pressure (BP) occurs due to the pooling of blood in the lower extremities, and the autonomic nervous system mediates compensatory mechanisms to increase the heart rate in order to maintain a normal BP [2,3]. Patients with OI struggle to regulate their BP, and thus, OI manifests as symptoms including lightheadedness, dizziness, syncope and heart palpitations [4–7]. Treatments and management plans for orthostatic symptoms are often challenging due to the varied etiology of OI and can range from vasopressin analogs to increasing salt intake to drinking cold water in the morning [8,9]. As such, a clear understanding of the origin of orthostatic symptoms is critical to determining the appropriate treatment.

BP and heart rate monitoring as well as orthostatic stress tests such as the supine-to-stand, supine-to-sitting and head-up tilt tests are commonly used to diagnose conditions of OI [10,11]. Although autonomic physiological responses during orthostatic stress tests are thought to be largely stable, studies have reported poor reproducibility upon repeated challenges [11–14]. Inconsistent assessment procedures and contextual differences can contribute to poor reproducibility, as OI can be influenced by factors such as time of day, diet and current medications [9,14,15]. A questionnaire tool that can help identify orthostatic symptoms in patients would be insightful by identifying contributing lifestyle factors.

The Orthostatic Discriminant and Severity Scale (ODSS) was developed by Baker and colleagues in 2018 [16]. It is aimed at understanding whether patients who experience OI-like symptoms, such as dizziness, faintness, heart palpitations, lightheadedness and syncope, have orthostatic or non-orthostatic symptoms [16]. The ODSS is more advantageous compared to previously developed questionnaires such as the Autonomic Symptom Profile (ASP) and Orthostatic Hypotension Question (OHQ), because it is more concise and does not focus on only orthostatic hypotension but also includes other types of OI [16].

As the ODSS was developed in Western populations, it is important to validate the translated Chinese version of the questionnaire to confirm that it is sufficiently reliable for application in the clinical setting in China. Other questionnaires also are available in Chinese for measuring orthostatic symptoms, including the orthostatic Symptom Questionnaire and orthostatic grading scale (OGS) [17]. However, the Symptom Score was largely developed to assess OI in children and adolescents and might not be appropriate for the general population, and the OGS is a brief 5-item questionnaire that does not provide sufficiently in-depth information. In the present study, we generated the first Chinese version of the ODSS by translating it from English to Chinese. We validated its effectiveness for screening and diagnosing patients with orthostatic intolerance syndrome (OIS), who presented with orthostatic intolerance symptoms and showed abnormal results in the supine-to-stand test.

## 2. Methods

### 2.1. Study design and participants

Patients with OI symptoms were recruited on a rolling basis from June 2019 to December 2020, from the outpatient or inpatient Affiliated 2nd Hospital of Hainan Medical University. Healthy controls were recruited from among staff members or the family members of patients who had no orthostatic symptoms. All control participants were assessed and confirmed to have had no syncope or fall incidents in the previous year. Patients were assessed by a neurologist to confirm the presence of orthostatic symptoms during postural changes, including dizziness, syncope, amaurosis, inattention, fatigue, heart palpitations, chest tightness and nausea. Additionally, healthy controls were also assessed to ensure the absence of any autonomic dysfunctions. The exclusion criteria for both patients and healthy controls included abnormal or unstable cerebral blood flow signal during transcranial doppler (TCD) ultrasound, inability to complete a supine-to-stand test, arterial stenosis $\geq$50 %, a history of cardiac procedures or surgeries for coronary artery disease, and the inability to comprehend or complete the assessment procedures. Basic information, including name, gender, age, smoking and drinking habits, and past medical history (relating to hypertension, diabetes, coronary heart disease, arrythmia, syncope/fall), were collected for all participants. All participants also completed various clinical tests, which are described below. In total, we collected data from 100 patients (85 included and 15 excluded in the study) and 20 healthy controls. Data are available upon request.

Ethical approval was obtained from the Second Affiliated Hospital of Hainan Medical University (2019R005-E02). Written informed consent was obtained from all participants, and they were allowed to withdraw from the study at any point. Written informed consent for participation of minors in the study was obtained from the individual patient' s parent or guardian.

### 2.2. Chinese version of the ODSS

The original English Orthostatic Discriminant and Severity Scale (ODSS) did not include any sociocultural-specific or lifestyle-related questions. As such, we carried out direct translation of the questionnaire without modifications. After translation of the text into Chinese, we back translated the text into English to ensure there were no mistranslations of the questionnaire text. Like the English version, the Chinese version of the ODSS has 33 items (see Appendix 1), of which 22 are related to orthostatic symptoms and 11 are related to non-orthostatic symptoms. Items 7, 8, 9, and 16 to 23 relate to non-orthostatic symptoms, while the remaining items are related to orthostatic symptoms. Questions relating to OIS include the frequency, severity, duration and resolution of symptoms during an orthostatic episode as well as factors that can contribute to orthostatic stress, such as prolonged standing, eating, and heat stress. The non-orthostatic questions are related to generalized weakness, fatigue, pain, as well as symptoms of dizziness unrelated to any postural changes. Participants are asked to self-report based on the symptoms they have experienced in the previous year.

The ODSS includes 10 conditional questions and 23 questions to be answered on a 7-point Likert scale. For the conditional questions, participants are asked to select "yes" or "no". A "yes" answer is scored as 1 point, whereas a "no" answer is scored as 0 points. Although this is different from the original ODSS published by Baker et al. we chose to score 0 and 1 for ease of calculation. After each

conditional question, participants then answer a follow-up 7-point Likert scale question. The scores for these questions correspond to the answers on a Likert scale. If a participant answers "no" on a conditional question, they then skip the corresponding Likert scale question and proceed to the next conditional question. The purpose of the Likert scale questions is to further understand the symptoms experienced by patients with respect to their frequency, duration, and severity, with each symptom rated on a scale from 1 to 7. The score out of 7 corresponds proportionally to the frequency and severity of the symptoms. For example, if symptoms are completely relieved after a positional correction, the item would be scored as 7, whereas if no relief occurs at all, the item would be scored as 1. Scores were summed for the orthostatic and non-orthostatic questions separately to obtain an orthostatic score (OS) and a non-orthostatic score (NS). The highest possible OS and NS scores are 100 and 71 points. respectively.

### 2.3. Orthostatic Symptom Questionnaire

A questionnaire was used to assess orthostatic symptoms during the previous month such as nausea, hand tremors, dizziness, heart palpitations, headache, profuse sweating, blurred vision, chest tightness, and difficulty concentrating (see Appendix 2) [17]. Participants were asked whether symptoms occurred as they transitioned from a supine to upright position or after they remained in an upright position for a long period of time. If a symptom was present, participants then rated the frequency of the symptom on a scale from 0 to 4, where 0: never, 1: once a month, 2: 2–4 times a month, 3: 2–7 times a week, and 4: at least once a day on average. The answers to these questions were summed to obtain an overall orthostatic symptom score based on symptom frequency.

### 2.4. Orthostatic grading scale

The Orthostatic Grading Scale (OGS) is a 5-item self-report scale that measures the severity of symptoms of orthostatic hypotension (see Appendix 3) [18]. We asked participants to complete the questionnaire, and the scores for the individual items were added to obtain a final score.

### 2.5. Supine-to-stand test

Headgear holding the TCD probe was first placed on the participants for cerebral blood flow monitoring. Participants also wore a wrist sphygmomanometer to measure BP and heart rate during the test. Participants were instructed to lie down in a supine position for 3 min, then stand up quickly within 8 s and remain standing for 10 min without leaning on any surfaces. Participants then had to quickly return to a supine position and maintain the position for another 3 min before the test was concluded.

BP and heart rate were recorded at six time points: after 3 min in the initial supine position (baseline reading) and at 0, 1, 3, 5, 8 and 10 min after standing. Changes in BP and heart rate were calculated by subtracting baseline readings collected after 3 min in the initial supine from the readings at 3 min after standing.

Changes in cerebral blood flow were recorded throughout the test, and the average cerebral blood flow velocity (CBFV) during the 3 min in supine position was taken as the baseline reading. Normal changes in cerebral blood flow typically include an initial dip in flow velocity, which reaches the lowest value within 30 s before rebounding back to the baseline reading, forming a "W" wave (above 80 % of baseline CBFV) [19]. Abnormal cerebral blood flow is identified by a lack of rebound in cerebral blood flow after 30 s of standing. For calculation of a velocity score, CBFV was measured at four time points: at baseline, and after 1, 5, and 10 min of standing. Baseline blood flow was taken as 100 %. After 1 min of standing, blood flow equal to 80–89 % that at baseline was scored as 1 point, 70–79 % as 2 points, and $<$70 % as 3 points. At 5 min, blood flow equal to 79–88 % that at baseline was scored as 1 point, 69–78 % as 2 points, and $<$69 % as 3 points. At 10 min, blood flow equal to 77–85 % that at baseline was scored as 1 point, 67–76 % as 2 points, and $<$67 % as 3 points. The scores at 1, 5, and 10 min were summed, and a score of 0 was considered normal, 1–2 mildly abnormal, 3–4

**Table 1**
Diagnostic criteria for subtypes of OI [20].

| Subtype | Diagnostic criteria | Differential |
|---|---|---|
| Orthostatic hypotension-compensated (OH–C) | OH with normal orthostatic CBFv. Systolic BP drop of $\geq$20 mmHg or diastolic BP drop of $\geq$10 mmHg within 3 min of standing. Orthostatic CBFV score = 0. | If systolic and diastolic BP drop after 3 min of standing, the diagnosis of delayed orthostatic hypotension (L-OH) is considered. |
| Orthostatic hypotension-uncompensated (OH–U) | OH with abnormal cerebral blood flow. Systolic BP drop of $\geq$20 mmHg or diastolic BP drop of $\geq$10 mmHg within 3 min of standing. Orthostatic CBFV score $>$1. | |
| Orthostatic hypertension (OH-T) | Systolic BP increase of $\geq$20 mmHg, or increase by 20 % of baseline. Orthostatic CBFV score = 0. No significant changes in heart rate upon standing. | |
| Postural tachycardia syndrome (POTS) | No significant drop in BP after standing. Average heart rate $<$100 beats per minute (bpm) when in supine position with increase by $\geq$ 30 bpm after standing up that persists for $\geq$3 min. Maximum heart rate $\geq$120 bpm. | If the maximum heart rate does not exceed 120 bmp, the diagnosis of chronic isolated OI is considered. |
| Orthostatic cerebral hypoperfusion syndrome (OCHOs) | Orthostatic CBFV score $>$1. No significant drop in BP or increase in heart rate upon standing. | |

moderately abnormal and >4 severely abnormal.

Based on the BP, heart rate and orthostatic CBFV in the supine-to-stand test, participants who met the criteria for an abnormal diagnosis were included in the OIS group, while those who did not meet the diagnostic criteria were included in the non-OIS (NOIS) group. Specifically, participants in the NOIS group did not have abnormal heart rate, blood pressure, and cerebral blood flow measurements during the clinical testing. The diagnostic criteria for each subtype of OIS are presented in Table 1, and representative traces are shown in Supplemental Fig. 1.

### 2.6. Valsalva maneuver

Blood pressure of the participants was measured before and after the test. Participants were instructed to continuously exhale with an expiratory pressure of 40 mmHg into a manometer for 15 s, while wearing the TCD headgear to measure cerebral blood flow. CBFV during the 3 min in the supine position was taken as the baseline. The Valsalva ratio (VR) was calculated by taking the highest heart rate during the Valsalva maneuver (VM) divided by the lowest heart rate occurring within 30 s of the VM peak heart rate. VM ratios were also calculated using the Quantitative Autonomic Reflex and Small Fibers Tests (QASAT) method, where VM1 was obtained by dividing the CBFV at the end of phase II by the baseline CBFV and VM2 was obtained by dividing the CBFV at the end of phase IV by the baseline CBFV [21].

### 2.7. Data analysis

Data collected from participants are presented as mean and standard deviation for a normally distributed population with homogenous variance. Differences between groups were analyzed using the analysis of variance (ANOVA) F-test. Data with unequal variances are presented as $M$ ($P_{25}$, $P_{75}$) and analyzed using the Kruskal-Wallis test. For data presented as percentages (%), we used the Chi-square test and Fisher's exact test. The Spearman's rank-order correlation was used to study correlations between questionnaires and tests. A Cronbach's alpha of <0.6 indicates poor internal consistency and reliability, while values of 0.7–0.8 indicate considerable reliability, and values of 0.8–0.9 indicate good reliability. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive ability of the Chinese version of the ODSS for OI, and an area under curve (AUC) value of 0.5–0.7 indicates low predictive ability, 0.7–0.9 indicates moderate predictive ability and >0.9 indicates good predictive ability. Youden's J statistic was used as a summary measure to estimate the sensitivity and specificity of the Chinese version of the ODSS. $P < 0.05$ was applied as the cut-off for statistical significance.

## 3. Results

A total of 100 patients with orthostatic symptoms and 20 healthy controls with no orthostatic symptoms were recruited into the study. From the patient group, 15 patients were excluded for having a pacemaker (n = 1), severe cerebral and arterial stenosis (n = 7), or poor temporal insonation window quality during TCD measurements (n = 7). The basic and clinical characteristics of the remaining 85 patients and the 20 control participants included in the statistical analyses are presented in Table 2. No significant differences in gender, age or the incidence rates of hypertension, diabetes and smoking history were observed between the control and patient groups (all $p > 0.05$). However, a significantly higher percentage of patients in the patient group had a history of syncope/fall (30.59 %) compared with that in the control group (10.0 %; $p < 0.05$).

### 3.1. Assessment of autonomic functions

The autonomic reflex screening results for the control, NOIS and OIS groups measured during the supine-to-stand test are presented in Table 3. Using the BP, heart rate and CBFV changes during the supine-to-stand test, 32 patients (37.6 %) met the diagnostic criteria for OIS in the supine-to-stand test, while none of the participants in the control group did. The OIS group consisted of 13 cases of orthostatic hypotension (OH–C), 7 cases of orthostatic hypotension with abnormal cerebral blood flow (OH–U), 1 case of orthostatic hypertension (OHT), 8 cases of orthostatic cerebral hypoperfusion syndrome (OCHOs) and 3 cases of postural tachycardia syndrome (POTS). The other 53 patients did not meet the diagnostic criteria for OIS and were included in the NOIS group. The supine-to-stand test showed that the changes in systolic and diastolic BP as well as the upright cerebral blood flow score were significantly higher in the

**Table 2**
General characteristics of the study population, comparing the control and patient groups using Fisher's exact test.

| | Control group (n = 20) | Patient group (n = 85) | *p* |
|---|---|---|---|
| Gender (male/female) | 15/5 | 52/33 | 0.185 |
| Age (years) | 55.65 ± 16.52 | 58.35 ± 16.50 | 0.512 |
| Hypertension, n (%) | 5 (25.0) | 34 (40.0) | 0.161 |
| Diabetes, n (%) | 3 (15.0) | 10 (11.8) | 0.468 |
| Smoking history, n (%) | 5 (25.0) | 23 (27.1) | 0.548 |
| History of syncope/fall, n (%) | 2 (10.0) | 26 (30.6) | 0.049* |

*$p < 0.05$.

**Table 3**
Autonomic function results in control, NOIS and OIS groups.

| | Control group (n = 20) | NOIS group (n = 53) | OIS group (n = 32) |
|---|---|---|---|
| Baseline heart rate (bpm) | 69 (64.5, 73.30) | 67 (61.93, 75.50) | 70.5 (57.44, 80.23) |
| △heart rate (bpm) | 9.38 (4.25, 14.75) | 8.77 (5, 14.23) | 11.39 (4.48, 19) |
| Supine systolic BP (mmHg) | 126 (107, 137) | 128 (113, 143) | 136.5 (114.5, 160) |
| Supine diastolic BP (mmHg) | 76 (70, 85.25) | 77 (67.5, 85) | 80 (71.5, 92) |
| △systolic BP (mmHg) | 2.5 (−4, 7) | −3 (−10, 3.5) | −21.5 (−33.75, 10.25)[b d] |
| △diastolic BP (mmHg) | 4.5 (−4.75, 8) | 2 (−2, 7) | −9.5 (−18.75, 1.5)[b d] |
| "W" wave rebound (n) | 3 | 5 | 6 |
| CBFV score | 0 (0, 0.75) | 0 (0, 0) | 2 (0, 4)[b d] |
| VM CBFV phase I | −8.1 (−12.03, −3.83) | −11 (−15.97, −6.05) | −16.37 (−20.38, −11.36)[a c] |
| VM CBFV phase II | 8.2 (5.90, 14.60) | 10.8 (5.65, 16.10) | 6.9 (3.3, 16.8) |
| VM CBFV phase III | 2.48 (−4.46, 6.5) | −1.2 (−5.04, 6.15) | −7.37 (−12.09, −1.22)[a c] |
| VM CBFV phase IV | 15.76 (8.95, 28.27) | 19.63 (12.49, 28) | 15.74 (8.43, 26.92) |
| VR | 1.48 (1.34, 1.65) | 1.35 (1.23, 1.54) | 1.25 (1.19, 1.46)[a] |

Data are presented as *M* ($P_{25}$, $P_{75}$), unless otherwise specified.
[a] $p < 0.05$ vs control.
[b] $p < 0.01$ vs control.
[c] $p < 0.05$ vs NOIS.
[d] $p < 0.01$ vs NOIS.

OIS group than in the control and NOIS groups ($p < 0.01$). No significant differences were detected between the groups when comparing baseline BP and heart rate in the supine position, as well as "W" wave rebound in the CBFV while standing ($p > 0.05$).

### 3.2. Validity of Chinese version of ODSS

Across all questionnaires, including the Chinese version of the ODSS, Symptom Score and OGS, healthy controls had significantly lower scores compared with patients in the OIS and NOIS groups (Supp Fig. 1A). Comparison of scores between the OIS and NOIS groups revealed that the OIS group had significantly higher scores on the OS component of the ODSS ($p = 0.003$; Fig. 1A), the Symptom Score ($p = 0.002$; Fig. 1C) and the OGS ($p = 0.019$; Fig. 1D). No significant difference in the NS component of the ODSS was detected between the OIS and NOIS groups ($p = 0.225$; Fig. 1B). Additionally, both the OS and NS values from the Chinese ODSS correlated significantly with the Symptom Score (OS: $r = 0.0813$, $p < 0.001$; NS: $r = 0.660$, $p < 0.001$; Fig. 1E) and the OGS score (OS: $r = 0.918$, $p < 0.001$; NS: $r = 0.748$, $p < 0.001$; Fig. 1F).

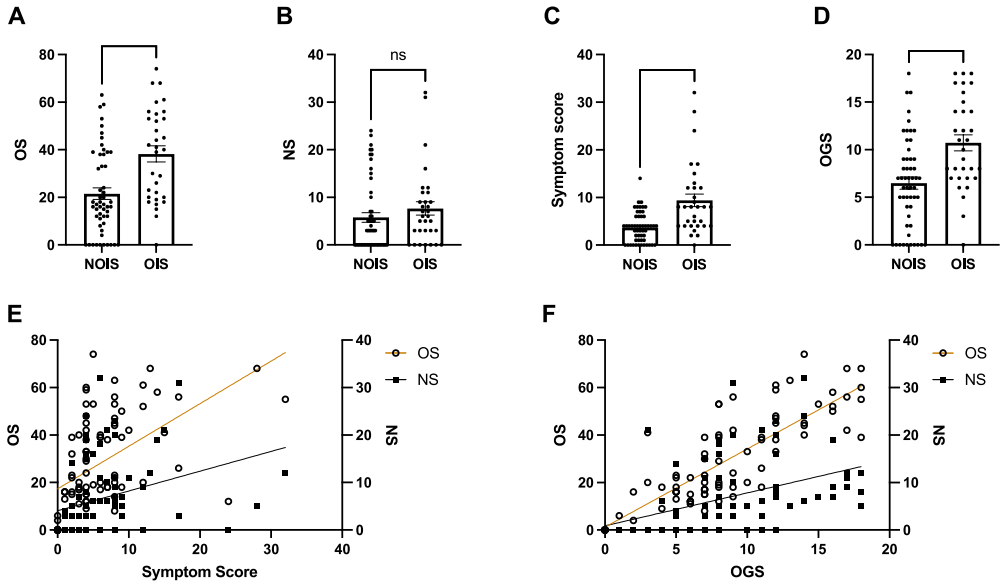



**Fig. 1.** Comparison of test scores and correlation between scores of NOIS and OIS groups. (A) The OIS group had a significantly higher OS from the ODSS than the NOIS group. (B) The NS did not differ significantly between the NOIS and OIS groups. (C) The Symptom Score of the OIS group was significantly higher than that of the NOIS group. (D) The OGS score of the OIS group also was significantly higher than that of the NOIS group. Both the OS and NS values correlated well with the Symptom Score (E) and OGS score (F).

Both the OS and NS from the ODSS showed significant negative correlations with the change in systolic BP (OS: $r = -0.273$; $p = 0.005$; NS: $r = -0.224$, $p = 0.022$; Fig. 2A) and the change in diastolic BP (OS: $r = -0.227$; $p = 0.020$; NS: $r = -0.223$, $p = 0.022$; Fig. 2B) in the supine-to-stand test. Both the OS and NS also were significantly correlated with the CBFV score in the supine-to-stand test (OS: $r = 0.438$; $p < 0.001$; NS: $r = 0.278$, $p = 0.005$; Fig. 2C). The OS also had significant negative correlations with the CBFV during phase I ($r = -0.337$, $p = 0.001$; Fig. 2D) and phase III ($r = -0.305$, $p = 0.004$; Fig. 2E) during the VM.

### 3.3. Predictive value of the Chinese ODSS for OI

To first understand the internal consistency and reliability of the ODSS, we calculated Cronbach's α values for the OS, NS and total ODSS score (Table 4). All three Cronbach's α values were greater than 0.8, suggesting the ODSS has good internal consistency and reliability.

ROC curve analysis was performed to evaluate the sensitivity and specificity of the ODSS, Symptom Score and OGS for OIS prediction (Fig. 3A–C). The AUC values for the OS and NS of the ODSS, the Symptom Score and the OGS were 0.754 ($p < 0.001$), 0.609 ($p = 0.092$), 0.779 ($p < 0.001$) and 0.735 ($p < 0.001$), respectively. The AUC value confidence interval of 0.65–0.808 for the OS of the ODSS indicated that the OS of the ODSS has moderate predictive value for the supine-to-stand test. The Symptom Score and OGS similarly showed good predictive value for OIS detection relative to the supine-to-stand test.

Next, we calculated the sensitivity and specificity of different OS scores as cut-off points for OIS detection. Since the scale scores cannot be 0.5, the cut-off value was selected from whole numbers. It was found that when 18 points were used, the Youden index was the highest, providing the best predictive results for both positive and negative outcomes of the supine-to-stand test. Specifically, the sensitivity was 87.5 % (n = 28/28 + 4), specificity was 52.8 % (n = 28/25 + 28), positive predictive value was 52.83 % (n = 28/28 + 25), and negative predictive value was 87.5 % (n = 28/4 + 28), with an accuracy rate of 65.88 % (n = 56/85) in identifying patients with positive and negative results in the supine-to-stand test. A cut-off score was not generated for the NS, because the NS did not differ significantly between the OIS and NOIS groups.

Comparing the different subtypes of OIS, we found that patients with POTS experience the largest change in heart rate during the supine-to-stand test, and the heart rate change in this group was significantly greater than that in the NOIS group and that in patients with the OH–C subtype within the OIS group ($p < 0.05$; Table 5). Patients with OH–C had the highest supine systolic BP. The OH–C and

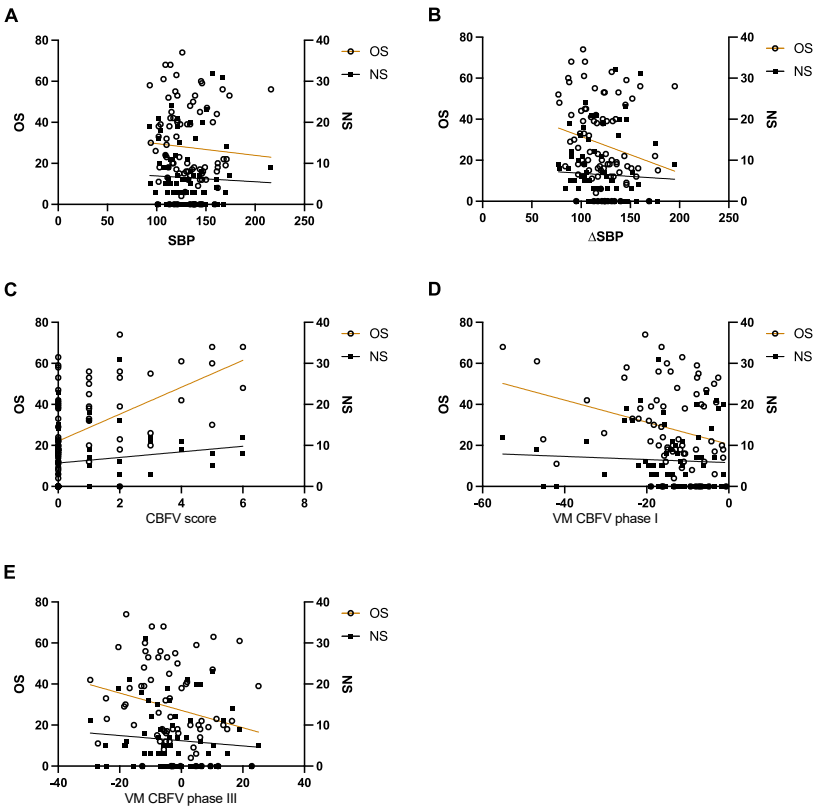



**Fig. 2.** Correlations between ODSS scores and various physiological measurements during supine-to-stand test and VM. Correlations of test scores with (A) systolic BP in baseline supine position, (B) change in systolic BP when standing, (C) CBFV score, and (D) VM CBFV during phase I and (E) phase III.

**Table 4**
Cronbach's α for each score in the Chinese version of the ODSS.

| ODSS test scores | Cronbach's α |
|---|---|
| Orthostatic score (OS) | 0.905 |
| Non-orthostatic score (NS) | 0.852 |
| Total ODSS score | 0.924 |

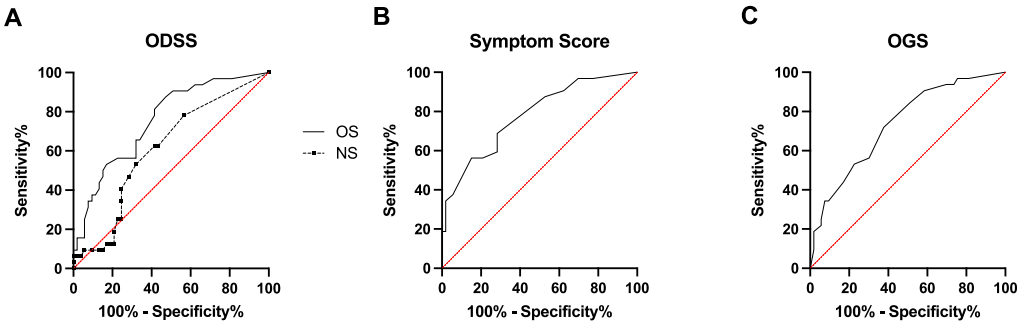



**Fig. 3.** ROC curve analysis evaluating the ability of the (A) OS and NS of the ODSS, (B) Symptom Score and (C) the OGS to detect OI.

OH–U subtypes experienced the greatest change in systolic BP, and specifically, patients with OH–U had significantly greater changes in systolic BP compared with the NOIS and OCHOs groups. The CBFV values for OH–U, OCHOs and POTS patients were also significantly higher than those of the NOIS group and OH–C patients ($p < 0.05$). Additionally, OH–U patients had significantly higher "W" wave rebound and lower VR and VM CBFV during phases II and III compared with the NOIS group ($p < 0.05$).

Among patients in the OIS group, patients with OH–U had the highest OS from the ODSS, followed by patients with OCHOs, POTS and finally OH–C. Only the OS of OH–U patients differed significantly from that of the NOIS group. The rankings of the four subtypes for the NS followed the same order as those for the OS, but none of the groups had an NS that was significantly different from that of the NOIS group. For the Symptom Score, the highest to lowest scores were observed in the POTS, OH–U, OH–C, and OCHOs groups, while the highest to lowest OGS scores were found in the OH–U, POTS, OCHOs and lastly, OH–C groups. None of the Symptom Scores and

**Table 5**
Comparison of scores, supine-to-stand results, and measurements of autonomic function among patients of the OIS group with different subtypes of OI.

| | NOIS group (n = 53) | OH–C group (n = 13) | OH–U group (n = 7) | OCHOs group (n = 8) | POTS group (n = 3) |
|---|---|---|---|---|---|
| Age (years) | 58 (49–68.5) | 66 (55.5, 70) | 55 (51, 56) | 54.5 (25.25, 62) | 15 (14, 21)[a] |
| Gender (Male/female) | 39/19 | 9/4 | 4/3 | 3/5 | 1/2 |
| OS | 17 (8.5, 38) | 29 (18.5, 44.5) | 56 (48, 68)[b] | 34.5 (19.25, 54.5) | 26 (20, 68) |
| NS | 3 (0, 8.5) | 5 (0, 8) | 9 (8, 12) | 4 (0.75, 11.25) | 5 (3, 11) |
| Symptom Score | 4 (1, 6) | 8 (4.5, 10)[b] | 10 (4, 13)[a] | 4.5 (2, 11.25) | 17 (8, 28)[a] |
| OGS score | 7 (2.5, 9) | 10 (7.5, 14)[b] | 16 (12, 17)[b] | 7.5 (5.5, 11) | 11 (7, 18) |
| Δ heart rate (bpm) | 8.77 (5, 14.23) | 6 (0.53, 12) | 14 (5.23, 20)[#] | 13.61 (4.25, 19) | 33 (32, 37)[a c] |
| Δsystolic BP (mmHg) | −3 (−10, 3.5) | −33 (−44.5, −21.5)[b d] | −27 (−56, −24)[b d] | −5.5 (−11, −1.75) | −10 (−15, −2) |
| "W" wave rebound (incomplete ratio %) | 9.43 | 27.27 | 42.86[a] | 0 | 0 |
| CBFV score | 0 (0, 0) | 0 (0, 1) | 5 (2, 6)[b##] | 2 (2, 3.75)[b##] | 3 (3, 5)[b c] |
| VM CBFV phase I | −11 (−15.97, −6.05) | −14.58 (−16.62, −7.83) | −18.75 (−39.71, −14.46) | −18.63 (−40.27, −9.25) | −16.37 (−30.37, −11.36) |
| VM CBFV phase II | 10.8 (5.65, 16.10) | 5.9 (1.35, 12.33) | 4.15 (2, 15.50) | 11.7 (5.78, 19.95) | 14.3 (10.6, 23) |
| VM CBFV phase III | −1.2 (−5.04, 6.15) | −5.38 (−9.45, 3.08) | −11.94 (−20.81, −11.11)[a] | −8.47 (−16.58, 8.46) | −5.77 (−7.37, 2.94) |
| VM CBFV phase IV | 19.63 (12.49, 28) | 15.59 (10.68, 18.95) | 6. (1.95, 15.24)[!] | 29.21 (15.71, 35.7) | 22.03 (8.43, 31.94) |
| VR | 1.35 (1.23, 1.54) | 1.22 (1.12, 1.54) | 1.21 (1.13, 1.23) | 1.32 (1.25, 1.70) | 1.46 (1.28, 2.05) |

Data are presented as *M ($P_{25}$, $P_{75}$)*, unless otherwise specified.
[a] $p < 0.05$ vs NOIS.
[b] $p < 0.01$ vs NOIS group.
[c] $p < 0.05$ vs OH–C.
[d] $p < 0.05$ vs OCHOs.

OGS scores of the four OIS subtypes differed significantly from the values of the NOIS group.

We used ROC curve analysis on data from the 85 participants with OI symptoms to evaluate the predictive value of the Chinese version of the ODSS for the different subtypes of OI, we found that only the OS from the ODSS had reliable predictive value for OH–U, whereas it was not as useful for OH–C, OCHOs or POTS (Fig. 4A–D). The AUC value for the OS for OH–U was 0.917, with a 95 % confidence interval of 0.916–0.978. Using a cut-off value of 41.5 points, the sensitivity and specificity of the OS for detecting OH–U were 100 % and 82.7 %, respectively.

## 4. Discussion

In this study, we aimed to evaluate whether the Chinese version of the ODSS can be a useful tool for identifying patients with OI symptoms and abnormal results in the supine-to-stand test. Participants were divided into NOIS and OIS groups based on the changes in heart rate, BP and CBFV observed during the supine-to-stand test. We also administered self-report tests including the Chinese ODSS, Symptom Score and OGS to gauge OI. As expected, the ΔSBP, ΔDBP, CBFV score, VM CBFV in phases I and III, and VR observed in the OIS group differed significantly from those of the NOIS group and healthy controls. Importantly, this was reflected in self-reported test scores, with the OIS group having significantly higher scores on the OS of the ODSS as well as higher Symptom Score and OGS scores. The NS of the ODSS did not differ among the groups. We also found good correlations between the OS and physiological measurements, with higher OS scores tending to correspond with larger changes in physiological measurements during autonomic function tests. ROC curve analyses indicated that the Chinese version of the ODSS had similar moderate sensitivity and specificity for detecting patients with OIS compared with the Symptom Score and OGS. These results suggest the OS of the ODSS can reliably identify patients with orthostatic symptoms and could be used as a screening tool within clinical settings. To further delineate the predictive value of the ODSS, we divided the OIS group according to different types of OI based on the various diagnostic criteria. We concluded that the OS of the ODSS had uniquely high specificity and sensitivity for identifying OH–U among patients in the OIS group, while having moderate specificity and sensitivity for the detection of OH–C, OCHOs and POTS.

Patients with OIS have a greater fall risk, and this can result in fractures, traumatic brain injury and soft tissue injuries [22,23]. Elderly patients are particularly vulnerable to falls due to OIS, and a fall can further lower their quality of life [24]. Therefore, it is critical to have a healthcare framework that can facilitate and support clear diagnosis of OIS and appropriate standardized management or treatment of these patients. Currently, the Chinese healthcare system faces a spectrum of challenges, mostly surrounding making healthcare affordable and accessible to its people while ensuring the load on the healthcare system does not increase [25,26]. With the increased use of mobile technology to provide healthcare in China, having a questionnaire that can aid the diagnostic process without medical equipment or healthcare workers on-site would be greatly beneficial [27]. The present study found that the Chinese version of the ODSS could be a useful tool for screening for orthostatic symptoms, and importantly, it can be administered by any healthcare worker via tele-consult without the need for additional equipment and being on-site [28]. Additionally, the original ODSS showed that good test-retest reliability within 2 weeks of testing, suggesting that the test can be potentially used on patients several times [16]. This is important as current orthostatic stress tests have limited reproducibility and can produce fluctuating results on repeated challenges [11,12]. The ODSS thus provides another avenue for accurate diagnosis and could potentially even be utilized to track a patient's progress throughout the treatment process. Accordingly, it will be worth exploring the test-retest reliability of the ODSS over longer periods of time in future studies. Our results further showed that the Chinese version of the ODSS achieved a 65.88 % accuracy in distinguishing between OIS and NOIS patients with a cut-off value of 18. Further investigations are warranted to optimize the selection of the cut-off value for the Chinese ODSS to improve its positive or negative predictive value. If the tool is intended for screening purposes, greater sensitivity may be required, whereas if it is intended as the gold standard for final diagnosis, higher specificity is essential.

One limitation of the present study is that the Chinese version of the ODSS showed only modest predictive value for patients with OIS, particularly for those with OH–C, OCHOs or POTS. This may be due to the small patient sample sizes of the OI subtype groups. Although non-significant, we still observed that patients with OH–C, OCHOs and POTS were more likely to have higher OS values compared with patients in the NOIS group. As such, the ODSS could still be used as an initial screening tool, and follow-up clinical tests can then be ordered to provide an accurate diagnosis and treatment plan if necessary. This would be particularly useful in the context of rural medicine, where community doctors can first use the tool to screen patients before referring them for more thorough examinations in city hospitals. It would be useful to recruit patients based on the different subtypes of OI to have a better understanding of whether the ODSS could also be useful for identifying these sets of patients. Given that the different subtypes of OI have different physiological signatures, it also will be possible to develop questionnaires in the future that can identify these conditions without the need for clinical tests. Another limitation was the lack of independence between the patients and controls, as we recruited some of the family members as controls. Although OI is not known to be primarily influenced by genetic factors, such factors may have contributed to some degree of statistical weakness. It would be useful to repeat this study with more control participants. Lastly, the Chinese version of the ODSS was scored and organized differently from the English version, which may introduce variability in interpretation.

In conclusion, the Chinese version of the ODSS can be used efficiently in the healthcare system to diagnose patients with OH–U and to identify patients that may have OIS and thus require further clinical testing to confirm. We foresee that the implementation of this questionnaire can help to alleviate both the burden on the healthcare system while providing affordable and accessible healthcare to patients.

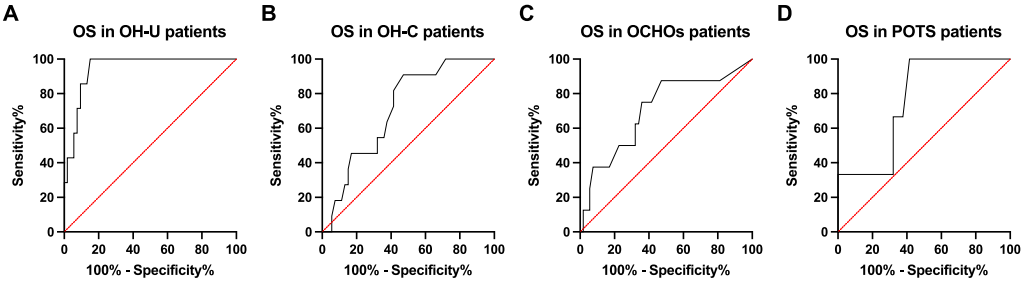



**Fig. 4.** ROC curves for evaluating the sensitivity and specificity of the Chinese version of the ODSS for detecting different types of OI. (A) The OS of the ODSS had very high sensitivity and specificity for detecting OH–U. (B–D) The OS did not show good sensitivity or specificity for detecting OH–C, OCHOs, or POTS, respectively.

## Data availability statement

The authors confirm that the data supporting the findings of this study are included in the supplementary materials.

## CRediT authorship contribution statement

**Weiting Tang:** Writing – review & editing, Writing – original draft. **Hui Gu:** Writing – review & editing, Formal analysis, Data curation. **Bin Chen:** Visualization. **Sheng Hu:** Data curation. **Wenjie Fan:** Data curation. **Yong You:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

The study is supported by the Scientific and technological cooperation projects of key R & D programs of Hainan Province (ZDYF2020227), and the National Natural Science Foundation of China, Regional Science Fund Project (82360230).

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e34724.

## References

[1] E.L. Williams, S.R. Raj, R. Schondorf, W.K. Shen, W. Wieling, V.E. Claydon, Salt supplementation in the management of orthostatic intolerance: vasovagal syncope and postural orthostatic tachycardia syndrome, Auton. Neurosci. 237 (2022) 102906, https://doi.org/10.1016/j.autneu.2021.102906.
[2] A. Fedorowski, O. Melander, Syndromes of orthostatic intolerance: a hidden danger, J. Intern. Med. 273 (2013) 322–335, https://doi.org/10.1111/joim.12021.
[3] H. Kaufmann, L. Norcliffe-Kaufmann, J.A. Palma, Baroreflex dysfunction, N. Engl. J. Med. 382 (2020) 163–178, https://doi.org/10.1056/NEJMra1509723.
[4] R. Freeman, W. Wieling, F.B. Axelrod, D.G. Benditt, E. Benarroch, I. Biaggioni, W.P. Cheshire, T. Chelimsky, P. Cortelli, C.H. Gibbons, Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome, Auton. Neurosci.: Basic and Clinical 161 (2011) 46–48.
[5] J. Baker, J.R. Paturel, D.M. Sletten, P.A. Low, K. Kimpinski, The orthostatic discriminant and severity scale (ODSS): an assessment of orthostatic intolerance, Clin. Auton. Res. 30 (2020) 69–77, https://doi.org/10.1007/s10286-018-00586-5.
[6] U. Hohtari-Kivimäki, M. Salminen, T. Vahlberg, S.-L. Kivelä, Orthostatic hypotension is a risk factor for falls among older adults: 3-year follow-up, J. Am. Med. Dir. Assoc. 22 (2021) 2325–2330, https://doi.org/10.1016/j.jamda.2021.07.010.
[7] V. Gupta, L.A. Lipsitz, Orthostatic hypotension in the elderly: diagnosis and treatment, Am. J. Med. 120 (2007) 841–847, https://doi.org/10.1016/j.amjmed.2007.02.023.
[8] S. Eschlböck, G. Wenning, A. Fanciulli, Evidence-based treatment of neurogenic orthostatic hypotension and related symptoms, Journal of neural transmission (Vienna, Austria 124 (2017) 1567–1605, https://doi.org/10.1007/s00702-017-1791-y, 1996.
[9] J.J. Figueroa, J.R. Basford, P.A. Low, Preventing and treating orthostatic hypotension: as easy as A, B, C, Cleve. Clin. J. Med. 77 (2010) 298–306, https://doi.org/10.3949/ccjm.77a.09118.
[10] J.B. Lanier, M.B. Mote, E.C. Clay, Evaluation and management of orthostatic hypotension, Am. Fam. Physician 84 (2011) 527–536.
[11] J.E. Naschitz, I. Rosner, Orthostatic hypotension: framework of the syndrome, Postgrad. Med. 83 (2007) 568–574, https://doi.org/10.1136/pgmj.2007.058198.
[12] W.S. Aronow, N.H. Lee, F.F. Sales, F. Etienne, Prevalence of postural hypotension in elderly patients in a long-term health care facility, Am. J. Cardiol. 62 (1988) 336, https://doi.org/10.1016/0002-9149(88)90243-3.

[13] W.H. Jost, C. Rapp, J. König, K. Schimrigk, Are heart rate responses reproducible in the tilt-table test? Clin. Invest. 72 (1994) 996–999, https://doi.org/10.1007/bf00577743.
[14] J. Frith, Diagnosing orthostatic hypotension: a narrative review of the evidence, Br. Med. Bull. 115 (2015) 123–134, https://doi.org/10.1093/bmb/ldv025.
[15] D.J. Irvin, M. White, The importance of accurately assessing orthostatic hypotension, Geriatr. Nurs. 25 (2004) 99–101, https://doi.org/10.1016/j.gerinurse.2003.10.022.
[16] J. Baker, J.R. Paturel, D.M. Sletten, P.A. Low, K. Kimpinski, Initial validation of symptom scores derived from the orthostatic discriminant and severity scale, Clin. Auton. Res. 29 (2019) 105–112, https://doi.org/10.1007/s10286-018-0511-5.
[17] H. Cai, S. Wang, R. Zou, P. Liu, H. Yang, Y. Wang, C. Wang, Symptom score: a new instrument to assess orthostatic intolerance in children and adolescents, J. Child Neurol. 35 (2020) 835–843, https://doi.org/10.1177/0883073820936025.
[18] C. Schrezenmaier, J.A. Gehrking, S.M. Hines, P.A. Low, L.M. Benrud-Larson, P. Sandroni, Evaluation of orthostatic hypotension: relationship of a new self-report instrument to laboratory-based measures, Mayo Clin. Proc. 80 (2005) 330–334, https://doi.org/10.4065/80.3.330.
[19] L. Norcliffe-Kaufmann, B. Galindo-Mendez, A.L. Garcia-Guarniz, E. Villarreal-Vitorica, V. Novak, Transcranial Doppler in autonomic testing: standards and clinical applications, Clin. Auton. Res. 28 (2018) 187–202, https://doi.org/10.1007/s10286-017-0454-2.
[20] P. Novak, Cerebral blood flow, heart rate, and blood pressure patterns during the tilt test in common orthostatic syndromes, Neurosciences J 2016 (2016) 6127340, https://doi.org/10.1155/2016/6127340.
[21] P. Novak, Quantitative scale for grading of cardiovascular autonomic reflex tests and small fibers from skin biopsies (QASAT), Journal of Neurological Disorders 3 (2015).
[22] A. Gangavati, I. Hajjar, L. Quach, R.N. Jones, D.K. Kiely, P. Gagnon, L.A. Lipsitz, Hypertension, orthostatic hypotension, and the risk of falls in a community-dwelling elderly population: the maintenance of balance, independent living, intellect, and zest in the elderly of Boston study, J. Am. Geriatr. Soc. 59 (2011) 383–389, https://doi.org/10.1111/j.1532-5415.2011.03317.x.
[23] A. Mol, P.T.S. Bui Hoang, S. Sharmin, E.M. Reijnierse, R.J.A. van Wezel, C.G.M. Meskers, A.B. Maier, Orthostatic hypotension and falls in older adults: a systematic review and meta-analysis, J. Am. Med. Dir. Assoc. 20 (2019) 589–597.e585, https://doi.org/10.1016/j.jamda.2018.11.003.
[24] H. Durgun, N. Turan, H. Kaya, Relationship between fall behavior and quality of life of elderly individuals, Psychol. Health Med. (2021) 1–8.
[25] C. Wang, K. Rao, S. Wu, Q. Liu, Health care in China: improvement, challenges, and reform, Chest 143 (2013) 524–531, https://doi.org/10.1378/chest.12-1839.
[26] K. Hu, Challenges facing the Chinese health care system, Asia Pac. J. Publ. Health 33 (2020) 160–161, https://doi.org/10.1177/1010539520968464.
[27] Z. Ni, B. Wu, C. Samples, R.J. Shaw, Mobile technology for health care in rural China, Int. J. Nurs. Sci. 1 (2014) 323–324, https://doi.org/10.1016/j.ijnss.2014.07.003.
[28] Y. Liu, Q. Kong, E.W. de Bekker-Grob, Public preferences for health care facilities in rural China: a discrete choice experiment, Soc. Sci. Med. 237 (2019) 112396, https://doi.org/10.1016/j.socscimed.2019.112396.