



ORIGINAL ARTICLE

# Psychometric properties of the Chinese version of 21-item Fall Risk Index for community-dwelling older adults with stroke

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## ABSTRACT

**BACKGROUND:** The 21-item Fall Risk Index questionnaire (FRI-21) was developed to screen for fall risk in older adults. It showed great potential in assessing the fall risk in stroke population. However, no previous study investigated its reliability and validity in people with stroke in Hong Kong.

**AIM:** This study aimed to translate FRI-21 to Chinese and investigate: 1) the FRI-21 scores between people with stroke and healthy older adults; 2) the test-retest reliability of the FRI-21 in people with stroke; 3) the convergent validity by correlated of the FRI-21 with Berg Balance Scale (BBS); 4) the predictive ability of FRI-21 on the fall occurrence in the 2 years follow-up; 5) the optimal FRI-21 cut-off score that distinguishes faller and non-faller among people with stroke in the 2 years follow-up; and 6) the ceiling and floor effects of the Chinese version of the FRI-21.

**DESIGN:** Cross-sectional study.

**SETTING:** University-based rehabilitation laboratory.

**POPULATION:** In total, 57 people with stroke and 31 healthy older adults.

**METHODS:** The FRI-21 test was assessed in people with stroke on Day1 and Day 2 (7 days after Day 1), and assessed in healthy older adults on Day 1 only. The BBS was also assessed in Day 1.

**RESULTS:** The mean FRI-21 scores in subjects with stroke was 7.37. The FRI-21 demonstrated good inter-rater reliability (intraclass correlation [ICC] 0.74) and good test-retest reliability (ICC=0.798) in people with stroke. The FRI-21 scores demonstrated significant negative correlations with the BBS ( $r=-0.308$ ). The FRI-21 score was found to be a significant predictor (OR 1.40 [95% CI 1.06-1.85],  $P=0.018$ ) of fall in the 2 years of follow-up. The receiver operating characteristic curve analysis identified an optimal FRI-21 cutoff score of 7.5, showing an acceptable diagnostic power in distinguishing faller and non-faller among people with stroke (area under curve = 0.723,  $P=0.002$ ), with moderate sensitivity (80.0%) and specificity (60.5%). Ceiling and floor effects are negligible.

**CONCLUSIONS:** This study reflects the reliability and validity of the FRI-21 as self-administered tool for assessing fall risk in individuals aged 50 and over with stroke, and without cognitive impairments. A cut-off score of 7.5 was identified to distinguish faller and non-faller in people with stroke. The FRI-21 score was a significant predictor of fall in people with stroke. It effectively differentiates fall risk between people with stroke and healthy older adults. Future research should increase the sample size to enhance the generalizability of the findings.

**CLINICAL REHABILITATION IMPACT:** Clinicians can use this tool to efficiently identify high-risk individuals among stroke survivors and implement targeted early interventions. This early fall risk screening tool allows healthcare providers to initiate preventive measures and intensive rehabilitation protocols for those at greatest risk, potentially reducing secondary complications, improving functional outcomes, and decreasing hospital readmission rates.

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**KEY WORDS:** Accidental falls; Stroke; Mass screening; Surveys and questionnaires.

Falls can cause various injuries, including bruises (11%), lacerations (16%), sprains (8%), and fractures (5%).<sup>1</sup> Falls are the cause of about 95% of all hip fractures,<sup>2</sup> which often necessitate emergency care or hospitalization. The consequences include further increased fall risk, greater dependence on daily activities, reduced social participation, and elevated rates of depression and mortality.<sup>1</sup> There were 52.6% individuals with chronic stroke experience falls,<sup>3</sup> a rate significantly higher than that among community-dwelling older adults (20%).<sup>4</sup> Therefore, it is crucial to screen people with stroke for a high fall risk. Clinicians require reliable measures to assess baseline fall risk and efficacy of interventions.

In people with stroke, fall risk is often evaluated using objective tests such as the Berg Balance Scale (BBS), Mini Balance Evaluation Systems Test, Timed Up and Go Test (TUG), and Five Times Sit to Stand Test, which primarily assess physical function. Subjective tools used to identify high-risk individuals, such as the Fall Risk Assessment Tool and Morse Fall Scale, overlook environmental and social factors. Additionally, these assessments are typically administered by healthcare professionals rather than being self-administered.

The 21-item Fall Risk Index questionnaire (FRI-21), which was developed by the Ministry of Health, Labor, and Welfare of Japan in 2009, is a tool used to screen older adults for fall risk.<sup>5</sup> It comprises 21 Yes/No questions that address cognitive function, physical ability, emotional status, environmental factors, and social factors. Previous studies found the area under the curve (AUC) of receiver operating characteristic (ROC) for the FRI-21 was 79.4% (95% confidence interval [CI]: 0.76-0.83) and a sensitivity of 0.68 and specificity of 0.76 at a cut-off point of 9/10, with satisfactory test-retest reliability (intraclass coefficient [ICC] 0.74).<sup>6, 7</sup> However, the original version of FRI-21 may not be able to accurately reflect fall risk of people in mainland China and Hong Kong. The translation of FRI-21 for the stroke population in China and Hong Kong are essential steps towards improving the assessment and management of fall risk. By ensuring that the FRI-21 accurately reflects the contexts to Chinese population, healthcare professionals can effectively identify and address fall risk factors among stroke survivors. This translation of FRI-21 will benefit the people with high level of fall risk and tailored interventions for patients in these areas. Additionally, although the FRI-21 has been applied to populations with different conditions, including community-dwelling older adults,<sup>8, 9</sup> people with dementia,<sup>7</sup> and osteoporosis,<sup>10</sup> it

has not been applied to people with stroke. Therefore, the reliability, divergent validity of FRI-21 and its predictive ability of fall among people with stroke, require investigation.

The aims of this study were to:

- translate the original FRI-21 to Chinese;
- compare the FRI-21 scores between people with stroke and healthy older adults;
- determine the test-retest reliability of the FRI-21 in people with stroke;
- calculate the correlations of the FRI-21 with BBS;
- assess the predictive ability of FRI-21 on the fall occurrence in the 2 years follow-up;
- identify the optimal FRI-21 cut-off score that distinguishes faller from non-faller in people with stroke in the 2 years follow-up;
- examine the ceiling and floor effects of the FRI-21.

## Materials and methods

### Study design

This was a cross-sectional study. All subjects received an explanation of the study objectives and assessment procedures, and informed written consents were given before starting the study. The study followed the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of The Hong Kong Polytechnic University (No. HSEARS20230807001).

### Translation

The original FRI-21 was translated by a forward-backward translation procedure, according to Cha's guideline.<sup>11</sup> First, two independent translators (2 physiotherapists who were native Chinese speakers) forward translated the original version of FRI-21 to Chinese version. Then, the 2 Chinese version of FRI-21 were assessed by the 2 independent bilingual translators. They identified the discrepancies between the 2 Chinese version of FRI-21 and syntheses them based on the original FRI-21. Then, two other bilingual translators (two native English speaker) were backward-translated the Chinese synthesized version to English. The two backward translated version of FRI-21 were integrated to one by the two bilingual translators. A panel board with four professionals (two physiotherapists, one nurse and professional translator) reviewed the Chinese version of FRI-21 and determined the final Chinese version of FRI-21.

**Sample size calculation**

The reliability of the FRI-21 in people with stroke remains unexamined. However, this tool has exhibited good inter-rater reliability (ICC=0.74) in people with dementia.<sup>7</sup> In this study, the FRI-21 was conducted twice in people with stroke with an interval of 7 to 10 days to enable a determination of test-retest reliability. An online sample size calculator<sup>12</sup> estimated that a sample size of at least 50 would be required to obtain an ICC of 0.5, a significance level of 0.05, and a power of 80%.

Additionally, the correlation between the FRI-21 and stroke-specific outcomes had not been investigated in previous studies. Assuming a significant moderate-to-good correlation ( $\rho=0.35$ ) between the FRI-21 and stroke-specific outcome measures, a sample size of at least 46 subjects would be required to achieve 80% power at a significance level of 0.05, as determined using G-Power 3.1.9.7 (Franz Faul, University of Kiel, Kiel, Germany).

To ensure sufficient subjects with complete data will be collected, 57 subjects with stroke were recruited to evaluate the reliability of the FRI-21 in this study.

**Participants**

The community-dwelling people with stroke were recruited through a Hong Kong local rehabilitation network using poster advertisements (Figure 1). The inclusion criteria were the following: 1) an age over 50 years; 2) an onset of stroke at least 12 months prior to the study; 3) a medically stable condition; 4) an ability to follow instructions; 5) an Abbreviated Mental Test score >7; 6) minimal upper extremity capacity for trunk stabilization when standing up; and 7) being able to shift independently or with the use of walking aids from a supine to a sitting position and from a sitting to a standing. The exclusion criteria included: 1) other neurological diseases; 2) orthopaedic issues; or 3) post-trauma problems that could affect the assessment performance.

Thirty-one older adults (10 men, 21 women) with a healthy, stable condition were also recruited, and were confirmed to meet the following inclusion criteria: 1) an age greater than 50 years; 2) an independent capacity to finish the Sit to Stand Test in a single attempt (with or without a stool for support); and 3) an ability to follow instructions. The exclusion criteria were as follows: 1) neurological disease; 2) orthopedic issues; 3) post-trauma problems; or 4) other medical condition(s) that might affect performance during the assessment.

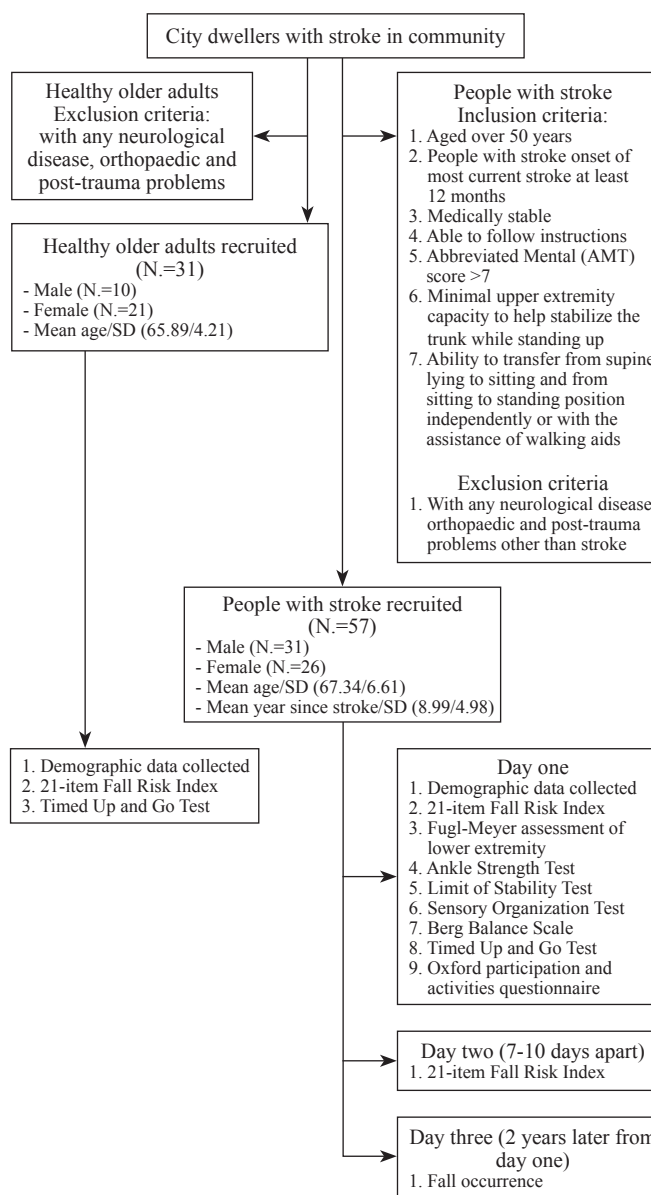


Figure 1.—Flow chart of the study.

**Testing procedures**

On Day 1, demographic data were collected from both the people with stroke and healthy older adults, and the FRI-21 was implemented. Subjects with stroke also completed the BBS test.

On Day 2 (7-10 days apart from Day 1), subjects with stroke who had been assessed on Day 1 performed the FRI-21 to determine its test-retest reliability. The test-retest reliability of the FRI-21 was evaluated using a second

trial, which was conducted 7-10 days after the first trial to reduce learning effects and account for any physical changes in the participants.

On Day 3 (2 years apart from Day 1), the subjects with stroke were followed up to assess the fall history in the past 2 years. Data from both faller and non-faller on Day 3 were used to establish cut-off scores for distinguish faller and non-faller in the 2 years of follow-up among people with stroke.

### Outcome measures

The FRI-21 is a screening tool for determining subjects' fall risk and contains 21 Yes/No questions.<sup>5</sup> Each affirmative response receives a score of 1 point, and the total scores fall between 0 to 21. A larger fall risk is indicated by a higher score. The 21 items address the presence of stumbling, stair climbing ability, decreased walking speed, crossing the street during a green signal, continuous walking for 1 km, standing on one leg for 5 seconds, cane use, squeezing a towel, dizziness, bent back, knee pain, vision problem, hearing problem, forgetfulness, anxiety about falls, usage of over five prescription drugs, perception of darkness at home, indoor obstacles, barriers on floor, everyday stair use at home, and steep slopes nearby. An optimal cut-off point for early fall risk detection was found to be 9/10 in a previous study with community-dwelling older adults.<sup>13</sup>

The BBS was used as balance assessment tool.<sup>14</sup> In this scale, the quality of task performance and time used to complete the tasks are rated on a 5-point scale from 0 (dependent) to 4 (independent), and the highest score is 56. A higher score indicates better balance ability. A previous study exhibited the excellent reliability (ICC=0.99) of the BBS in people with stroke.<sup>14</sup>

### Statistical analysis

Statistical Package for the Social Sciences software (version 29; IBM Corporation, Armonk, NY, USA) was used for data analysis. The level for significance was established at  $\alpha=0.05$ . Using descriptive statistics, the participants' demographic data are compiled. The Levene's Test and the Kolmogorov-Smirnov Test were used to evaluate homogeneity of variance and normality, respectively. Parametric and nonparametric data were compared between subjects with stroke and healthy older adults with the independent *t*-test and Mann-Whitney U Test. The FRI-21 scores of subjects with stroke on Day 1 and Day 2 were compared using the paired-sample *t*-test.

ICCs were used to assess test-retest reliability (ICC3,1).

Since fixed raters were used and a single measurement was taken in this study, Model 3 was used to analyze the test-retest reliability. Poor, moderate, good, and excellent reliability was indicated by an ICC value of <0.5, 0.5-0.75, 0.75-0.90, and >0.90, respectively.<sup>15</sup>

For the convergent validity, Pearson's correlations (*r*) for parametric data and Spearman's rho for nonparametric data were used to calculate the correlations of the FRI-21 scores with BBS score in people with stroke. No, fair, moderate-to-good, or good-to-excellent correlation was indicated by an *r* value of <0.25, 0.25-0.49, 0.5-0.75, or >0.75, respectively.<sup>15</sup>

Binary logistic regression with enter method was employed to evaluate the predictive ability of the FRI-21 for fall occurrence in people with stroke over a two-year follow-up period. Odds ratios (ORs) and Nagelkerke *R*<sup>2</sup> values were calculated to assess the strength and explanatory power of the FRI-21 in predicting falls during this timeframe.

A ROC curve was plotted to determine the FRI-21 score cut-off for distinguishing the faller and non-faller in the 2 years of follow-up among people with stroke, and the trade-off between sensitivity and 1-specificity was determined by Youden's index. The AUC was used to calculate the discrimination accuracy. Outstanding, excellent, acceptable, poor, or no discrimination accuracy was indicated by an AUC value of  $\geq 0.9$ , 0.8 to <0.9, 0.7 to <0.8, 0.5 to <0.7, and 0.5, respectively.<sup>15</sup>

## Results

### Characteristics of the participants

This study recruited 57 people with stroke and 31 healthy older adults, with mean ages of  $67.34 \pm 6.61$  and  $65.89 \pm 4.21$  years, respectively. Table I presents the subjects' demographic characteristics. The mean FRI-21 scores of people with stroke on days 1 (N.=57) and 2 (N.=57), along with the scores for healthy older adults are presented in Table II. A notable difference in body mass index was observed between the subjects with stroke and healthy controls.

### Test-retest reliability

The FRI-21 demonstrated a good test-retest reliability (ICC=0.798) in people with stroke (Table III).

### Correlation of the FRI-21 with other outcome measures

The correlation between the FRI-21 scores and BBS was shown in Table IV. Significant correlations were found be-

TABLE I.—Demographics of people with chronic stroke and healthy older adults.

Parameters	People with chronic stroke (N.=57)	Healthy older adults (N.=31)	P value
Mean age, years	67.34±6.61	65.89±4.21	0.214
Sex, M/F	31/26	10/21	0.045
Body Mass Index, kg/m <sup>2</sup>	24.23±3.31	21.80±2.85	<0.001
Stroke type, ischemic/hemorrhagic	41/16	—	—
Year since stroke, years	8.99±4.98	—	—
Affected side (left/right)	30/27	—	—

TABLE II.—Mean 21-item Fall Risk Index result for people with stroke and healthy subject.

Parameters	People with chronic stroke (N.=57)	Healthy older adults (N.=31)	P value	P value (Day 1 vs. Day 2)
Day 1 FRI-21	7.37±2.79	5.39±2.526	<0.0010	0.458
Day 2 FRI-21	7.54±2.78	—	—	—

FRI-21: 21-item Fall Risk Index.

TABLE III.—Test-retest reliability of the FRI-21 performance time of subjects with stroke.

Parameter	Test-retest-ICC <sub>3,1</sub>	95% CI	P value
FRI 21 (T1)	ICC=0.798	0.680-0.876	<0.001

TABLE IV.—Concurrent validity of the FRI-21 for people with stroke and BBS (N.=57).

Parameters	People with chronic stroke	Spearman	P value
BBS	50.88±6.78	-0.308	0.020

BBS: Berg Balance Scale.

tween the FRI-21 and BBS ( $r=-0.308$ ,  $P=0.020$ ), which indicated the significant convergent validity to measure the balance function and fall risk in people with stroke.

**Cut-off score**

The ideal FRI-21 cut-off score in this study was 7.50, with 80.0% sensitivity, 60.5% specificity, and 0.723 AUC, suggesting that the FRI-21 has an acceptable discriminative accuracy for identifying individuals with a high fall risk.<sup>16</sup> This cut-off effectively differentiated faller from non-faller in people with stroke based on their fall risk (Figure 2, Table V).

**Logistic regression analysis**

In the 2 years of follow-up, there were 53 subjects responded and four subjects dropout (one dead and three lost contact). Among the 53 subjects, there were 15 of them

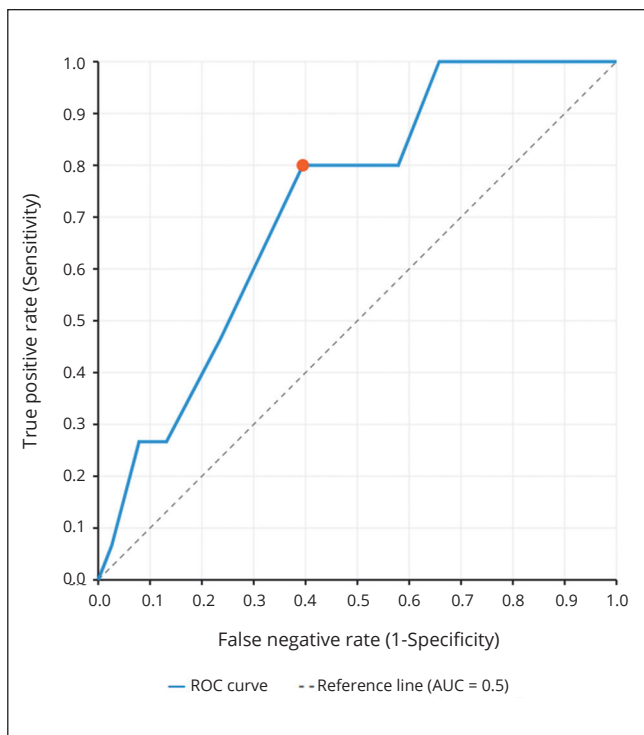


Figure 2.—The ROC curve of FRI-21 to distinguish the faller and non-faller in people with stroke.

(28.3%) fell in the past 2 years. The ORs (95%CI) was 1.401 (1.06-1.85). The Nagelkerke R<sup>2</sup> was 0.179 (Figure 3, Table V).

TABLE V.—The predictive ability and diagnostic power of FRI-21 to fall occurrence in people with stroke in the 2 years' follow-up.

Optimal cutoff score (N.=53)	Area under the curve	Sensitivity	Specificity	Odd ratio (95% CI)	Nagelkerke R <sup>2</sup>
7.5	0.723	80.0%	60.5%	1.401 (1.06-1.85)	0.179

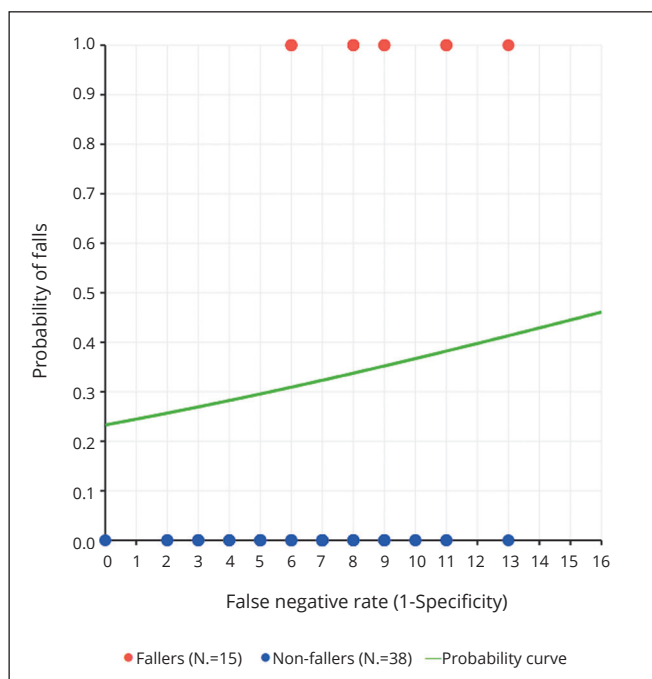


Figure 3.—The logistic regression analysis: FRI-21 score to predict the fall in people with stroke in 2 years' follow-up.

### Ceiling and floor effect

There were 2.3% of the subjects scored 13/21 in the FRI-21, the highest score in this study, while 1.1% scored 0/21. Typical significant ceiling and floor effects have been set at 15%,<sup>17</sup> with rates of 10 to <15% and 5 to <10% accepted as moderate and minor effects, respectively,<sup>18</sup> suggesting a negligible ceiling and floor effect.

### Discussion

This was a pioneer study to evaluate the psychometric properties of the Chinese version of FRI-21 in people with stroke. The FRI-21 score in the stroke group was significantly higher than that of healthy group. It also showed good test-retest reliability when assessing people with stroke. Furthermore, the FRI-21 exhibited convergent validity to measure balance function and fall risk as indicated by negative significant correlation with BBS score. The FRI-21 score was found to be a significant predictor of fall in the 2 years of follow-up, with each 1-point increase of FRI-21 score associated with 40% higher odds of falling. The ROC curve analysis identified an optimal FRI-21 cut-off score of 7.5 with acceptable diagnostic power in distinguishing faller and non-faller among people with stroke. Ceiling and floor effects of FRI-21 are negligible.

### Performance of stroke

The mean FRI-21 score of subjects with stroke was 7.37, lower than the cut-off of 9/10 reported in a previous study<sup>6</sup> which reported mean ages of 74.60±6.70 years in the high fall risk group and 67.34±6.61 years in the stroke group. Additionally, people who were unable to shift from supine to sitting or from sitting to standing independently or with a walking aid were excluded from the current study. The differences in age and inclusion criteria between the studies may explain the superior performance of subjects in the current study.

Subjects with stroke in the current study showed a higher FRI-21 score (mean=6.31) than those with Alzheimer's disease (AD).<sup>7</sup> Poor balance and visuospatial abilities are the main risk factors for falls in individuals with AD, according to research, while cognitive impairment poses a less significant risk.<sup>19</sup> Tsujimoto's study included newly diagnosed people with AD, indicating an early phase of disease in which memory loss was the primary manifestation.<sup>7</sup> In contrast, people with stroke face physical challenges such as sensory loss, reduced muscle strength, and limb spasticity, which adversely affect their gait stability and balance. The increased FRI-21 scores in stroke patients compared to AD patients may be explained by these variations.

### Between-group difference in the FRI-21

The FRI-21 scores differed significantly between subjects with stroke and healthy older adults ( $P<0.001$ ), with the score for subjects with stroke being 1.98 points higher than that for healthy controls. Upper motor neuron lesions can increase the susceptibility to damage of brain areas related to movement control, including the motor cortex, insula, putamen, and descending motor tracts, and damage in these areas leads to altered muscle activation patterns, sensory organization disturbances, and reduced muscle strength.<sup>20</sup> All of these consequences cause reduced muscle strength, increased spasticity and reduced balance which increase the fall risk of people with stroke.

### Test-retest reliability of the FRI-21

This study adds to the body of literature by offering novel data on the test-retest reliability of the FRI-21 in people with stroke (ICC=0.798). The observed good test-retest reliability is attributed to clear translation of the items in the questionnaires, consistent tester instructions, and use of a 7- to 10-day interval between trials, which reduced the learning effect and minimized actual changes in subjects' conditions.<sup>21</sup>

### Correlation of the FRI-21 Questionnaire with BBS

A significant, fair, and negative correlation was found between the FRI-21 and BBS scores ( $r=-0.308$ ,  $P=0.020$ ), which suggested the convergent validity of FRI-21 to assess the functional balance and fall risk in people with stroke. A previous study reported that 48.1% of people with stroke have balance impairments, which are contributors for falls and fear of falling.<sup>22</sup> The BBS measures subjects' balance ability, a significant predictor of falls among people with stroke.<sup>23</sup> The significant correlation between these measures suggests that the FRI-21 effectively assess the balance-related components of fall risk, which are particularly impaired in people with stroke, caused by altered muscle tone, and sensory deficits directly impact postural control.<sup>24</sup>

### The FRI-21 score to distinguish faller and non-faller in people with stroke

The FRI-21 demonstrated acceptable ability assess the fall risk in people with stroke. Comparing with previous study<sup>6</sup> which assessed FRI-21 in community older adults, our finding showed a comparable AUC of FRI-21 to distinguish faller and non-faller in people with stroke. It may suggest that the FRI-21 maintains relatively consistent overall discriminative ability across different populations.

The optimal cut-off point identified in previous work with community-dwelling older adults was 9/10, which is higher than our threshold of 7.50 for the stroke population. This lower cut-off in stroke patients suggests that individuals with stroke may exhibit fall risk at lower FRI-21 scores, consistent with the known increased fall risk following stroke due to specific neurological impairments including hemiparesis, balance deficits, and sensory disturbances.<sup>3</sup>

A precaution should be noticed that there were only 53 subjects with stroke included in the ROC analysis in this study. The sample size was related small when compare with the previous study<sup>6</sup> which included 1053 community older adults. The different finding on the optimal cutoff FRI-21 score can be attributed the difference in sample size.

### The predictive ability of FRI-21 on the fall in the 2 years' follow-up

This was the first study to use FRI-21 to predict the fall in the 2 years follow-up among people with stroke. The finding showed that for each one-point increase in the FRI-21 score, the odds of falling increased by approximately 40%, which demonstrated the FRI-21's predictive capability for

actual fall events. In clinic, the physiotherapist can use the FRI-21 as a foundation for targeted intervention design represents an innovative and practical clinical approach to fall prevention in stroke rehabilitation. By focusing interventions specifically on items where patients score 1 (indicating risk), physiotherapists can develop personalized, efficient protocols that directly address each individual's unique fall risk issue. This item-level intervention approach offers several distinct advantages over generic fall prevention programs.

The Nagelkerke  $R^2$  value of 0.179 suggests that the FRI-21 accounts for approximately 17.9% of the variance in fall occurrence among people with stroke. Future study can investigate the impact of additional factors (*e.g.* emotion, education) beyond those captured by the FRI-21 influence fall events in this population.

### Ceiling and floor effect of FRI-21

This is the first study to demonstrate the negligible ceiling and floor effects of Chinese version of FRI-21 in people with stroke. The absence of such effects suggests that the FRI-21 maintains good discriminative ability across the full spectrum of the construct being measured, allowing for accurate assessment of both individuals with minimal impairment and those with severe limitations. This enhances the instrument's responsiveness to change in longitudinal studies and its utility in detecting differences between groups in comparative research. However, it should be noticed that there were only 57 subjects included in the analysis. The sample size was relatively small for definitive psychometric validation. Future validation studies with larger, more diverse samples are warranted to make more robust conclusions regarding the ceiling and floor effects of the FRI-21.

### Limitations of the study

There are several limitations in this study. First, the gender ratios in between subjects with stroke differed from healthy older adults, with the healthy group having fewer male; additionally, the between-group difference in BMI may have affected physical performance outcomes.<sup>25</sup> Second, the sample size for this study was based on effect sizes derived from reliability and correlation analyses in previous study<sup>7</sup> or assumption involving community-dwelling older adults. However, this sample size may not be sufficient for conducting ROC analysis, logistic regression analysis, and assessing floor or ceiling effects in patients with stroke. To enhance the robustness of these analyses, future studies should consider recruiting a larger sample of

stroke survivors with varying mobility levels. Lastly, this cross-sectional study can only detect correlation but not causal relationship.

## Conclusions

The Chinese version of FRI-21 can effectively assess fall risk in people with stroke and was found to exhibit strong test-retest reliability and correlations with measures of stroke outcome. A cut-off score of 7.5 was identified to distinguish faller and non-faller in people with stroke. The FRI-21 score was a significant predictor of fall in people with stroke. Clinicians can use this tool to efficiently identify high-risk individuals and provide early intervention. Future studies should involve larger samples to enhance the generalizability of the findings.

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### Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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### Authors' contributions

Shamay S. Ng and Peiming Chen gave substantial contributions to the conception and the design of the study; K. Cheng, Y. Hui, C. Law, H. Leung, T. Cheung, Peiming Chen to acquisition, analysis and interpretation of the data. All authors have participated to draft the manuscript, Shamay S. Ng, Billy C. So, Richard H. Xu, C. Hsu, Kim J. Li, Cynthia Y. Lai, Mimi M. Tse revised it critically. All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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