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# **OPEN** Differences in symptom clusters based on multidimensional symptom experience and symptom burden in stroke patients

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In the study of stroke symptoms, a significant unresolved issue remains: What are the similarities and differences in the use of three symptom dimensions—occurrence, severity, and distress—and symptom burden to identify symptom clusters, and which level is recommended for constructing symptom clusters? This study aimed to identify the number and types of symptom clusters in stroke patients on the basis of these dimensions and to determine the most suitable dimension for extracting symptom clusters. Data were collected from 656 stroke patients via a convenience sampling method at a tertiary-level hospital in Wuhan, China, between August 2023 and March 2024. Exploratory factor analysis was conducted to extract symptom clusters on the basis of the three dimensions of the symptom experience scale and symptom burden. Four similar symptom clusters were identified: the mood disturbance symptom cluster, the physical symptom cluster, the cognitive dysfunction symptom cluster, and the slurred speech and choking cough symptom cluster. The symptom of "fatigue" within the physical symptom cluster was not identified only in the dimension of distress (with a percentage agreement of 83.3%), whereas the symptom composition of other clusters remained consistent across all three symptom dimensions (with a percentage agreement of 100%). Moreover, all four symptom clusters exhibited high consistency in terms of both occurrence and symptom burden, regardless of whether the symptom with the highest factor loading or the overall symptom composition was considered. The use of symptom occurrence and symptom burden is recommended for identifying symptom clusters in stroke patients. Subsequently, trajectory studies of symptom clusters and symptom network analyses should be conducted on the basis of these two dimensions to establish a solid theoretical foundation for future clinical interventions and related scientific research.

Keywords Symptom management, Stroke, Symptom clusters, Factor analysis, Chronic illness

Stroke is the second leading cause of death and the third leading cause of disability worldwide, accounting for nearly 7 million fatalities each year<sup>1</sup>. Common symptoms of stroke include hemiplegia, sensory impairment, aphasia, and visual impairment. These symptoms often cooccur, resulting in a synergistic effect that significantly reduces both the quality of life and the prognosis of patients<sup>2,3</sup>. Therefore, the implementation of effective assessment and prevention strategies is crucial for alleviating the burden of stroke on individuals and healthcare systems<sup>4</sup>.

Stroke symptoms are characterized by persistence and complexity. Current assessment and intervention studies that focus on individual symptoms cannot fully elucidate the occurrence of symptoms, the interactions between symptoms, and their impact on patient prognosis<sup>5</sup>. Scholars are increasingly investigating these issues from the perspective of multidimensional symptoms (i.e., symptom clusters)<sup>6</sup>. A symptom cluster is defined as "two or more symptoms that are related to each other, occur together, composed of stable groups of symptoms, are independent of other clusters, and may reveal specific underlying dimensions of symptoms." [p.278]<sup>6</sup>. The rationale for this research approach is that symptoms that occur in clusters may share a common etiology or mechanism(s)<sup>7,8</sup>. The significance of studying symptom clusters lies in the ability to manage multiple symptoms

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simultaneously, thereby enhancing the efficiency of symptom management<sup>9</sup>. For example, in a study by Yeh et al., the application of auricular acupressure to intervene in the "pain-fatigue-sleep disturbance" symptom cluster among breast cancer patients resulted in a 30% reduction in symptom severity after 7 days<sup>10</sup>. Therefore, stroke symptom management on the basis of symptom clusters is expected to alleviate patient discomfort to a greater extent and effectively promote poststroke rehabilitation.

Assessing and extracting symptom clusters on the basis of symptom experience is a crucial step in the scientific management of symptoms<sup>5,8,11</sup>. However, most studies on symptom clusters have focused primarily on cancer patients<sup>12</sup>. As the prevalence of chronic diseases increases, approximately 80% of people over the age of 65 worldwide suffer from at least one chronic disease<sup>13</sup>. To further advance research in symptom science, it is essential to investigate symptom clusters associated with chronic diseases. In contrast, in the field of stroke, only seven studies have assessed symptom clusters<sup>14–20</sup>. Three of the studies used the Neuropsychiatric Inventory (NPI)<sup>14</sup>, the Poststroke Depression Rating Scale<sup>15</sup>, and a 26-item questionnaire<sup>16</sup> to extract three to six psychiatric symptom clusters in stroke patients. Additionally, one of the studies used the Memorial Symptom Assessment Scale to identify six symptom clusters in patients with cerebral hemorrhage<sup>19</sup>. Notably, there were variations in the number and types of symptom clusters identified across these four studies, which may be attributed to the differences in the symptom scales used and the content of the assessments. In contrast, the remaining three studies used the Common Symptoms of Stroke Questionnaire to assess symptom clusters in stroke patients<sup>17,18,20</sup>. Among these studies, two employed<sup>17,20</sup> severity to identify symptom clusters, whereas one study<sup>18</sup> used the average of the three symptom dimensions-namely, symptom burden-for identifying symptom clusters. Numerous studies have demonstrated that symptom experience is multidimensional and includes symptom dimensions such as occurrence, severity, and distress<sup>12,21,22</sup>. Consequently, symptom clusters derived from symptom experiences may also exhibit multidimensional characteristics. Therefore, despite the consistency of the assessment tools, there are still differences in the number and types of symptom clusters reported across these studies, possibly due to differences in the symptom dimensions extracted. The use of a single symptom dimension to extract symptom clusters offers greater simplicity in data collection, while employing the symptom burden may better reflect the comprehensive characteristics of symptoms<sup>23</sup>. However, relying solely on averages for symptom cluster extraction may overlook the nuanced differences in patients' experiences across various symptom dimensions<sup>18</sup>. Current research on patients' symptom experiences relies predominantly on self-reports, making patients' perceptions and understanding of symptom dimensions crucial for our assessments<sup>24</sup>. Therefore, comparing the similarities and differences among the three dimensions of symptom experience and symptom burden facilitates an examination of the nuanced variations in patients' symptom experiences at both the individual and aggregate levels, as well as the exploration of potential universal patterns in symptom experiences.

As noted above, a critical question in stroke symptom management remains unanswered: What are the similarities and differences in identifying symptom clusters using the three symptom dimensions versus the symptom burden? Additionally, which level is recommended for constructing symptom clusters? Given the limited research in this area, the purpose of this study was to assess 23 symptoms in stroke patients on the basis of three dimensions and symptom burden. Additionally, it aims to compare the number and types of identified symptom clusters and determine the most appropriate dimension for symptom cluster identification. We hypothesized that while the symptom clusters identified through the three dimensions and the symptom burden may exhibit overall similarities, there could be subtle differences in the composition of symptoms within the clusters.

# Methods

#### Patients and settings

This study adopted a cross-sectional design. This study recruited participants through convenience sampling between August 2023 and March 2024. According to the requirements of exploratory factor analysis, the ratio of sample size to scale items needed to be at least 1:5<sup>25</sup>. Given that the Stroke Symptom Experience Scale comprises a total of 23 symptom items, at least 115 samples were required for accurate estimation. A total of 700 stroke patients were hospitalized in the Neurology Department of a tertiary-level hospital in Wuhan, China. A total of 656 questionnaires were effectively recovered, with an effective recovery rate of 93.7%. The inclusion criteria were as follows: (1) met international stroke diagnostic standards and were diagnosed with stroke by CT or MRI examination<sup>26</sup>; (2) had a stroke diagnosis within two weeks (during hospitalization); (3) were aged 18 years or older; and (4) participated voluntarily, with informed consent obtained. The exclusion criteria included (1) a history of drug dependence, anxiety, depression or other mental illnesses; (2) dementia or severe cognitive dysfunction; (3) severe organ dysfunction, cachexia, or end-stage disease; and (4) visual, hearing, or speech communication impairments. This study received approval from the hospital ethics committee (approval number: HBZY2023-C26-01). All research methods were conducted in accordance with the relevant guidelines and regulations. All patients provided informed consent.

# Data collection procedure

This study selected stroke patients from the inpatient department of neurology at a tertiary hospital as participants and conducted face-to-face surveys via paper-based questionnaires. Prior to the survey, investigators who had undergone uniform training provided patients with a detailed explanation of the study's purpose, methods, and significance. The survey officially commenced after patients signed informed consent forms. Patients were also informed that they could withdraw from the survey at any time and that the survey process would not have any adverse effects on them. Additionally, the study pledged to strictly maintain the confidentiality of patients' personal information, ensuring that all data would be securely stored and used solely for scientific research purposes.

#### Instrument

A demographic questionnaire was used to obtain information on age, sex, body mass index (BMI), ethnicity, marital status, employment status, medical payments, education level, income, smoking status, drinking status, eating habits, residence, stroke type, number of comorbid chronic diseases, and family history of cardiovascular disease.

The Common Symptoms of Stroke Questionnaire, compiled by Shi Dan<sup>27</sup>, was used to assess the frequency, severity, and pain of 23 common stroke symptoms. When conducting surveys, researchers explain each symptom in a language that is easily understandable to patients, ensuring that they can make accurate assessments on the basis of their actual experiences. For example, regarding 'limitation of limb movement,' patients receive a straightforward explanation: it refers to difficulty in using the hands, feet or other parts of the body or the inability to perform certain movements. These include difficulty walking or standing, being unable to maintain these positions for long periods of time, insufficient arm or hand strength to lift objects or perform fine tasks, and difficulty performing self-care activities such as bathing, dressing, or eating independently. Using the questionnaire, patients were asked to indicate whether they had experienced each symptom in the past week. Among these, the incidence rate refers to the proportion of cases in which a specific symptom occurs relative to the total number of participants. For example, if 563 out of 656 patients exhibited limb weakness, the incidence rate would be calculated as 563/656 = 85.8%. For any symptom experienced, they were asked to rate its frequency of occurrence, severity, and distress. Symptom occurrence and severity were measured via a 4-point Likert scale (i.e., occurrence: 1 = seldom, 2 = sometimes, 3 = often, 4 = always; severity: 1 = slight, 2 = moderate, 3 = severe, 4 = very severe). Symptom distress was measured via a 5-point Likert scale (i.e., 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much). The average scores of the three dimensions—Occurrence, Severity, and Distress-reflect the symptom burden for a specific symptom experienced by patients, whereas the average symptom burden across all 23 symptoms represents the total symptom burden of the patients<sup>27</sup>. The content validity index (CVI) of the scale ranges from 0.8 to 1.0, and the internal consistency (Cronbach's alpha coefficient) is 0.805<sup>27</sup>. In this study, the Cronbach's alpha value for this scale was 0.854. The reliability and validity of this questionnaire have been demonstrated in studies of stroke patients<sup>17,18,20</sup>.

#### Data analyses

IBM SPSS 29 was used to analyze the data. Descriptive statistics and frequency distributions were calculated for the demographic and clinical characteristics.

#### Creation of symptom clusters

The objective of this study was to identify potential symptom clusters from the 23 symptoms associated with stroke and to explore the relationships among these symptoms. Exploratory factor analysis (EFA) is a suitable approach for our research, as it allows researchers to extract latent factors (i.e., symptom clusters) from a set of observed variables (e.g., symptoms), thereby uncovering hidden structures within the data<sup>28</sup>. In practice, EFA is typically used in combination with rotation methods<sup>29</sup>. Therefore, during the analysis, we employed EFA for factor extraction and refined the interpretation of factors via oblique rotation. This approach ensures that the extracted factors more accurately reflect the relationships among the variables<sup>30</sup>.

Thus, this study used exploratory factor analysis combined with oblique rotation to identify the types and compositions of symptom clusters on the basis of the three symptom dimensions of occurrence, severity, and distress. The internal consistency of these symptom clusters was assessed via Cronbach's alpha coefficient. The extraction criteria for the symptom clusters were as follows: (1) When the KMO values for all dimensions are greater than 0.77 and the significance of Bartlett's test of sphericity is less than 0.05, the data meet the criteria and are suitable for factor analysis<sup>31</sup>. For the three symptom dimensions of stroke, the KMO values were 0.866, 0.917, 0.892, and 0.896, respectively, and the significance levels of Bartlett's test of sphericity were all less than 0.001, confirming that the data met the standards for factor analysis. (2) To ensure sufficient variation and covariation, the incidence rate of symptoms had to be greater than 20% and less than  $80\%^{12}$ . (3) Each factor loading was required to be  $\geq 0.40$ ; if the loading values of the same symptoms in multiple factors were  $\geq 0.40$ , the maximum loading value was used to determine the symptom's attribution<sup>32</sup>. (4) Each factor contained at least two symptoms<sup>32</sup>. (5) Cronbach's alpha symptom coefficient within each factor was  $\geq 0.4^{32}$ . Solutions for each factor were subsequently examined to determine clinically appropriate names for the symptom clusters. Symptom clusters were named on the basis of the majority of symptoms in the cluster.

#### Differences in the number and types of symptom clusters

To evaluate the percentage agreement among the symptoms within the same cluster via occurrence, severity, and distress ratings, we used the criteria proposed by Kirkova and Walsh<sup>33</sup>. In their study, the researchers proposed that to establish the consistency of a symptom cluster across three dimensions, the following criteria must be satisfied: within each dimension, at least 75% of the symptoms in the cluster should be present; additionally, each dimension must include the symptom with the highest factor loading, indicating the most prominent and significant symptom. The percentage agreement refers to the extent to which the composition of symptoms within the same symptom cluster remains consistent across different symptom dimensions.

While Kirkova and Walsh<sup>33</sup> employed the term "stability" to describe these criteria, the definition and use of stability within symptom cluster research are inconsistent<sup>34</sup> and have led to the subjective application of

these criteria. Consequently, in this study, the term "stability" is used to describe whether the same clusters are identified across dimensions and/or studies.

### Results

#### Demographic and clinical characteristics

The demographic and clinical characteristics of the patients are summarized in Table 1. Among the total sample of 656 patients, the mean age was  $66.31 \pm 11.21$  years. Among these patients, 64.9% were male, 68.0% had a normal weight, 98.6% were Han Chinese, 84.3% lived in urban areas, and 91.3% were married. The majority of the patients were retired (79.9%). In terms of lifestyle habits, 63.7% currently do not smoke, 64.2% currently do not drink alcohol, and 39.0% have a salty diet. In terms of clinical characteristics, 96.5% of the patients suffered from cerebral infarction, 80.5% had one to three chronic diseases, and 67.4% reported no family history of cerebrovascular diseases.

Characteristics	Mean ± SD						
Age(years)	66.31±11.21						
Count(%)	Count(%)						
Gender							
Male	426(64.9)						
Female	230(35.1)						
BMI							
Low weight	48(7.3)						
Normal weight	446(68.0)						
Overweight	162(24.7)						
Ethnicity							
Han	647(98.6)						
Other	9(1.4)						
Residence							
Urban	553(84.3)						
Rural	103(15.7)						
Marital status	. ,						
Married	599(91.3)						
Unmarried	13(2.0)						
Divorced or widowed	44(6.7)						
Employment status							
Employed	133(20.3)						
Retired	523(79.7)						
Smoking							
Current	238(36.3)						
Non-current	418(63.7)						
Alcohol drinking							
Current	235(35.8)						
Non-current	421(64.2)						
Eating habits							
Salty diet	256(39.0)						
Moderate diet	193(29.4)						
Light diet	207(31.6)						
Stroke type							
Cerebral infarction	633(96.5)						
Intracerebral haemorrhage	21(3.2)						
Subarachnoid Hemorrhage	2(0.3)						
Number of comorbid chronic diseases							
0	109(16.6)						
1-3	528(80.5)						
>3	19(2.9)						
Family history of cardiovascular disease.							
With	214(32.6)						
Without	442(67.4)						

**Table 1**. Demographic and clinical characteristics of stroke patients (n = 656). SD standard deviation.

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# Symptom ratings

The incidence rates of symptoms in stroke patients are shown in Table 2. The results indicate that the incidence rate of symptoms in this population ranges from 3.5 to 85.8%. Notably, the occurrence rate of 18 out of the 23 assessed symptoms fell between 20% and 80%. The symptoms with an occurrence rate of less than 20% or greater than 80% included limb weakness (85.5%), shoulder pain (12.0%), upper limb flexion (7.6%), foot drop (5.3%), and varus (3.5%). These symptoms do not meet our inclusion criteria for EFA. Limb weakness, decreased self-care ability, fatigue, limited limb movement, and inability to maintain body balance ranked among the top five across the four levels: occurrence, severity, distress, and symptom burden.

#### Symptom clusters based on symptom occurrence

On the basis of the occurrence of symptoms, four symptom clusters were identified, as shown in Table 3. The detailed factor loadings of each symptom in the symptom clusters extracted on the basis of the three symptom dimensions and symptom burden can be found in Appendices 1 to 4. Factor 1, with six symptoms, was named the mood disturbance symptom cluster. Factor 2, with six symptoms, was named the physical symptom cluster. Factor 3, with three symptoms, was named the cognitive dysfunction symptom cluster. Factor 4, with two symptoms, was named the slurred speech and choking cough symptom cluster.

#### Symptom clusters based on symptom severity

On the basis of the severity of the symptoms, four symptom clusters were identified, as shown in Table 3. The naming and composition of the symptom clusters are consistent with those extracted on the basis of occurrence.

	Incidence Rates <sup>b</sup>	Occurrence Ratings <sup>c</sup> Severity Ratings <sup>d</sup>		Distress Ratings <sup>e</sup>		Symptom Burden Ratings <sup>f</sup>			
Symptoms <sup>a</sup>	n(%)	Mean ± SD	Rank Order	Mean ± SD	Rank Order	Mean ± SD	Rank Order	Mean ± SD	Rank Order
Limb weakness	563(85.8)	$2.82 \pm 1.361$	1	$2.14 \pm 0.270$	1	$2.51 \pm 1.331$	1	$2.82 \pm 1.361$	1
Decreased self-care ability	500(76.2)	$2.38 \pm 1.519$	2	$1.98 \pm 1.408$	2	$2.22 \pm 1.496$	2	$2.38 \pm 1.519$	2
Fatigue	492(75.0)	$2.15 \pm 1.447$	4	$1.85 \pm 1.395$	3	$1.94 \pm 1.401$	4	$2.15 \pm 1.447$	4
Limited limb movement	465(70.9)	$2.34 \pm 1.647$	3	$1.84 \pm 1.446$	4	$2.09 \pm 1.547$	3	$2.34 \pm 1.647$	3
Inability to maintain body balance	402(61.3)	$2.00 \pm 1.717$	5	$1.66 \pm 1.547$	5	$1.82 \pm 1.641$	5	$2.00 \pm 1.717$	5
Memory decline	397(60.5)	$1.70 \pm 1.497$	8	$1.42 \pm 1.406$	8	$1.51 \pm 1.405$	8	$1.70 \pm 1.497$	8
Decreased limb sensation	363(55.3)	$1.71 \pm 1.667$	7	$1.47 \pm 1.519$	7	$1.52 \pm 1.562$	7	$1.71 \pm 1.667$	7
Troubled by not being able to do what you want	354(54.0)	$1.41 \pm 1.432$	10	1.23±1.333	9	1.31±1.396	10	$1.41 \pm 1.432$	10
Limb uncoordinated	352(53.7)	$1.73 \pm 1.714$	6	$1.47 \pm 1.576$	6	$1.58 \pm 1.634$	6	$1.73 \pm 1.714$	6
Slurred speech	312(47.6)	$1.50 \pm 1.701$	9	$1.14 \pm 1.378$	10	$1.40 \pm 1.605$	9	$1.50 \pm 1.701$	9
Unhappy	309(47.1)	$1.21 \pm 1.378$	13	$1.05 \pm 1.272$	12	$1.17 \pm 1.373$	11	$1.21 \pm 1.378$	12
Slowed reaction	304(46.3)	$1.26 \pm 1.462$	12	$1.05 \pm 1.310$	13	$1.08 \pm 1.305$	14	$1.26 \pm 1.462$	13
Easily anxious	294(44.8)	$1.32 \pm 1.563$	11	$1.13 \pm 1.423$	11	$1.08 \pm 1.319$	13	$1.32 \pm 1.563$	11
Lack of initiative	289(44.1)	$1.17 \pm 1.416$	14	$0.99 \pm 1.260$	14	$1.09 \pm 1.345$	12	$1.17 \pm 1.416$	14
Attention decline	267(40.7)	$1.10 \pm 1.419$	15	0.96±1.314	15	$1.00 \pm 1.333$	15	$1.10 \pm 1.419$	15
No interest in surrounding activities	247(37.7)	$0.96 \pm 1.322$	16	$0.88 \pm 1.247$	16	$0.95 \pm 1.317$	16	$0.96 \pm 1.322$	16
Choking cough	221(33.7)	0.89±1.345	17	$0.82 \pm 1.307$	17	$0.92 \pm 1.395$	17	$0.89 \pm 1.345$	17
Disappointed with the future	199(30.3)	0.78±1.252	18	0.73±1.202	18	$0.76 \pm 1.246$	18	$0.78 \pm 1.252$	18
Limb pain	137(20.9)	$0.58 \pm 1.209$	19	$0.51 \pm 1.091$	19	$0.55 \pm 1.171$	19	$0.58 \pm 1.209$	19
Shoulder pain	79(12.0)	$0.32 \pm 0.937$	20	$0.30 \pm 0.889$	20	$0.31 \pm 0.915$	20	$0.32 \pm 0.937$	20
Upper limb flexion	50(7.6)	$0.21 \pm 0.792$	21	$0.17 \pm 0.645$	21	$0.18 \pm 0.664$	21	$0.21\pm0.792$	21
Foot drop	35(5.3)	$0.15 \pm 0.701$	22	$0.12 \pm 0.531$	22	$0.14 \pm 0.638$	22	$0.15 \pm 0.701$	22
Varus	23(3.5)	$0.09 \pm 0.477$	23	0.06±0.373	23	$0.07 \pm 0.430$	23	$0.09\pm0.477$	23

**Table 2.** Symptom occurrence rates, severity, distress and symptom burden ratings for symptoms in stroke patients (n = 656). SD standard deviation. <sup>a</sup>Symptoms with an incidence rate of less than 20% or greater than 80%, including limb weakness, shoulder pain, upper limb flexion, foot drop, and varus, do not meet our criteria for inclusion in the Exploratory Factor Analysis (EFA). <sup>b</sup>Symptoms are listed in descending order of occurrence; Incidence Rates: The number of cases for a specific symptom divided by the total sample size. <sup>c</sup>Occurrence Ratings: 1 = rarely, 2 = sometimes, 3 = often, 4 = almost always. <sup>d</sup>Severity ratings: 1 = slight, 2 = moderate, 3 = severe, 4 = very severe. <sup>e</sup>Distress ratings: 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much. <sup>f</sup>The average scores across the three dimensions of occurrence, severity, and distress reflect the patient's symptom burden for that particular symptom, while the mean symptom burden across all 23 symptoms represents the patient's overall symptom burden level. Symptom Burden Ratings = the average score of the three dimensions (occurrence, severity, and distress) / 23.

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Symptom Cluster	Symptoms Within the Cluster	Occurrence	Severity	Distress	Symptom Burden
Mood disturbance symptom cluster	No interest in surrounding activities	0.835	0.846	0.847	0.846
	Disappointed with the future	0.811	0.852	0.828	0.832
	Unhappiness	0.797	0.817	0.792	0.804
	Troubled by not being able to engage in desired activities	0.728	0.761	0.772	0.759
	Lack of initiative	0.715	0.766	0.775	0.756
	Easily anxious	0.518	0.568	0.497	0.539
	Percent agreement <sup>a</sup>	100%	100%	100%	100%
Physical symptom cluster	Inability to maintain body balance	0.817	0.849	0.829	0.835
	Limitation of limb movement	0.785	0.848	0.811	0.827
	Decreased self-care ability	0.746	0.785	0.783	0.784
	Limb uncoordinated	0.778	0.788	0.746	0.775
	Decreased limb sensation	0.558	0.659	0.574	0.597
	Fatigue	0.429	0.489	-	0.444
	Percent agreement	100%	100%	83.3%	100%
Cognitive dysfunction symptom cluster	Memory decline	0.854	0.829	0.845	0.850
	Attention decline	0.822	0.848	0.838	0.837
	Slowed reaction	0.796	0.758	0.769	0.777
	Percent agreement	100%	100%	100%	100%
Slurred speech and choking cough symptom cluster	Slurred speech	0.866	0.904	0.891	0.898
	Choking cough	0.604	0.580	0.616	0.596
	Percent agreement	100%	100%	100%	100%

**Table 3.** Identifying symptom clusters using the frequency, severity, distress, and symptom burden of symptoms in stroke patients. - = Factor loadings for these symptoms were < 0.40. <sup>a</sup>Example of Percentage Agreement Calculation Method: percentage agreement for the physical symptom cluster, that consisted of a total of 6 symptoms across all three dimensions, was calculated as follows for the distress dimension: 5 symptoms / 6 symptoms×100=83.3% agreement.

#### Symptom clusters based on symptom distress

On the basis of the symptoms of distress, four symptom clusters were identified, as shown in Table 3. Factor 1, with six symptoms, was named the mood disturbance symptom cluster. Factor 2, with five symptoms, was named the physical symptom cluster. Factor 3, with three symptoms, was named the cognitive dysfunction symptom cluster. Factor 4, with two symptoms, was named the slurred speech and choking cough symptom cluster.

#### Symptom clusters based on symptom burden

Four symptom clusters were identified on the basis of symptom burden, as shown in Table 3. The naming and composition of the symptom clusters are consistent with those extracted on the basis of occurrence.

#### Agreement in the types of symptoms within each symptom cluster

Table 3 presents a summary of the percentage agreement among the symptoms within each cluster across the occurrence, severity, distress dimensions, and symptom burden. For the mood disturbance symptom cluster, the total number of symptoms was six, and the percentage agreement was 100%. The six symptoms that were included in the occurrence, severity, distress, and symptom burden clusters were as follows: no interest in surrounding activities, disappointment with the future, unhappiness, inability to engage in desired activities, lack of initiative, and easy anxiety. The symptom "no interest in surrounding activities" had the highest factor loading in both the occurrence and distress dimensions, consistent with symptom clusters based on symptom burden. In the severity dimension, this symptom ranked second.

For the physical symptom cluster, the total number of symptoms ranged from five to six, and the percentage agreement ranged from 83.3 to 100%. The five symptoms that were included in the occurrence, severity, distress, and symptom burden clusters were as follows: inability to maintain body balance, limitation of limb movement, decreased self-care ability, uncoordinated limb, and decreased limb sensation. The symptom "inability to maintain body balance" had the highest factor loading across occurrence, severity, and distress, aligning with symptom clusters based on symptom burden.

For the cognitive dysfunction symptom cluster, the total number of symptoms was 3, and the percentage agreement was 100%. The three symptoms that were included in the occurrence, severity, distress, and symptom burden clusters were as follows: memory decline, attention decline, and slowed reaction. The symptom "memory decline" had the highest factor loading in both the occurrence and distress dimensions, consistent with symptom clusters based on symptom burden. In the severity dimension, this symptom ranked second.

For the slurred speech and choking cough symptom cluster, the total number of symptoms was two, and the percentage agreement was 100%. The two symptoms included slurred speech and choking cough. The symptom

"inability to maintain body balance" had the highest factor loading across occurrence, severity, and distress, aligning with symptom clusters based on symptom burden.

#### Discussion

In this study, the top five symptoms across all three dimensions and symptom burden levels are limb weakness, decreased self-care ability, fatigue, limited limb movement, and inability to maintain body balance. Limb weakness and limited limb movement may be linked to damage to the motor cortex, motor pathways, or associated neural structures, significantly impacting the patient's capacity to perform self-care activities<sup>35</sup>. Fatigue in stroke patients typically results from multiple factors, including abnormal energy metabolism due to neurological damage, impaired muscle function, and psychological stress<sup>36</sup>. Balance dysfunction is typically associated with damage to the cerebellum, brainstem, or vestibular system<sup>37</sup>. These symptoms can influence one another; for example, limb weakness and limited limb movement can exacerbate balance disorders, which in turn further restrict a patient's mobility, thereby creating a vicious cycle<sup>35</sup>.

This study is the first to evaluate differences between symptom clusters on the basis of occurrence, severity, distress and symptom burden in a larger sample of stroke patients. These symptom clusters meet the criteria of Kirkova and Walsh<sup>33</sup> in terms of consistency across three dimensions and symptom burden. Overall, four similar symptom clusters were identified across four different levels, which aligns with our research hypothesis. A more detailed analysis is presented in the subsequent discussion section. Our findings are consistent with studies on other diseases, which have also identified analogous symptom clusters using three symptom dimensions<sup>12,38-44</sup>. In patients with gastrointestinal (GI) cancer, four similar symptom clusters were identified on the basis of three symptom dimensions (i.e., psychological distress, CTX-related, GI, and weight change)<sup>12</sup>. In another study involving patients with various types of tumors, five similar symptom clusters were identified on the basis of three symptom dimensions (i.e., psychological, gastrointestinal, weight gain, respiratory, and hormonal clusters)<sup>39</sup>. Similarly, in studies involving patients with chronic kidney disease<sup>40</sup>, lung cancer patients undergoing chemotherapy<sup>41</sup>, pediatric cancer patients<sup>42</sup>, breast cancer patients<sup>43</sup>, and prostate cancer patients<sup>44</sup>, similar symptom clusters were identified on the basis of both occurrence and severity. All of these studies<sup>12,39,41-44</sup> employed the Memorial Symptom Assessment Scale (MSAS)<sup>45</sup> for evaluation. Furthermore, in research involving HIV patients<sup>38</sup>, the 20-item HIV Symptom Index<sup>46</sup> was used, which identifies four similar symptom clusters on the basis of occurrence and distress. (i.e., gastrointestinal, psychological, pain, body image). The stroke symptom experience scale used in this study closely resembles the setup of both the MSAS and the 20-item HIV Symptom Index, as all three instruments assess three experiential dimensions of symptoms through patient self-reports. The identification of symptom clusters on the basis of these three dimensions is conducted in accordance with the symptom management model<sup>7,47</sup>. This suggests that when symptom clusters are identified under the framework of this model, the symptom composition extracted using these three dimensions may not exhibit significant differences. Second, this might indicate that the scope of adopting these three dimensions to define "multidimensionality" is relatively narrow. Contemporary symptom science theory advocates for a more diverse perspective in assessing patients' symptom sensations, experiences, and burden<sup>48</sup>. Consequently, we can proceed with a multidimensional assessment of symptom clusters by considering the intensity of symptoms (primarily measurable manifestations, such as occurrence and severity), the nature of symptoms (primarily nonmeasurable manifestations, such as the nature of pain, including distending pain, dull pain, and stabbing pain), and the scope of impact (primarily the magnitude of influence on quality of life, such as effects on sleep quality and appetite)<sup>49</sup>.

#### Mood disturbance symptom cluster

Mood disturbance symptom clusters are common in a variety of chronic conditions, such as heart failure, chronic obstructive pulmonary disease, HIV, and decompensated hepatocirrhosis<sup>38,40,50-60</sup>. In this study, the mood disturbance symptom clusters were consistent in the types and number of symptoms across the three symptom dimensions and symptom burden. Although the incidence rates of "no interest in surrounding activities" and "disappointed with the future" were relatively low at 37.7% and 30.3%, respectively, these symptoms displayed high factor loadings in the extracted symptom clusters. This pattern likely reflects their association with more severe mood disturbances, potentially indicating poststroke depression<sup>61</sup>. Thus, these symptoms significantly contributed to the explanatory power of the statistical model. Combined with previous studies, we found that the most consistent mood disturbance symptoms among stroke patients include unhappiness, being easily anxious and being troubled by not being able to engage in desired activities<sup>17,18,20</sup>. In follow-up, we can further investigate whether these three symptoms are sentinel symptoms or core symptoms in the stroke symptom network. The mechanisms underlying these symptoms may represent the fundamental mechanism of the mood disturbance symptom cluster. Numerous mechanisms have been proposed for the development of mood disturbance symptoms in stroke, including the brain damage hypothesis<sup>62,63</sup>, stroke lesions in the limbic-cortical-striatalpallidal-thalamic circuit<sup>64</sup>, and the monoamine hypothesis<sup>65</sup>. Recent studies have shown that proinflammatory cytokines, such as immortal-like and functional T cells, interleukin-1, interleukin-6, and interleukin-18, are closely associated with this syndrome<sup>66-68</sup>. Future research could focus on verifying and characterizing the role of these proinflammatory cytokines in brain cells, aiming to identify intervention targets for the poststroke mood disturbance symptom cluster to improve poststroke mood disorders.

#### Physical symptom cluster

In this study, physical symptom clusters were extracted across all three symptom dimensions and symptom burden; however, fatigue symptoms were identified only in the occurrence and severity dimensions and not in the distress dimension. This observation may be attributed to the fact that the majority of patients in this study were mildly affected. This finding suggests that poststroke fatigue is a general feeling of fatigue that is not related to specific structural damage to the brain<sup>69</sup>. This fatigue can be alleviated with rest and does not significantly affect a patient's quality of life<sup>70</sup>. "Inability to maintain body balance" demonstrated the highest factor loadings across the three symptom dimensions and symptom burden within the physical symptom clusters. This symptom directly reflects the location and severity of brain injury and is also associated with an increased risk of falls, which can adversely affect the rehabilitation process<sup>37</sup>. Combined with previous studies on stroke, we found that limitations in limb movement were the most consistent symptom within the physical symptom cluster<sup>17,18,20</sup>. A common neurological consequence of stroke is the loss or limitation of unilateral muscle function, which may lead to restrictions in exercise, mobility, and overall functional ability<sup>71</sup>. The American Heart Association's physical activity and exercise recommendations recommend that stroke survivors engage in at least 150 min of moderate-intensity physical activity per week to improve physical function<sup>72</sup>. Future intervention strategies could specifically target sentinel symptoms within this symptom group to more effectively improve general physical symptoms after stroke.

#### Cognitive dysfunction symptom cluster

The cognitive dysfunction symptom cluster extracted from the three symptom dimensions and symptom burden exhibited a high degree of consistency in its composition. Among these, "memory decline" and "attention decline" demonstrated high factor loadings across all three symptom dimensions and symptom burden. The presence of these symptoms may impair a patient's ability to remember rehabilitation exercises or follow medical instructions, as well as maintain focus<sup>73</sup>. Consequently, this directly affects their comprehension and execution of rehabilitation training, potentially delaying the recovery process. Additionally, Liu<sup>19</sup> researched the symptom cluster in patients with intracerebral hemorrhage and reported that the cognitive dysfunction symptom cluster coalesced with the limb dysfunction cluster. This may be because 96.5% of patients suffer from cerebral infarction, and symptoms related to hemorrhagic stroke caused by hypertension are often more severe than those related to cerebral infarction, resulting in a more complex combination of symptom groups in this study<sup>74,75</sup>. Stroke subtypes are highly complex, and the presence of various comorbidities requires segmentation of the study population, emphasizing the importance of addressing the comorbidity phenomenon. Combined with previous studies<sup>19,58</sup>, we found that memory decline is the most consistent symptom within the cognitive dysfunction symptom cluster and may represent the core mechanism of this symptom cluster. Mechanisms that may contribute to the occurrence of cognitive dysfunction symptom clusters include increased cerebrospinal fluid amyloid levels following a stroke, neurodegenerative changes associated with tau pathology, and hippocampal atrophy<sup>76,77</sup>. The generation of new neurons is crucial for promoting hippocampal function, thereby enhancing cognitive function and recovery after stroke<sup>78-80</sup>. Currently, various intervention methods to promote neuron generation include repetitive transcranial magnetic stimulation, elements of virtual rehabilitation, high-intensity intermittent training and computer game-assisted task-specific exercises<sup>81-84</sup>. In the future, it is possible to use the scientific research paradigm as a guide to comprehensively examine which intervention methods can improve the cognitive dysfunction symptom cluster of stroke patients and determine the most effective intervention measures.

#### Slurred speech and choking cough symptom cluster

The slurred speech and choking cough symptom cluster extracted across the three symptom dimensions and symptom burden exhibited a high degree of consistency in its composition. Slurred speech not only showed the highest factor loadings across all symptom dimensions and symptom burdens in this study but was also the most consistent symptom, as supported by the research findings of Luo<sup>18</sup> and Liu<sup>20</sup>. Both slurred speech and choking cough are associated with a reduced ability of the central nervous system to control laryngeal muscles in the cerebral cortex, subcortical areas, and brainstem networks<sup>85,86</sup>. The mechanisms underlying the occurrence of these two symptoms are similar. Therefore, both language training and swallowing training can improve muscle control in the same nerve center, possibly resulting in a synergistic effect<sup>87</sup>. Ko<sup>88</sup> employed naryngopharyngeal neuromuscular electrical stimulation as an intervention method in 18 patients. This approach improved vocal fold vibration, restored laryngeal muscle function, and significantly enhanced both speech and swallowing functions. Thus, investigating the common pathophysiological mechanisms underlying these symptom clusters is essential for developing effective intervention strategies.

The symptom with the highest factor loading demonstrates the most explanatory power for its respective symptom cluster, serving as the core representative of that cluster. A comparison of the highest factor loadings across the four symptom clusters revealed that "no interest in surrounding activities" in the mood disturbance symptom cluster and "memory decline" in the cognitive dysfunction symptom cluster both presented the highest factor loadings in occurrence, distress, and symptom burden but slightly lower loadings in severity. This suggests that patients' perceptions and experiences of such symptoms with strong subjective characteristics are highly consistent in terms of occurrence and distress and align closely with symptom burden. On the one hand, while the severity of such symptoms may not be inherently high, they can significantly impact and distress patients<sup>61</sup>. On the other hand, the occurrence and distress of these symptoms reflect their frequency and impact on quality of life, which patients can easily understand and assess<sup>11</sup>. However, because mood and cognitive symptoms are more subjective experiences for patients and their impact on daily life is indirect, coupled with the lack of clear evaluation standards and scales for symptom intensity, patients may generally perceive these symptoms as less severe<sup>89</sup>. Therefore, we recommend prioritizing the use of occurrence, distress, and symptom burden to identify symptom clusters when assessing these types of symptoms. Additionally, this highlights the need to develop specific scales in the future to help patients evaluate the severity of such symptoms more accurately. Healthcare professionals should, on the one hand, pay attention to symptoms that are perceived as significant by patients despite their low severity and, on the other hand, guide patients to recognize the seriousness of their emotional and cognitive symptoms<sup>89</sup>. In contrast, "inability to maintain body balance" in the physical symptom cluster and "slurred speech" in the slurred speech and choking cough symptom cluster presented the highest factor loadings across all three symptom dimensions and symptom burden, demonstrating a high degree of consistency. This is because these two symptoms, as manifestations of reduced physical function<sup>18,90</sup>, are more objective indicators, and patients' experiences of such symptoms across dimensions are highly consistent. However, the symptom of "fatigue" in the physical symptom cluster was not identified in the distress dimension, and this incomplete recognition may affect clinical staff's judgment of patients' symptom clusters<sup>43</sup>. Therefore, occurrence, severity, and symptom burden are recommended for identifying the physical symptom cluster, whereas any dimension combined with symptom burden can be used for identifying slurred speech and choking cough symptom clusters. In summary, to ensure both accurate assessment of emotional and cognitive symptoms and comprehensive identification of symptoms in the physical symptom cluster, we recommend extracting symptom clusters on the basis of occurrence and symptom burden.

### Limitations

This study has several limitations. First, it is a cross-sectional analysis that assesses symptoms at a single time point during treatment. In future studies, our team will use the optimal symptom experience dimension to track changes in symptom clusters longitudinally and the interactions of these symptom clusters over time and assess their impact on patient outcomes. Second, this study did not analyze whether stroke patients experienced their first stroke, which is a crucial factor influencing outcomes. In the future, our research team will focus on incorporating this factor into our studies and conduct in-depth analysis and exploration. Thirdly, although limb weakness is prevalent among stroke patients and holds significant clinical importance, its inclusion in the exploratory factor analysis was precluded due to its occurrence rate exceeding 80% in the study population, in accordance with the methodological requirements for symptom cluster extraction. This exclusion may influence the composition of the physical symptom cluster and potentially diminish its clinical interpretability. It is recommended that future research employ novel analytical methods to more comprehensively identify clinically meaningful symptom cluster patterns. Additionally, our sample was drawn primarily from a single hospital, which may limit the generalizability of the research results. Therefore, future studies should be conducted across multiple centers, include diverse ethnic groups, and use larger sample sizes. Finally, because this study relied on a questionnaire format, patient reporting may be subject to subjective bias. Thus, future research could incorporate more objective evaluation indicators.

#### Conclusion

In summary, this study identified four symptom clusters in stroke patients: a mood disturbance symptom cluster, a physical symptom cluster, a cognitive dysfunction symptom cluster, and a slurred speech and choking cough symptom cluster. The four symptom clusters demonstrated a high degree of consistency in terms of occurrence and symptom burden, whether with respect to the symptoms with the highest factor loadings or their overall composition. Therefore, we recommend the use of occurrence and symptom burden data to extract symptom clusters. To more comprehensively identify and evaluate these clusters, future research should develop a multidimensional scale that incorporates factors such as the intensity, nature, and scope of impact of symptoms. This will enable a more thorough assessment of the true symptom manifestations and experiences of stroke patients. This approach provides a solid theoretical foundation for future studies on stroke symptom networks and empirical intervention research, facilitating the transition from theory to implementation science.

# Data availability

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

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# Author contributions

S.Z. designed the research topic and conducted data analysis on stroke patients. D.Y. prepared the tables and wrote the manuscript. H.H. and M.L. supervised the entire article and provided supervision and management. Y.Z. and J.X. were responsible for collecting data on stroke patients. X.W., L.L. and D.Y. contributed to the revision and improvement of the paper. All the authors read and approved the final manuscript.

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# Declarations

# **Competing interests**

The authors declare no competing interests.

# Ethics approval and consent to participate

Ethical approval was granted from the hospital ethics committee (approval number: HBZY2023-C26-01), Hubei, China. Informed consent was obtained from all participants. All participants were advised that participating in the study was voluntary and free to withdraw without any consequences.

# Additional information

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