Original Article

Identifying Symptom Clusters Among People Living With HIV on Antiretroviral Therapy in China: A Network Analysis

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Abstract

Context. There exists a research interest shift from separate symptoms to symptom clusters among people living with HIV (PLWH), which may provide a better understanding of symptom management in HIV/AIDS care. However, the symptom clusters among Chinese PLWH are still unknown.

Objectives. The aim of our study was to identify symptom clusters and to examine demographic and health-related factors associated with these symptom clusters among PLWH prescribing antiretroviral therapy (ART) in China.

Methods. From April to September 2017, we recruited 1116 participants through a convenience sampling in five HIV/AIDS designated facilities in the eastern, middle, and southwest regions of China. The principal component analysis was used to identify the symptom clusters. Association network was adopted to describe the relationships among symptoms and clusters. A multiple linear model was used to investigate the associated factors for the severity of overall symptoms and the prevalence of each symptom clusters.

Results. Five symptom clusters were identified, including cognitive dysfunction, mood disturbance, wasting syndrome, dizziness/headache, and skin-muscle-joint disorder. Cognitive dysfunction was the most central symptom cluster. Variables including primary caregiver during ART treatment, years of HIV diagnosis and ART use, having comorbidity, self-rated health, and quality of life were associated with the prevalence of these five symptom clusters.

Conclusion. Our study suggests that there is a need to evaluate symptom clusters for the improvement of symptom management among PLWH. It is particularly important to include assessment and treatment of cognitive symptoms as an essential component of the HIV care.   J Pain Symptom Manage 2019;57:617−626. © 2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words
Symptom cluster, symptom management, HIV/AIDS, China

Introduction

People living with HIV (PLWH) suffer from severe symptoms caused by the HIV infection, the adverse effects of antiretroviral therapy (ART), opportunistic infections, and comorbidities.[1] Previous studies found that most PLWH experience multiple symptoms.[2,3] These symptoms are likely to have a negative impact on the quality of life, functional performance, and adherence to treatment among PLWH.[4−6] A symptom cluster is described as two or more symptoms independently co-occurring, which may or may not share a common mechanism.[7] However, current studies have focused on isolated symptoms and thus may fail to represent the real-world situation where PLWH usually have experienced more than one symptom.

After an exhaustive search, we found only six studies reporting symptom clusters among PLWH. In studies conducted by Sousa et al. and Cook et al., six clusters

were identified among 917 male PLWH and 246 male PLWH in the U.S., including malaise/weakness/fatigue, confusion/distress, fevers/chills, gastrointestinal discomfort, shortness of breath, and nausea/vomiting[8,9] However, the data used by these two studies were collected before the introduction of ART. It is known that ART often has adverse effects.[10] Therefore, these two studies may fail to reflect the symptoms patients may experience now.

Four studies have evaluated symptom clusters among PLWH in the ART era.[11−14] Besides the symptom clusters being identified in previous studies before the advent of ART, several new symptom clusters have been emerged among PLWH for the past five years, which include pain and sensory disturbance, neurological and cognitive problems, and dermatological symptoms. The emerging of these new symptoms may be mainly due to the side effect of ART side effect and the aging of the HIV population.

Previous studies have already shown that race is significantly associated with symptom cluster membership.[15,16] However, current studies have mainly focused on PLWH in the U.S., Uganda, and South Africa; there is a dearth of knowledge of symptom clusters among Chinese PLWH. To address this knowledge gap, the aim of our study was to explore symptom clusters in PLWH in China. Specifically, this study addresses the following research questions: 1) What is the most common and severe single symptom in this population? 2) What are the most common symptom clusters? 3) What are some of the demographic and health-related factors associated with these symptom clusters?

Methods
Sample
A cross-sectional design was conducted to answer these research questions. From April to September 2017, we recruited participants through a convenience sample from five HIV/AIDS designated hospitals in five cities in the eastern (Shanghai), middle (Hengyang), and southwest regions (Kunming, Nanning, and Changning) of China, which are responsible for HIV/AIDS-related treatment and care in these areas. The eligible participants were 1) diagnosed with HIV infection; 2) aged 18 years and older; and 3) receiving ART treatment in inpatient or outpatient departments of these five HIV/AIDS designated hospitals. Participants were excluded if 1) they were unable to complete the questionnaire due to severe comorbidities such as acute infection and cardiopulmonary disease or 2) they were diagnosed with severe or end-stage HIV-associated neurocognitive disorder. Ninety participants were excluded due to missing data. As a result, this study included a total of 1116 eligible PLWH.

Procedure
Ethical approval for our study was obtained from the Institutional Review Board of the School of Nursing, Fudan University (IRB#TYSA2016-3-1). All data collection was completed in the aforementioned five hospitals. Research nurses in these five designated hospitals were trained to collect data and verify demographic data based on the patients' medical records. Research nurses explained to patients the purpose and content of the research. After providing written informed consent, participants who met the inclusion criteria were asked to fill out the questionnaire. For those participants who were unable to complete the questionnaire by themselves or could not understand the content of the questions, research nurses conducted in-person interviews in Mandarin or the appropriate dialect to collect the data. Participants in the survey were compensated by receiving an electronic pill dispenser and AIDS care pamphlet.

Measures
Sociodemographic and clinical data were collected with a structured questionnaire. The sociodemographic variables included age, gender, ethnicity, marital status, employment status, educational attainment, number of children, and place of residence. The clinical variables included years since HIV diagnosis, on ART (yes/no), duration (years) of ART, the latest CD4+ T cell count, and comorbidities. Among these clinical variables, the latest CD4+ T cell count, years since HIV diagnosis, morbidities, and duration of ART were verified by the clinical nurses through the patients' medical records.

Twenty-seven HIV/AIDS-related symptoms were measured by a self-reported symptom checklist. Before conducting this study, our team reviewed eight HIV-specific symptom checklists such as the Self-Completed HIV Symptom Index (Justice Scale), the HIV Assessment Tool, the revised Sign and Symptom Check-List for HIV (SSC-HIVrev), and the Riverside Symptom Checklist. Based on the previous studies we have conducted, we decided to create our own measure by choosing 20 highly prevalent HIV-specific symptoms from the Self-Completed HIV Symptom Index (Justice Scale).[17] However, among 20 included symptoms, we believed that depression and anxiety could not be assessed by only one item. Therefore, we used well-validated tools including the Chinese version of the Patient Health Questionnaire-2[18] and the Chinese version of the Generalized Anxiety Disorder 2-Item Questionnaire[19] to assess self-report depression and anxiety. Because of a large proportion of HIV population being over 45 years old in China, many PLWH reported having cognitive impairments that were related to HIV. However, previous

symptom checklists fail to detect changes in PLWHs' cognitive ability. Therefore, we included five items from the cognition-related domain of the AIDS Health Assessment Questionnaire[20] to assess self-reported cognitive ability.

The checklist was translated into Chinese by two research members who had extensive expertise in AIDS care and their mother tongue was Chinese. Conflicts regarding language expressions of the items were solved through discussion. The translated version was modified based on the input from the members of the expert committee from five sites. The content validity was identified by four experts in our expert committee who had enough expertise in AIDS care. The internal consistency of the final version checklist was tested in a pilot study with a sample of 90 PLWH in Shanghai. The content validity index for the whole checklist was 0.918. This checklist had good internal consistency, with a Cronbach's alpha of 0.916 in this sample.

This symptom checklist contains 27 items specific to the severity of HIV/AIDS-related symptoms, with a higher score indicating a higher level of symptom severity. Participants were asked to indicate their responses by answering on a four-point scale. This scale described symptom severity in the past four weeks, with responses ranging from not at all (0) to severe (3). Symptom severity was determined by summing the scores of all items (the final scores ranged from 0 to 81).

Data Analysis

Statistical analyses were conducted using SPSS 22 for Windows (IBM, Armonk, NY). We used frequencies, percentages, means, and SDs to describe the demographic variables and symptom severity.

To detect symptom clusters among the 27 HIV/AIDS-related symptoms, principal component analysis (PCA) was conducted to identify the dimensions of the symptoms (severity score) via R. Kaiser-Meyer-Olkin test was performed to analyze the suitability of our data for factor analysis. The number of factors was determined using a scree plot in the factor analysis. Orthogonal transformation (varimax rotation) was used in the PCA. Factors with Eigen values greater than 1.0 were included.[21] The number of factors was confirmed with Horn's parallel analysis.[22] Symptoms with factor loadings greater than 0.45 were included in clusters. We used Cronbach's α coefficient to assess the internal consistency and reliability of the derived factors. A discussion was held among the research team members to ensure the clinical relevance of the derived symptom clusters.

An association network was performed to describe the relationships among symptoms and clusters via the R package, *qgraph*.[23] In the symptom network, Spearman correlations estimated the relationships between pairs of symptoms (severity score) and symptom clusters (standardized severity score). The edges represented the conditional independent relationships among nodes. The thickness of the edges represented the magnitude of the association. This network was weighted and undirected. By implementing the Fruchterman-Reingold algorithm, the nodes with the strongest correlations were placed in the center of the network. Nodes in the same factor had stronger spearman correlations and were placed more closely.[24,25] Owing to using orthogonal transformation in principal component analysis which may minimize the impact of individual items, we included all symptom clusters and individual symptoms in the network analysis to detect centrality indices.

We used three centrality indices, namely, strength, closeness, and betweenness, to identify the most central symptoms and symptom clusters. Strength represented the absolute sum of the correlation coefficients of the edges connected to the edges. This means the probability that activation of a certain symptom would co-occur with other symptoms. Closeness represented the distance of a certain node to all other linked nodes. The shorter weighted path indicates a larger value of closeness. Betweenness represented the number of times that a node was placed on the shortest path between two nodes. Symptoms that serve as bridges between two symptoms have high betweenness centrality.

This study used exploratory multiple linear models to investigate factors associated with the severity of overall symptoms and five symptom clusters among PLWH. The model included the following demographic and clinical variables: gender (male = 0, female = 1), age, ethnicity (Han = 0, minority = 1), educational attainment (high school or above = 0, otherwise = 1), religion (no religion = 0, otherwise = 1), place of residence (urban = 0, rural = 1), employment status (employed = 0, otherwise = 1), marital status (single = 0, otherwise = 1), primary caregiver during ART treatment (patient = 0, otherwise = 1), years since HIV diagnosis, duration of ART (years), comorbidity (no = 0, yes = 1), CD4 count, self-rated health (1 = very bad to 5 = very good), QOL (1 = very bad to 5 = very good). A two-tailed *P* value less than 0.05 indicated statistical significance in all analyses.

Results

The full sample included 1116 PLWH aged 18 years and older. The characteristics of the patients are shown in Table 1. The majority of participants were

Table 1
Participant Characteristics (N = 1116)

Characteristics	n (%), M (Q25, Q75)
Age	40.0 (32.0, 50.0)
Gender	
Male	804 (72.04)
Female	312 (27.96)
Race/ethnicity	
Han	888 (79.57)
Minority	228 (20.43)
Education level	
Middle school or below	586 (52.51)
High school or equivalent	220 (19.71)
Post grad or equivalent	279 (25.00)
Master's or above	31 (2.78)
Having religion	118 (10.57)
Region	
Urban	855 (76.61)
Rural	261 (23.39)
Employment	
Employed	494 (44.27)
Otherwise	622 (55.73)
Marital status	
Single	381 (34.14)
Married	544 (48.75)
Otherwise	191 (17.11)
Primary caregiver	
Myself	436 (39.07)
Family members (spouse, parents, kids, or other relatives)	624 (55.91)
Otherwise	56 (5.02)
Years of HIV diagnosis	3.0 (1.0, 6.0)
<1 yrs	414 (37.10)
1−3 yrs	214 (19.18)
3−5 yrs	186 (16.67)
>5 yrs	302 (27.06)
Years of ART use	2.0 (0.5, 5.0)
<1 yrs	512 (45.88)
1−3 yrs	235 (21.06)
3−5 yrs	157 (14.07)
>5 yrs	212 (18.90)
Having comorbidities	
Yes	442 (39.61)
No	674 (60.39)
CD4+ T cell count[a]	312 (135, 483)
<50	112 (10.04)
50−350	449 (40.23)
350−500	202 (18.10)
>500	227 (20.34)

ART = antiretroviral therapy.
[a]Due to missing data, description of CD4+ T cell count was based on data from 990 participants.

male (72.04%), Han Chinese (79.57%), married (48.75%), and urban residents (76.61%). The median age was 40 years. Among all the PLWH, 52.51% had a middle school education level or less. Over 44% of the PLWH were employed, and approximately 39% of the participants were their own primary caregivers during ART treatment. The participants were diagnosed as HIV positive with a median of three years before the study and had received ART for a median of two years. Nearly 60% of the participants did not have comorbidities (60.39%).

Table 2 shows the frequency and severity of HIV/AIDS-related symptoms among PLWH. The median number of symptoms was nine. The most common symptoms were fatigue (50.27%), sleep disturbance (44.18%), memory loss (39.87%), dizziness (38.08%), and slow reactions (36.02%). The most severe symptom was fatigue (0.75 ± 0.88), followed by sleep disturbance (0.67 ± 0.88), memory loss (0.55 ± 0.78), dizziness (0.51 ± 0.75), and appetite loss (0.50 ± 0.82).

Figure 1 shows the association network and centrality indices among 27 symptoms. The three strongest edges were between "uncontrollable worrying" and "feeling nervous" ($r = 0.77$), "slow reactions" and "difficulty concentrating" ($r = 0.67$), and "becoming confusing" and "having difficulty reasoning" ($r = 0.66$). In the entire network, "feeling nervous" ($r_S = 0.95$, $r_C = 1.30$, $r_B = 10$) was the most central symptom across the three centrality indices, followed by "fatigue" ($r_S = 0.91$, $r_C = 1.26$, $r_B = 4$).

The factor loading of each symptom and final symptom clusters are presented in Table 3. The Kaiser measure of sampling adequacy was high for the PCA (Kaiser-Meyer-Olkin = 0.933). The following five symptom clusters had Eigen values greater than 1.0 and above the intersection of two lines in the parallel analysis: 1) cognitive dysfunction; 2) mood disturbance; 3) wasting syndrome; 4) dizziness/headache; and 5) skin-muscle-joint disorder. Seven symptoms, including fatigue, cough, sleep disturbance, blurry vision, lipodystrophy, decreased sex drive, and hair loss, had low loading on all factors. The most common symptom cluster was wasting syndrome (37.46%), followed by cognitive dysfunction (35.93%), mood disturbance (32.44%), skin-muscle-joint disorder (28.23%), and dizziness/headache (17.47%). The Cronbach's α coefficient values showed acceptable internal consistency among the five derived symptom clusters.

Figure 2 shows the association network and centrality indices among the five symptom clusters and seven symptoms. The three strongest edges were between "mood disturbance" and "cognitive dysfunction" ($r = 0.56$), "wasting syndrome" and "fatigue" ($r = 0.54$), and "wasting syndrome" and "skin-muscle-joint disorder" ($r = 0.51$). In the entire network, "cognitive dysfunction" ($r_S = 0.45$, $r_C = 3.41$, $r_B = 10$) was the most central symptom cluster across the three centrality indices, followed by "mood disturbance" ($r_S = 0.44$, $r_C = 3.27$, $r_B = 8$).

The results of the exploratory multiple linear regression models of overall symptoms and five symptom clusters are shown in Table 4. Participants who were younger ($P < 0.01$), rural residents ($P < 0.01$), unemployed ($P < 0.001$), taken care of by other people ($P < 0.01$), had comorbidities ($P < 0.001$), and had a lower level of CD4 count were more likely to report having a higher level of overall symptom

Variable of Symptom	Number of Participants	Prevalence (%)	Severity (0−6) (Mean ± SD)
Fatigue	561	50.27	0.75 ± 0.88
Sleep disturbance	493	44.18	0.67 ± 0.88
Memory loss	445	39.87	0.55 ± 0.78
Dizziness	425	38.08	0.51 ± 0.75
Slow react	402	36.02	0.46 ± 0.70
Appetite loss	364	32.62	0.50 ± 0.82
Little interest in doing things	364	32.62	0.46 ± 0.75
Feeling down	355	31.81	0.44 ± 0.75
Muscle/joint ache	332	29.75	0.41 ± 0.72
Rash	325	29.12	0.41 ± 0.74
Having difficulty in concentrating	321	28.76	0.37 ± 0.66
Fever	318	28.49	0.48 ± 0.87
Weight loss	316	28.32	0.44 ± 0.81
Cough	310	27.78	0.38 ± 0.70
Hair loss	307	27.51	0.41 ± 0.75
Vision blur	307	27.51	0.39 ± 0.72
Feeling nervous	302	27.06	0.37 ± 0.69
Diarrhea	292	26.16	0.37 ± 0.72
Hand/foot pain	285	25.54	0.35 ± 0.67
Low sex drive	283	25.36	0.41 ± 0.79
Uncontrollable worrying	278	24.91	0.34 ± 0.66
Headache	243	21.77	0.30 ± 0.63
Nausea/vomit	206	18.46	0.26 ± 0.60
Having difficulty in reasoning	190	17.03	0.22 ± 0.54
Becoming confusing	180	16.13	0.22 ± 0.54
Mouth ulcer	175	15.68	0.22 ± 0.58
Lipodystrophy	152	13.62	0.17 ± 0.48

severity. Variables including gender, age, educational attainment, current residence, working status, comorbidities, and CD4 count were associated with the severity of five symptom clusters.

Discussion

This study demonstrated that the most prevalent symptoms in Chinese PLWH were fatigue, sleep disturbance, memory loss, dizziness, and slow reactions. Five symptom clusters were identified, including cognitive dysfunction, mood disturbance, wasting syndrome, dizziness/headache, and skin-muscle-joint disorder. In the entire symptom network, cognitive dysfunction was the most central symptom cluster across the three centrality indices (strength, closeness, and betweenness). Primary caregivers during ART treatment, having comorbidities, self-rated health, and self-rated QOL, were associated with the prevalence of these five symptom clusters.

Five symptom clusters were derived from the data. Cluster 1 is cognitive dysfunction. Consistent with Namisango's study, we also found that cognitive dysfunction was a crucial symptom cluster among PLWH and it is the most central symptom cluster across the three centrality indices.[12] Previous studies demonstrated that cognitive impairment was a "whole body" issue, which had a strong relationship with viral activity and inflammation.[26,27] The extent of cognitive impairment was also associated with the scale of long-term

HIV replication, which caused significant comorbidity and mortality and ultimately led to the prevalence of other symptoms.[28] Thus, the evaluation and treatment of cognitive dysfunction should be considered a crucial component of HIV care and support.

In addition, PLWH living in rural China were more likely to report having cognitive dysfunction. Cognitive dysfunction has strong associations with the self-rated health and QOL of PLWH. In our study, the average age of PLWH was higher in rural areas than in urban areas. This is mainly due to internal migration, which leads to the migration of young people from rural areas to urban areas. AIDS care services in rural areas should be prepared to manage an aging population and other demographic challenges. In the future, PLWH will face more challenges associated with cognitive problems because of population aging and long-term HIV infection as these people grow older.[29,30]

Cluster 2 was mood disturbance, which showed an overlap between depression and anxiety among PLWH. In this study population, depression was more prevalent among PLWH than anxiety, which was consistent with the findings of previous studies.[31,32] Our study also showed that younger PLWH were more likely to report having this cluster of symptoms. This finding is consistent with the results of the National Comorbidity Survey Replication in the U.S. that showed that the younger cohort of PLWH has a higher rate of current and lifetime depression
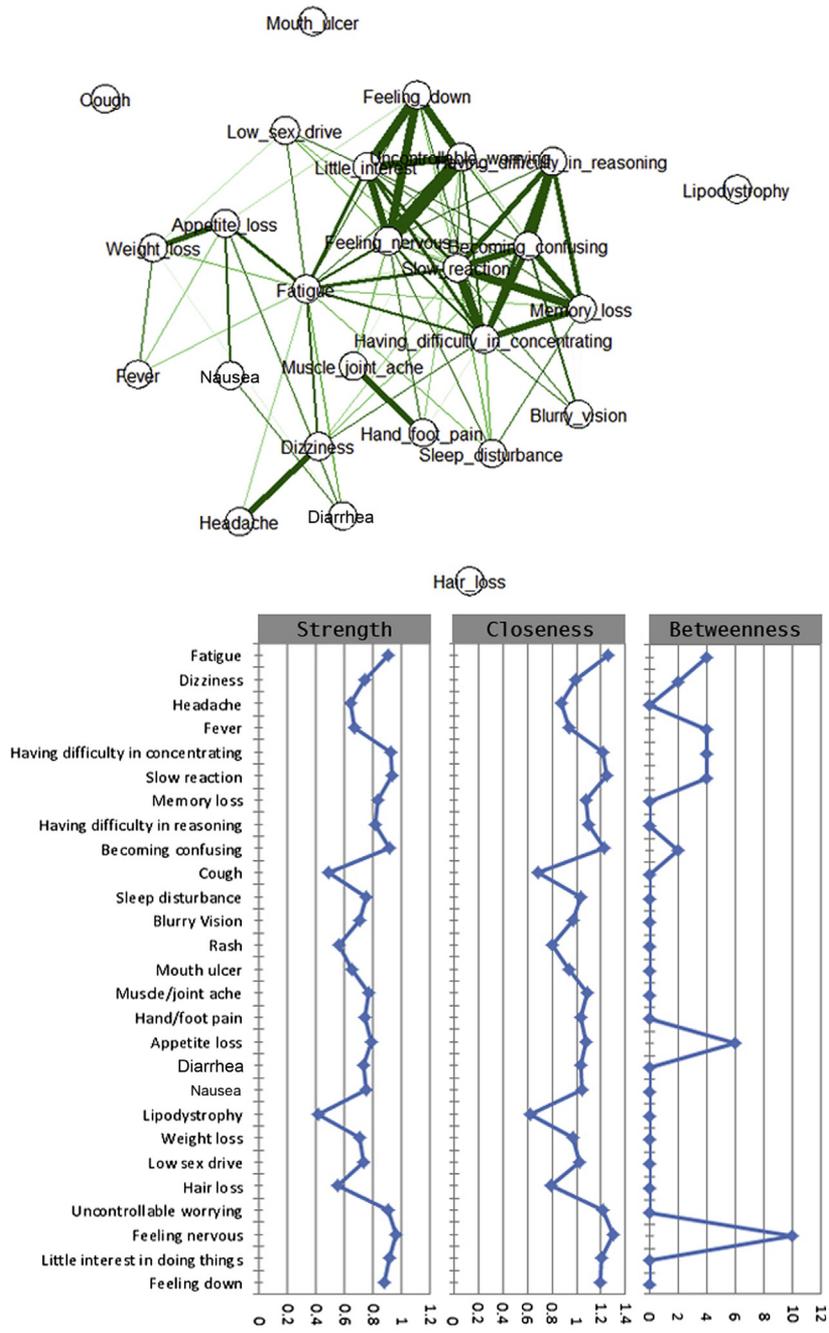
Fig. 1. Network of symptoms and centrality indices.

than their older counterparts.[33] In addition, similar to cognitive dysfunction, we found high coefficients of the three centrality indices in mood disturbance among all included symptoms. Mood disturbance, especially depression and anxiety, was related to a broad range of symptoms, such as insomnia, lack of motivation, pain, and cognitive problems.[34,35] Physical symptoms caused by either depression or comorbidity can trigger or worsen depression. These changes may lead to the deterioration of health conditions resulting in both somatic and psychological symptoms.[36]

Cluster 3 was wasting syndrome, which showed an overlap among fever, appetite loss, diarrhea, nausea/vomiting, and weight loss. Inconsistent with previous studies sharing a GI symptom cluster,[11−14] we found that fever and weight loss were also included in this cluster. We labeled this cluster as "wasting syndrome" because participants who were younger, had a longer duration of HIV diagnosis, and had a lower level of CD4 count were more likely to report having a co-occurrence of these symptoms. This cluster may be associated with inflammation. A previous study

Table 3
Summary of Cluster Symptoms (N = 1116)

| Cluster	Cluster Composition	Factor Loading	Number of Participants (%)	Cronbach's Alpha
Cognitive dysfunction	Having difficulty in concentrating	0.724	401 (35.93)	0.855
	Slow reaction	0.758		
	Memory loss	0.732		
	Having difficulty in reasoning	0.699		
	Becoming confusing	0.723		
Mood disturbance	Uncontrollable worrying	0.800	362 (32.44)	0.872
	Feeling nervous	0.797		
	Little interest in doing things	0.710		
	Feeling down	0.742		
Wasting syndrome	Fever	0.536	418 (37.46)	0.747
	Appetite loss	0.724		
	Diarrhea	0.502		
	Nausea/vomit	0.470		
	Weight loss	0.771		
Dizziness/headache	Dizziness	0.732	195 (17.47)	0.690
	Headache	0.807		
Skin-muscle-joint disorder	Rash	0.500	315 (28.23)	0.637
	Muscle/joint ache	0.453		
	Hand/foot pain	0.628		
	Mouth ulcer	0.625		
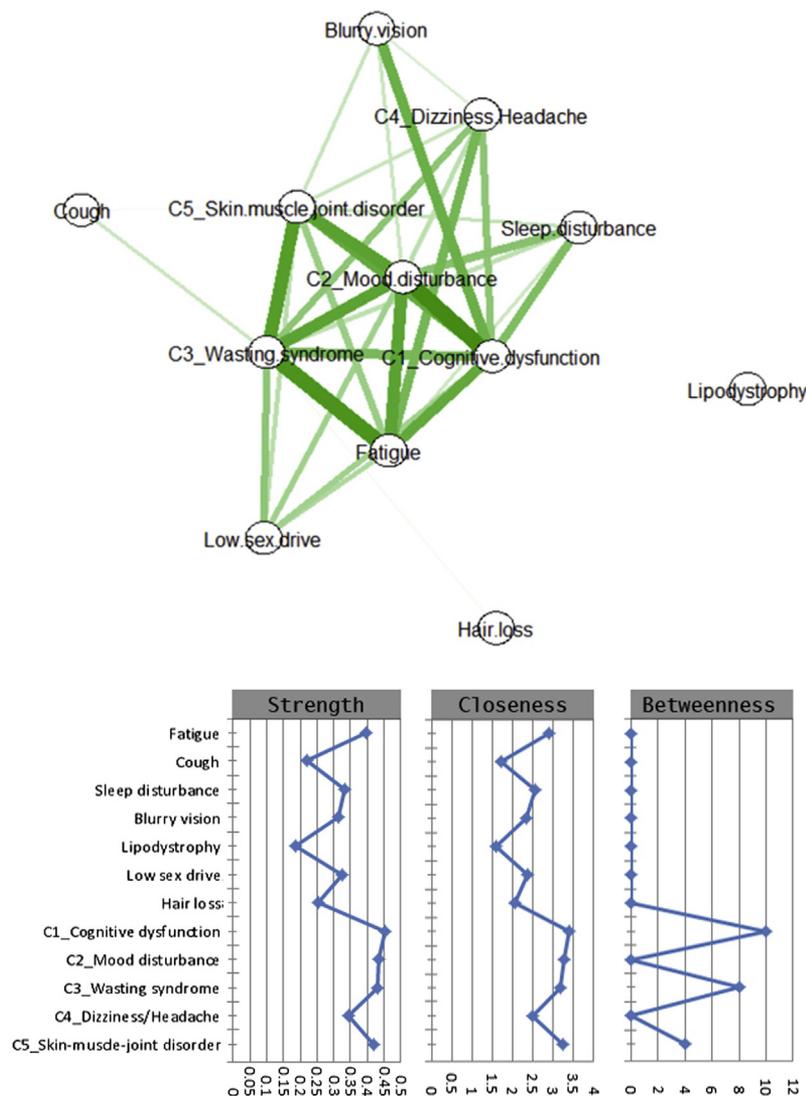
Fig. 2. Network of symptoms and symptom clusters, and centrality indices.

Table 4
Multiple Linear Regression of Five Symptom Clusters ($N = 1116$)

Variable	Model 1 Overall	Model 2 Cognitive Dysfunction	Model 3 Mood Disturbance	Model 4 Wasting Syndrome	Model 5 Dizziness/Headache Cluster	Model 6 Skin-Muscle-Joint Disorder
Male (compared to female)	0.060	0.071[a]	0.050	0.019	0.072[a]	0.003
Age	−0.114[b]	−0.042	−0.116[b]	−0.131[c]	−0.035	−0.084[a]
Han ethnicity (compared to minority)	0.028	0.021	0.057	−0.029	0.042	0.041
High school or above (compared to middle school or less)	−0.055	−0.012	−0.029	−0.102[b]	−0.039	−0.084[a]
Having religion (compared to having no religion)	0.040	0.038	0.049	0.027	0.034	0.026
Living in urban (compared to living in rural)	0.085[b]	0.146[c]	0.097[b]	0.006	0.028	0.075[a]
Employed (compared to otherwise)	0.199[c]	0.116[c]	0.146[c]	0.194[c]	0.122[c]	0.145[c]
Marital status: single (compare to otherwise)	−0.058	−0.053	−0.040	−0.040	−0.076	−0.009
Primary caregiver during treatment: myself (compared to otherwise)	0.083[b]	0.054	0.011	0.112[c]	0.086[b]	0.048
Years of HIV diagnosis	0.075	0.094	−0.030	0.102[a]	0.029	0.040
Years of having ART	0.008	0.003	0.025	−0.084	−0.017	0.041
Having comorbidity (compared to having no comorbidity)	−0.154[c]	−0.145[c]	−0.116[c]	−0.088[b]	−0.079[a]	−0.131[c]
Lg (CD4 count)[d]	−0.102[b]	0.005	0.003	−0.197[c]	−0.068	−0.085[a]

ART = antiretroviral therapy.
Model 1: $F = 11.446$, $P = 0.000$, $R^2_{adj} = 0.121$; Model 2: $F = 6.699$, $P = 0.000$, $R^2_{adj} = 0.070$; Model 3: $F = 5.091$, $P = 0.000$, $R^2_{adj} = 0.051$; Model 4: $F = 14.213$, $P = 0.000$, $R^2_{adj} = 0.148$; Model 5: $F = 4.758$, $P = 0.000$, $R^2_{adj} = 0.047$; Model 6: $F = 7.362$, $P = 0.000$, $R^2_{adj} = 0.077$.
[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.001$.
[d]Due to missing data, description of CD4+ T cell count was based on data from 990 participants.

showed that the level of inflammation in the HIV-positive population was associated with age, duration of HIV diagnosis, and type of ART.[37] Inflammation in patients with chronic HIV infection may lead to wasting syndrome, especially in the advanced HIV stage.[38] Effective ART can control the chronic inflammatory process. Thus, initiating ART as early as possible and having high medication adherence are important to control wasting syndrome.

Cluster 4 is a dizziness/headache cluster. Symptoms of dizziness and headache have been shown to be highly prevalent in previous studies.[11,12] Our results were consistent with the findings from these studies. We also found that after controlling for self-rated health condition, PLWH caring for themselves was a protective factor against having this symptom cluster. People who are able to manage their own health care usually have a high level of ability to relieve less distressing symptoms, including headache, dizziness, weight loss, and rash, by themselves.[39] Therefore, clinical nurses need to work with PLWH and enhance their self-care capacity to help them alleviate these symptoms more effectively.

Cluster 5 is a skin-muscle-joint disorder. The participants in our study had a relatively lower prevalence of muscle/joint aches compared to the results of Wilson's study (28% vs. 48%).[11] Many studies conducted in the U.S. and African countries also found a high prevalence of muscle/joint aches among PLWH.[40−42]

It is noteworthy that a study conducted among 176 Chinese individuals in Taiwan showed that 35% of PLWH reported having muscle aches and joint aches.[43] Previous studies have already shown that racial differences in symptom experiences are crucial.[15,16] Further studies are warranted to examine whether the difference in the prevalence of muscle/joint aches was caused by race.

Limitation
Although this is the first study to explore the symptom clusters among PLWH in China and had adequate statistical power to identify the relevant clusters, there were some limitations. First, this study only included 27 HIV/AIDS-related symptoms based on three full-scale measurements and one subdomain of a QOL scale. These symptoms were selected according to the ranking of the prevalence of symptoms in previous studies. Other symptoms that are potentially associated with medication side effects and comorbidities were not included in our study. We used only one item to represent each of the self-reported physical symptoms that could affect the reliability of the findings. Second, we used convenience sampling at five hospital sites. Our findings cannot be generalized to the entire Chinese population. Third, information about the type of comorbidities was not collected. In addition, we only included PLWH who were able to complete

the questionnaires by themselves. Therefore, the level of cognitive status in this sample was relatively high. Our study may have underestimated the degree of the relationship between cognitive dysfunction and other clusters.

Conclusion

Our study generated new knowledge of symptom clusters among PLWH in China by identifying five symptom clusters, including cognition dysfunction, mood disturbance, wasting syndrome, dizziness/headache, and skin-muscle-joint disorder. Cognitive dysfunction was the most central symptom cluster. Our study suggests that there is a need to evaluate symptom clusters for the improvement of symptom management among PLWH. It is particularly important to include assessment and treatment of cognitive symptoms as an essential component of the HIV care.

Disclosures and Acknowledgments

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