

Symptom Burden and Quality of Life in Patients with Chronic Obstructive Pulmonary Disease

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DOI: <https://doi.org/10.5281/zenodo.6640942>

Published Date: 14-June-2022

Abstract: Background: Chronic Obstructive Pulmonary Disease (COPD) with highly prevalence, disability, and mortality was a common health problem worldwide. And the COPD patients experienced seriously symptom and disease burden, as well as poor health-related quality of life (HQOL). The aims of this study were to describe the prevalence of symptoms, symptom burden and HQOL, and examine the relationship between the symptom burden and HQOL.

Methods: 197 hospitalized patients with COPD (mean (SD) age 68.12 (10.41) years) were recruited between December 2016 and November 2017. The symptom was assessed using the Memorial Symptom Assessment Scale (MSAS), including four subscales: the psychological (MSAS-PSYCH) subscale, the physiological (MSAS-PHYS), the global distress index (MSAS-GDI), and the MSAS total score (TMSAS). The HQOL was evaluated by Chinese version of the Clinical COPD Questionnaire (CCQ).

Results: The patients reported multiple symptoms with a median number of 7.00. The commonly reported symptoms were dry mouth, cough, shortness of breath, and lack of energy, and the psychological symptom included difficulty sleeping, worrying, feeling sad, feeling irritable, difficulty concentrating, and feeling nervous. The medians for the MSAS- PSYCH, MSAS-PHYS, MSAS-GDI, and TMSAS were 0.44, 0.47, 0.60, and 0.41, respectively. And the CCQ had moderate score. There were association between impaired quality of life and symptom burden (number of MSAS symptoms, MSAS-PHYS, MSAS-PSYCH, MSAS-GDI, the TMSAS) ($P < 0.001$).

Conclusions: The overall moderate symptom burden and poor HQOL suggests that detailed multidimensional symptom assessments are warranted in the care of COPD inpatients, with the purpose of focusing on severe and distressing symptoms in order to improve symptom management and reduce symptom burden progression.

Keywords: Chronic Obstructive Pulmonary Disease; symptom; symptom burden, quality of life.

1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), a common health problem worldwide, is a progressive illness with highly prevalent, disability, and mortality. According to the World Health Organization, 251 million cases experienced COPD in 2016, and about 3.17 million people died of COPD in 2015, which is approximately 5% of all deaths globally (<http://www.who.int/mediacentre/factsheets/fs315/en/>, Accessed April 02, 2018)¹. In China, the prevalence of COPD was 8.2% (male, 12.4%; female, 5.1%) in individuals 40 years of age or older¹.

Symptom was defined as a subjective perception of changes in biopsychosocial functioning, sensations, or cognition^{2,3}. The symptom experience of COPD patients was extremely complex, which was multidimensional including the dimensions frequency, severity and distress that can be assessed separately or in combination⁴. Previous studies have described multiple co-occurring symptoms in COPD patients⁵⁻⁹, however, rarely studies reported that among the Chinese COPD patients¹⁰. On average, COPD patients experienced between seven and eighteen co-occurring symptoms^{5,10,11}. The commonly reported symptoms included shortness of breath/ dyspnea, cough, sputum product, fatigue/ lack of energy and so on⁹⁻¹².

Symptom burden was defined as the mean number of symptoms per patient and a composite of symptom frequency, severity and distress¹³, and it related with physical, psychological, social functioning, and decreased health-related quality of life (HQOL)¹¹. The goal of symptom management was to reduce frequency, minimize severity, and relieve distress (<http://education.goldcopd.org/>, Accessed January 02, 2017). As COPD was incurable, symptom control was necessary for improving patients' HQOL¹⁴, and nurses played a key role in symptom management since they were involved in all stages of care¹⁵. In addition, the previous studies that researched HQOL in COPD patients focused only on the association of HQOL with symptoms^{16,17}. Therefore, the aim of this study was to describe the symptom burden and HQOL in COPD admitted patients and examine the relationship between the symptom burden and HQOL.

2. METHODS

2.1 Design

This study design was a cross-sectional by using a questionnaire. The study was approved by the the Research Ethics Committee of Nursing Scholl, Jilin University.

2.2 Sample and setting

Hospitalized patients with COPD who visited the pulmonary department at two university – affiliated - hospitals in Changchun, China between December 2017 and November 2018. Inclusion criteria for this study were (1) the patients had been diagnosed with COPD; (2) the patients were aged ≥ 40 years. Exclusion criteria were (1) patients lack of capacity to give informed consent; (2) patients with cognitive impairment; and (3) patients had a past history of other major health issues that could influence the symptoms and HQOL, such as active cancer and/or chronic renal disease. All patients were provided for informed consent before participation. Ethical approval and permissions were also obtained in the selected hospitals in this study. For the purposes of this study, 312 patients met the included criteria, 220 agreed to enter the study, finally 197 effective questionnaires were recovered.

3. MEASURES

3.1 Demographic and clinical characteristics

Demographic and clinical characteristics consisted of eight items: age; gender; Body Mass Index (BMI); marital status (married/cohabitant, widowed, and unknown); employed (working / retired); smoking status (current smoker, former smoker, and never smoker); disease duration; self-reported coexisting diseases (hypertension, heart disease, metabolic disease, and others).

3.2 Charlson Comorbidity Index

Based on the information from the medical records, the Charlson Comorbidity Index was used to characterize the degree the comorbid factors¹⁸. 19 categories of comorbid conditions were enrolled in the Charlson Comorbidity Index. Each category is weighted based on estimated risk for one-year mortality, and the overall Charlson score reflects the cumulative likelihood of one-year mortality. Charlson scores range between 0 and 35, and higher scores indicate greater comorbid burden.

3.3 Symptoms

The Memorial Symptom Assessment Scale (MSAS), originally designed to evaluate the symptom among the patients with cancer, was applied to measure the prevalence (yes or no) of 32 common symptoms (26 physical and 6 psychological) during the past week¹⁹. If the patients experienced the symptom, they would be asked to rate its severity, frequency, and

distress. The score of each symptom was calculated by averaging the scores on frequency, severity, and distress scales. If the symptom was absent, each dimension was scored as 0 and the score of this symptom was 0. Due to the hair loss is not associated with COPD, the “hair loss” is replaced with “weight gain” in this study^{5, 20}.

The MSAS had four subscales: the psychological (MSAS-PSYCH) subscale, the physiological (MSAS-PHYS), the global distress index (MSAS-GDI), and the MSAS total score (TMSAS). The MSAS-PSYCH was the average symptom score of worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating. The MSAS-PHYS was the average symptom score of lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness. The MSAS-GDI was the average of the frequency of feeling sad, worrying, irritable, feeling nervous, and the distress scores of lack of appetite, lack of energy, pain, feeling drowsy, constipation and dry mouth. The TMSAS was the average of all 32 symptoms with a range of 0 - 4¹⁹.

The Cronbach's alpha coefficient in this study was as follows: MSAS-PHYS, 0.679; MSAS-PHYS, 0.603; MSAS-GDI, 0.625; TMSAS, 0.730.

3.4 Health-related quality of life

Chinese version of the Clinical COPD Questionnaire (CCQ)²¹, which consists of 10 items and 3 domains (Symptom [4 items], Functional state [4 items] and Mental state [2 items]), was used to evaluate the health-related quality of life among the patients with COPD in the past week. Symptoms included dyspnea, cough, and phlegm; function state refers to the limitations in different activities of daily life due to the lung disease; mental state was the questions about feeling depressed and concerns about breathing. All scores range from 0 to 6, and the score was calculated as the mean of the sum of all items, with a higher score indicating lower health status. The Cronbach's alpha coefficient in this study was as follows: Symptom, 0.538; Functional state, 0.871; Mental state, 0.886; total CCQ, 0.825.

3.5 Data analysis

Data were analyzed using SPSS version 22.0 (IBM SPSS Statistics, SPSS, Chicago, Illinois). Categorical variables were described by frequency (percent), normal distributed variable by mean \pm standard deviation (SD), and skewed variables by median (minimum, maximum). Although the MSAS scores tend to be skewed, they were presented as mean \pm SD for the sake of historical comparison.

The HQOL score was the primary outcome for univariate correlation and for multivariate regression analyses. Pearson correlations were first calculated between the HQOL and all other measures. Categorical variables were coded to facilitate the calculation of correlations. Based on these univariate correlations, a potential pool of predictors was selected for multivariate regression analyses, with the HQOL score as the dependent variable. Several multiple regression models with stepwise entry were first analyzed to select the best set of nonredundant variables for predicting the HQOL score. All measures showing a correlation with $P < 0.05$ with HQOL score were included for multivariate modeling. Interim stepwise analyses were done on subscales from the same measure to minimize the number of predictors entering the final multivariate model. A 2-tailed $P < 0.05$ is considered statistically significant.

4. RESULTS

4.1 Patient characteristics

One hundred and ninety-seven COPD patients were enrolled in the study. The demographics and baseline characteristics of the population studied were presented in Table 1. Of those 197 participants, 53.30% were male, and 46.70% were female, with a mean age of 68.12 (± 10.41) years for the patients. The disease duration median was 6 years. The majority (75.13%) of patients were married or cohabitating. In addition, 88.32% were retired, and 26.90% of the patients were still smoking, 37.06% had stopped smoking. The mean BMI (kg/m^2) was 22.13 (± 4.11). There were relatively low levels of comorbidity (Charlson Comorbidity Index median = 2). The commonly comorbid conditions were hypertension, heart disease and metabolic disease.

Table 1: Demographics and Related Characteristics (N = 197)

Demographic characteristics	Number	Percentage
Age (years) (mean ± SD)	197	68.12 ± 10.41
Gender		
Male	105	53.30
Female	92	46.70
Marital status		
Married/cohabitant	148	75.13
Widowed	43	21.83
Unknown	6	3.05
Employed		
Working	23	11.68
Retired	174	88.32
Smoking status		
Current smoker	53	26.90
Former smoker	73	37.06
Never smoker	71	36.04
BMI (kg/m ²) (mean ± SD)	197	22.13 ± 4.11
Disease duration (years) (median [min, max])	197	6.00 (0, 66.00)
Charlson Comorbidity Index (median [min, max])	197	2.00 (1.00, 6.00)
Self-reported coexisting diseases		
Hypertension	41	20.81
Heart disease	59	29.95
Metabolic disease	24	12.18
Others	46	23.35

Abbreviations: BMI: Body Mass Index

4.2 Symptom Prevalence and Characteristics

The patients reported multiple symptoms with a median number of 7.00 (rang, 0 – 19) for the total patients. Table 2 displayed symptom prevalence and the percentage of patients reporting higher scores (3 or 4 on a scale of 0 – 4) for frequency, severity, and degree of distress. The highly prevalent symptoms ($\geq 50\%$ of the total patients) were dry mouth (80.20%), cough (79.19%), shortness of breath (67.51%), and lack of energy (54.82%). Four additional physical symptoms, feeling drowsy, pain, lack of appetite, and sweat, were reported by between 25% and 50% of the patients. The most commonly reported psychological symptom were difficulty sleeping (49.75%), followed by worrying (30.96%), feeling sad (27.41%), feeling irritable (26.90%), difficulty concentrating (25.38%), and feeling nervous (25.38%). The MSAS also evaluated the frequency, severity, and distress of the symptoms, which given a comprehensive picture of symptom burden. More than half patients rated dry mouth and shortness of breath as being particularly distressful during they stayed in hospital.

Table 2: Prevalence and Characteristics of Symptoms and Total MSAS Score (N=197)

Symptoms	Prevalence Number (%)	Frequency a Number (%)	Severity b Number (%)	Distress c Number (%)	MSAS Score d Mean ± SD
Dry mouth	158 (80.20)	72.78	67.09	57.59	2.16 ± 1.36
Cough	156 (79.19)	12.82	11.54	7.05	1.39 ± 0.88
Shortness of breath	133 (67.51)	18.80	15.04	53.38	1.29 ± 0.98
Lack of energy	108 (54.82)	24.07	16.67	52.78	1.09 ± 1.06
Difficulty sleeping	98 (49.75)	72.44	63.27	54.08	1.36 ± 1.45
Feeling drowsy	83 (42.13)	30.12	24.10	10.84	0.91 ± 1.15
Pain	70 (35.53)	41.43	38.57	27.14	0.79 ± 1.16
Lack of appetite	70 (35.53)	27.14	22.86	70.00	0.74 ± 1.03
Sweats	61 (30.96)	27.87	14.75	63.93	0.62 ± 0.96
Worrying	61 (30.96)	24.59	16.39	11.46	0.61 ± 0.96
Feeling sad	54 (27.41)	9.26	7.41	27.78	0.47 ± 0.80

Feeling irritable	53 (26.90)	13.21	3.77	13.21	0.51 ± 0.87
Difficulty concentrating	50 (25.38)	24.00	58.00	30.00	0.40 ± 0.80
Feeling nervous	50 (25.38)	22.00	22.00	22.00	0.48 ± 0.88
Weight loss	37 (18.78)	NE	2.70	0.00	0.18 ± 0.41
Numbness/tingling in hands/feet	34 (17.26)	20.59	14.71	11.76	0.34 ± 0.79
Itching	32 (16.24)	21.88	6.25	56.25	0.30 ± 0.72
Feeling boated	27 (18.78)	37.04	33.33	33.33	0.32 ± 0.81
Problems with urination	23 (11.68)	47.83	47.83	34.78	0.30 ± 0.87
Change in the way food tastes	16 (8.12)	NE	31.25	62.50	0.16 ± 0.57
Dizziness	9 (4.57)	0	0.00	33.33	0.08 ± 0.36
Nausea	7 (3.55)	28.57	14.29	57.14	0.06 ± 0.36
Weight gain	7 (3.55)	NE	0.00	0.00	0.03 ± 0.19
Mouth sores	5 (2.54)	NE	60.00	0.00	0.05 ± 0.34
“I don’t look like myself”	4 (2.03)	NE	25.00	25.00	0.04 ± 0.25
Problems with sexual interest or activity	3 (1.52)	0.00	0.00	0.00	0.02 ± 0.21
Difficulty swallowing	3 (1.52)	0.00	0.00	66.67	0.04 ± 0.29
Diarrhea	2 (1.02)	0.00	0.00	0.00	0.02 ± 0.22
Vomiting	1 (0.05)	0.00	0.00	0.00	0.01 ± 0.14
Change in skin	1 (0.05)	NE	0.00	0.00	0.01 ± 0.11
Swelling of arms of legs	0 (0.00)	NE	NE	NE	NE

^a Percentage of patients with symptom describing the frequency of the symptom as “frequently” or “almost constantly.”

^b Percentage of patients with symptom describing the severity of the symptoms as “severe” or “very severe.”

^c Percentage of patients with symptom describing the distress associated with the symptom as “quite a bit” or “very much.”

^d Mean ± SD provided for historical comparison. MSAS score ranges from 0 to 4.

4.3 MSAS subscales scores and health-related quality of life

The symptom rated with the highest MSAS symptom burden score, mean (± SD), in the patients was dry mouth 2.16 (± 1.36), followed by cough 1.39 (± 0.88), difficulty sleeping 1.36 (± 1.45), shortness of breath 1.29 (± 0.98), and lack of energy 1.09 (± 1.06). The MSAS symptom burden scores were listed in Table 2. And the MSAS subscales were displayed in Table 3. The scores varied from 0 to 4. The medians (min, max) for the MSAS- PSYCH, MSAS-PHYS, MSAS-GDI, and TMSAS were 0.44 (0, 2.78), 0.47 (0, 1.32), 0.60 (0, 4.00), and 0.41 (0, 1.28), respectively. The medians (min, max) for the total CCQ, symptom, functional state, and mental state were 2.60 (1.10, 4.90), 3.25 (1.25, 5.00), 2.50 (0.50, 5.75), and 2.00 (0.00, 4.50), respectively.

Table 3: the MSAS subscales scores and health-related quality of life scores (N = 197)

	Median	(min, max)	Possible range
MSAS Subscales			
MSAS-PSYCH	0.44	(0.00, 2.78)	0 - 4
MSAS-PHYS	0.47	(0.00, 1.32)	0 - 4
MSAS-GDI	0.60	(0.00, 4.00)	0 - 4
TMSAS	0.41	(0.00, 1.28)	0 - 4
QOL			
Total CCQ	2.60	(1.10, 4.90)	0 - 6
Symptom	3.25	(1.25, 5.00)	0 - 6
Functional state	2.50	(0.50, 5.75)	0 - 6
Mental state	2.00	(0.00, 4.50)	0 - 6

Abbreviation: MSAS-PHYS: The overall physical symptom score, MSAS-PSYCH: Psychological Symptom score, MSAS-GDI: The Global distress index, TMSAS: Total MSAS index score. QOL: health-related quality of life

4.4 Health-related quality of life: Univariate Relationships

Health-related quality of life, measured by the CCQ score, showed a strong association with all indices of symptom burden (Table 4). The strongest association between global symptom burden and impaired quality of life was seen with the TMSAS ($r = 0.603, P < 0.001$), followed by number of MSAS symptoms ($r = 0.584, P < 0.001$), MSAS-GDI ($r = 0.574, P < 0.001$), MSAS-PSYCH ($r = 0.481, P < 0.001$), and MSAS-PHYS ($r = 0.453, P < 0.001$). The age, smoking status, disease duration, and the Charlson Comorbidity Index were significantly related to health-related quality of life. No association with HQOL was observed with any of the other baseline patient characteristics, including gender, marital status, employed, and BMI.

Table 4: Univariate Correlations with health-related quality of life Score

Measures	Total CCQ	
	Correlation r	P-value
Age	0.326	< 0.001
Gender	0.000	0.998
Marital status	0.150	0.073
Employed	0.075	0.369
Smoking status	0.212	0.011
Disease duration (years)	0.231	0.005
BMI (kg/m ²)	-0.070	0.404
Charlson Comorbidity Index	0.191	0.022
Number of MSAS symptoms	0.584	< 0.001
MSAS-PSYCH	0.481	< 0.001
MSAS-PHYS	0.453	< 0.001
MSAS-GDI	0.574	< 0.001
TMSAS	0.603	< 0.001

4.5 Health-related quality of life: multivariate Relationships

The results of these interim regressions were entered into a stepwise regression model along with the variables that were significantly associated with the CCQ in univariate analysis (Table 4), specifically TMSAS (model 1). One predictor was selected by model 1 (beta = 0.603, $P < 0.001$). The R^2 for this model was 0.363, indicating that 36.3% of the variance of the CCQ was explained by this predictor (Table 5). TMSAS and age were selected in Model 2: TMSAS (beta = 0.564, $P < 0.001$) and age (beta = 0.234, $P < 0.001$). The R^2 for this model was 0.417, indicating that 41.7% of the CCQ was explained by these two predictors. In the Model 3, TMSAS (beta = 0.540, $P < 0.001$), age (beta = 0.267, $P < 0.001$), and smoking status (beta = 0.203, $P = 0.002$) were selected. The R^2 for this model was 0.457, indicating that 45.7% of the variance of the CCQ was explained by the three predictors selected by Model 3.

Table 5: Factors Associated with Quality of Life: Results of Multivariate Regression Models

Predictor	Regression Coefficients		P-value
	Unstandardized (Beta)	Standardized (Beta)	
Model 1 ($R^2 = 0.363$)			
TMSAS	1.946	0.603	< 0.001
Model 2 ($R^2 = 0.417$)			
TMSAS	1.822	0.564	< 0.001
Age	0.020	0.234	< 0.001
Model 3 ($R^2 = 0.457$)			
TMSAS	1.744	0.540	< 0.001
Age	0.022	0.267	< 0.001
Smoking status	0.201	0.203	0.002

5. DISCUSSION

In this cross-sectional study, the MSAS was used to describe the detailed multidimensional symptom profile in the inpatients with COPD. The participants experienced multiple symptoms, a moderate symptom burden and moderate impairment in overall HQOL.

In this study, the patients reported that they experienced 7.00 symptoms, which were similar to those in previous studies whose participants were mainly outpatients or patients lived at home^{6,10,11,22}. However, some symptoms that often occur in COPD, such as chest tightness, wheezing and sputum production, were not included in the present study. If those symptoms were added to the MSAS instrument, the total symptom prevalence might have been even higher.

The commonly reported physical symptoms included those typical associated with COPD: dry mouth, cough, shortness of breath, lack of energy. These findings are consistent with previous studies of symptom prevalence in COPD^{6,7,10,11,22}. However, the prevalence of psychological symptoms, including difficulty sleeping, worrying, feeling sad, feeling irritable, difficulty concentrating, and feeling nervous, was lower than in earlier studies whose participants were mainly Western COPD patients^{6,7,11,23}. The difference in the prevalence of emotional symptoms may be attributable to cultural differences. In Asian cultures, negative emotions are strongly discouraged and hence suppressed²⁴. Certain psychological symptoms, especially depression, may be expressed differently in Asians than in Westerners. Chinese people reportedly tend to express their depression as physical rather than psychological, differently from Westerners²⁵. Due to the culture different, the Chinese patients reported lower prevalence of sexual problem than the Westerners^{5-7,11}.

In this study, the symptoms that the patients reported highly prevalence, severity, frequency, and distress included dry mouth, cough, shortness of breath, lack of energy, difficulty sleeping, which were similar to those in previous studies^{6,11,22}. Dry mouth was the highest prevalence symptoms in admitted patients, which might be explained by the high use of anticholinergic medication. Dry mouth was a reversible adverse event²⁶. Patients who were suffering from dry mouth tend to change their food consumption behavior to ease their suffering²⁷, which may contribute to the risk of developing malnutrition. In clinical practice, nurses should evaluate this symptom in all patients to prevent the risk of altered food consumption, and should suggest treatment for dry mouth²⁸. Cough was often considered to be the first symptom of COPD (<http://education.goldcopd.org/>, Accessed January 02, 2017), and it was usually described only in prevalence²⁹. Patients with cough had an increased risk of disease progression and exacerbations that might require hospitalization^{29,30}. Patients with COPD should be provided support and knowledge to manage cough, and thereby reduce the symptom burden and avoid exacerbation. Shortness of breath was a “subjective experience of breathing discomfort”³¹, and could be missed by care professionals due to the different barriers to help-seeking behaviors³². In the study by Gysels et al³², patients experienced breathlessness had low access to services due to the nature of the symptom development, patients’ adaptation to restrictions with different activities, reaction from the social environment, and non-response from healthcare services. Lack of energy had a negatively effect on both health and function, leading to limitations in cognitive, physical and psychosocial function, and needed to be prevented in patients with COPD^{12,33}. Compared with general population, patients with airflow limitations were more likely to experience insomnia and difficulty in initiating and maintaining sleep³⁴. However, COPD patients reported that support from healthcare providers was rare concerning sleeping difficulties³⁵. These findings indicated the importance of symptom management in COPD patients. In order to improving management of symptom, it should be practical to start with multidimensional symptom assessment.

The MSAS subscale scores in this study were lower than those in previous studies^{5,6,11,22}. Because the participations in this study included the mild airflow limitation, it was logical that they didn’t report more severe symptom than patients with more advanced COPD. Compared participations in the previous studies, the inpatients in this study had lower health-related quality of life with higher CCQ scores³⁶⁻³⁹, which might be caused by the differences of participations and approach of measure.

The relationship between symptom burden and HQOL was complex. In the study the HQOL was correlated with age, smoking status, disease duration, Charlson Comorbidity Index, number of symptoms, and MSAS subscales. The previous studies presented that age, smoking status, education level, some symptoms (e.g. cough, dyspnea), and number of comorbidities were significantly associated with poor HQOL⁴⁰⁻⁴³. There were some other factors, such as coping or support from family or health professionals that might influence HQOL. A study including 4418 COPD patients suggested that the patients’ ability to cope with dyspnea might attenuate the relationship between symptom severity and patient satisfaction with the primary care provider⁴⁴. Therefore, additional studies are needed to clarify the extent to other factors affected HQOL.

The study had some limitations. First, the results were based on participations’ self-report and could not be independently verified through clinical documentation; thus, their accuracy might be subject to self-report and recall biases. Second, the

MSAS instrument was designed to assess the symptoms in cancer patients¹⁹ and may miss some COPD-related symptoms. Third, the patients included in this study were all recruited from pulmonary departments at two hospitals and might not necessarily be representative sample of all COPD patients, but the results ought to be transferable to patients in a similar context.

6. CONCLUSION

The overall moderate symptom burden and poor HQOL suggests that detailed multidimensional symptom assessments are warranted in the care of COPD inpatients, with the purpose of focusing on severe and distressing symptoms in order to improve symptom management and reduce symptom burden progression. Longitudinal studies are needed to evaluate for changes over time in multidimensional of the symptom experiences and HQOL.

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International Journal of Novel Research in Healthcare and Nursing

 Vol. 9, Issue 2, pp: (59-68), Month: May - August 2022, Available at: www.noveltyjournals.com

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Vol. 9, Issue 2, pp: (59-68), Month: May - August 2022, Available at: www.noveltyjournals.com

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