

Intervention for Symptom Cluster Management of Fatigue, Loss of Appetite, and Anxiety among Patients with Lung Cancer undergoing Chemotherapy

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ABSTRACT

Objective: Patients with lung cancer can experience various distressing symptoms. The present study aims to use symptom cluster management intervention based on symptom management theory to moderate the severity of symptom clusters, including fatigue, loss of appetite, and anxiety, in patients with lung cancer undergoing chemotherapy. **Methods:** A quasi-experimental study was conducted using historical controls to assess and compare the effect of a novel symptom cluster management intervention on the severity of fatigue, loss of appetite, and anxiety in patients with lung cancer undergoing chemotherapy. Lung cancer patients were recruited from an outpatient chemotherapy unit at a university hospital in Thailand. Eighty participants were assigned equally to the experimental and control groups. The study outcomes, including fatigue, loss of appetite, and anxiety, were assessed with the Edmonton Symptom Assessment System at baseline and days 7, 14, and 28 postintervention. Repeated-measures ANOVA was analyzed to determine mean differences between groups across

time. **Results:** Overall, anxiety decreased gradually on days 7, 14, and 28 ($P < 0.001$ for all time points) in the experimental group. Fatigue and loss of appetite also declined after days 14 ($P < 0.001$) and 28 ($P < 0.001$) compared to baseline. The significant effects of the interaction terms time \times group ($P < 0.001$) for all symptoms within the cluster indicate the benefit of the intervention over time. **Conclusions:** The pattern of changes in the symptom cluster across the study period was significantly different between the two study groups. Patients in the experimental group reported an improvement in fatigue, loss of appetite, and anxiety over time after receiving the intervention. The results suggested that the symptom cluster management intervention provided a promising approach for the simultaneous treatment of multiple symptoms within a cluster.

Key words: Anxiety, chemotherapy, fatigue, loss of appetite, lung cancer, symptom cluster, symptom cluster management

Introduction

Lung cancer is one of the most frequently diagnosed cancers and the leading cause of cancer death globally.^[1] Patients with lung cancer usually experience a variety of

distressing symptoms, many of which begin before diagnosis and continue throughout the course of the disease and its

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treatment.^[2,3] Most of these patients also have advanced or metastatic cancer at diagnosis (85%), which further contributes to their high rate of multiple physical and psychological symptoms.^[4] Chemotherapy is the most common treatment option for lung cancer, but it also involves several side effects.^[2,3,5] Both disease-related and treatment-related symptoms may adversely affect the functional status and quality of life (QOL).^[3]

Part of the symptom burden experienced by patients with lung cancer may result from the simultaneous occurrence of symptoms, also known as a “symptom cluster.” A symptom cluster is defined as two or more concurrent symptoms that are related, and they may or may not have a common cause.^[6,7] Studies have found that the number or severity of symptom clusters inversely correlate with patient outcomes such as morbidity, disease prognosis, functional status, QOL, and mortality.^[8-10] Subjective symptoms such as fatigue, loss of appetite, and anxiety are common among all patients with lung cancer.^[2,3,5] Still, they are often underdiagnosed by clinicians, particularly once patients complete each cycle of chemotherapy and are discharged from hospital.^[4] Thus, lung cancer patients have reported high rates of unmet needs for symptom management and psychological support.^[11] It is crucial for clinicians to apply the science of symptom clusters in clinical practice for a more thorough symptom assessment and more efficient symptom management.

A meta-analysis of randomized trials and a Cochrane review of nonpharmacological interventions for lung cancer patients found preliminary evidence that nurse-delivered psycho-educational intervention, skill training, and therapeutic counseling are effective in alleviating significant problems among these patients.^[12,13] However, most trials have excluded advanced lung cancer patients and have rarely obtained the feedback of patients during the research process. In intervention design, eliciting feedback from the participants along with modifying the format or content of the intervention in collaboration with the needs, goals, beliefs, and preferences of participants will help enhance feasibility and decrease retention.^[14]

The present study tested a novel symptom cluster management intervention with advanced symptomatic lung cancer patients undergoing chemotherapy. The intervention is based on the concept of symptom clusters^[15] and symptom management theory (SMT).^[16] SMT is grounded on the interrelatedness of three essential concepts: symptom experience, symptom management strategies, and outcomes [Appendix 1].^[16] The theory highlights the importance of taking the perceptions of the patient into account when studying symptoms. The current study incorporated the concept of symptom clusters into the SMT

to provide an understanding of the symptom experience component; particularly, multiple concurrent symptoms, their implications, and the changes in the symptoms experienced by an individual over time. This new approach combining the concept of symptom clusters and SMT enables researchers and clinicians to guide an individual into finding intervention components that contribute to improvements in patient outcomes.^[17]

In 2011, a study by Chan *et al.*^[18] demonstrated the positive effect of providing an intervention to treat a symptom cluster as a whole. They applied a psychoeducational intervention for the symptom cluster of breathlessness, fatigue, and anxiety in lung cancer patients receiving palliative radiation therapy (RT). Education on symptom management and coaching in progressive muscle relaxation was delivered to patients 1 week before RT initiation and repeated 3 weeks after radiation. The changes in the intensity of the symptom cluster were measured at four time points: before the intervention and 3, 6, and 12 weeks postintervention. Results suggest that the intervention provides a promising approach for the simultaneous treatment of multiple symptoms within a cluster. Several studies also demonstrate improvements in breathlessness, cough, fatigue, pain, depression, and anxiety in symptom clusters among lung cancer patients after treating multiple symptoms simultaneously.^[15,19] However, fewer studies have focused on alleviating fatigue, loss of appetite, and anxiety symptoms.

The symptom cluster management intervention used in the current study consisted of evidence-based cognitive-behavioral strategies to reduce the symptom cluster usually found in patients with lung cancer undergoing chemotherapy and include fatigue, loss of appetite, and anxiety.^[15] The researchers conducted a qualitative study to gain insights and feedback from symptomatic advanced lung cancer patients undergoing chemotherapy at the study site. Then, the intervention protocol was derived from the convergence of findings from the qualitative study.^[20] The protocol was designed to help patients address their symptom, experience and provide education regarding treatment side effects, dietary behavior changes, exercise, relaxation strategies, and emotional support. A specially trained nurse offered interventions during patient visits and phone calls. Each participant received tailored instructions to practice new symptom management skills relevant to their preference. Throughout every session, the nurse emphasized the benefits of practicing the skills and changing maladaptive thoughts. These activities were the key factors underlying behavior changes associated with symptom reduction and improved treatment adherence.

This present study aimed to examine the effect of the symptom cluster management intervention based on SMT

on the severity of symptom clusters, including fatigue, loss of appetite, and anxiety, in patients with lung cancer undergoing chemotherapy. We hypothesized that the interventions would lead to a reduction in the severity mean score of each symptom when compared to existing treatment.

Methods

Study design

The study was a quasi-experimental study using historical controls to assess and compare the effect of a novel symptom cluster management intervention on the severity of fatigue, loss of appetite, and anxiety in patients with lung cancer undergoing chemotherapy. Patients who underwent chemotherapy from November 2017 to February 2018 were assigned to the control group and received routine care. Patients enrolled at the same unit during March 2018 and November 2018 were screened for eligibility and assigned to the experimental group receiving routine care and symptom management intervention [Figure 1]. The participants in the experimental group were purposively selected to match demographic characteristics (age, gender, stages of cancer, and chemotherapy regimens) with the participants in the control group. There was no significant change in treatment for lung cancer during that period.

Participants and setting

Lung cancer patients were recruited from an outpatient chemotherapy unit at a university hospital in the lower northern region of Thailand between November 2017 and November 2018. Study procedures were approved by the university's institutional review board (NU IRB 591/59). Patient inclusion requirements were (1) aged older than 18 years, (2) a diagnosis of primary advanced nonsmall-cell lung cancer, (3) chemotherapy was the sole treatment, (4) previously received 2–3 cycles of chemotherapy, and (5) fluent in Thai and had access to a telephone. Patients were excluded from participating in the study if they (1) had cognitive impairment or (2) were enrolled in other clinical trials. A review of medical records and consultation with oncologists confirmed these eligibility criteria. During a clinical visit, a research assistant described the study, and the patient's written consent was obtained.

An adequate sample size was determined using power analysis. The anticipated mean changes from the control and experimental groups were obtained from a previous study,^[21] and the effect size of 0.08 was determined. A sample of 34 participants in each group was required to detect any significant difference level with a power of 0.90.^[22] To ensure the desired power, an anticipated dropout

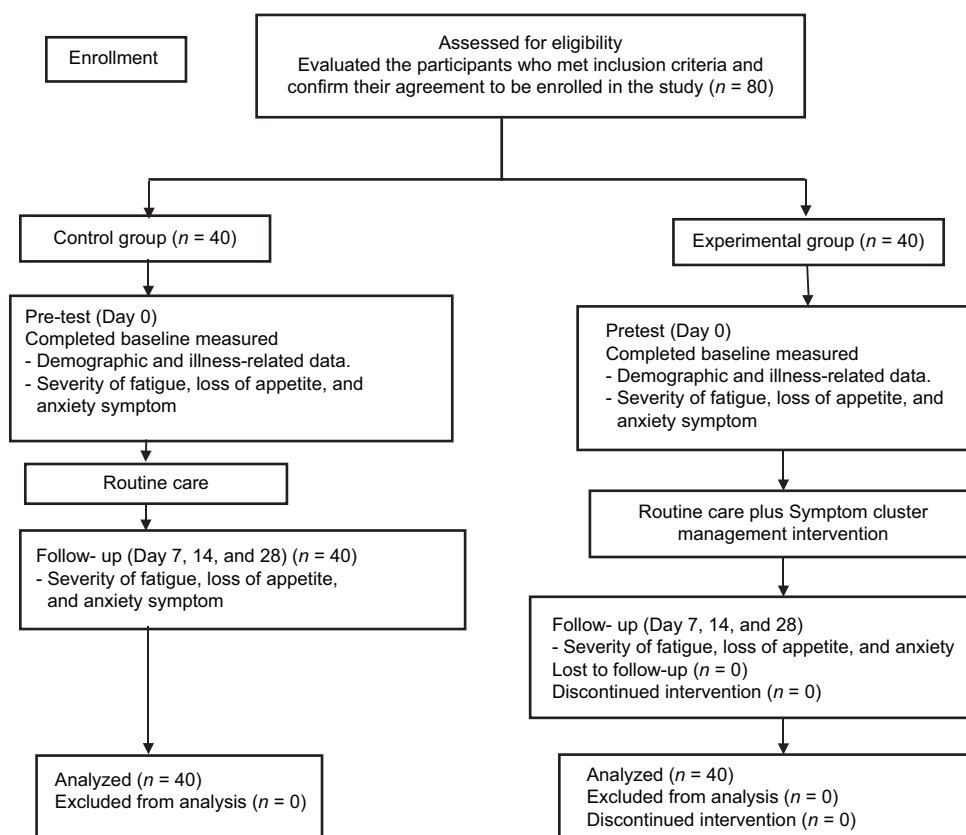


Figure 1: Participant flow diagram

rate of 15% was adjusted to the initial sample size. A total of forty participants were then assigned to each group.

Procedures

The case report form was developed by the research team to collect demographic data (age, gender, and marital status) and medical information (stage of cancer, cycle of chemotherapy, and chemotherapy protocol). All participants completed an individual baseline assessment regarding the severity of fatigue, loss of appetite, and anxiety. Then, a diary was handed out to each participant, and he/she was asked to record their symptom and activities every day continuously. Patients completed an individual assessment at 7, 14, and 28 days postintervention. The 28-day period is the duration between the day after patients received chemotherapy and the day before starting the next cycle. This period was chosen because we were interested in the short-term effects of the intervention. A research assistant who was blind to the study conditions collected the dairies on day 28.

General aspects of the symptom cluster management intervention and nurse training

The intervention was developed based on the SMT.^[16] A four-session intervention was derived including (1) symptom experience, (2) symptom cluster management strategies, (3) patient check-in, and (4) outcome evaluation. Session 1 and 2 were conducted in the outpatient unit, where the participants were asked to assess the symptom experience. Inaccuracy and misconception about symptom clusters were clarified and discussed during the first session. Then, in session 2, a specially trained nurse provided evidence-based instruction in physiological, behavioral, and psychological strategies to manage the symptom clusters. The content of these strategies was designed to cover appropriate exercises, dietary behavioral change, as well as relaxation and distraction techniques. Patients' needs, goals, beliefs, and preferences were discussed and a tailored program for each participant was derived. Then, an information booklet containing instructions for the symptom management strategies was handed out. In session 3, the nurse called each patient at home to check-in, identifying the patient's concerns, and providing emotional support. The last session was conducted at the outpatient unit, and the severity of symptom clusters was evaluated systematically. Figure 2 illustrates the conceptual model of the symptom cluster management intervention based on SMT, and Appendix 2 provides a summary of the intervention components.

The protocol intervention was reviewed and validated by five experts: two oncologists who specialize in chemotherapy and nutrition for cancer patients, one occupational oncology nursing instructor, and two cancer nursing instructors. The

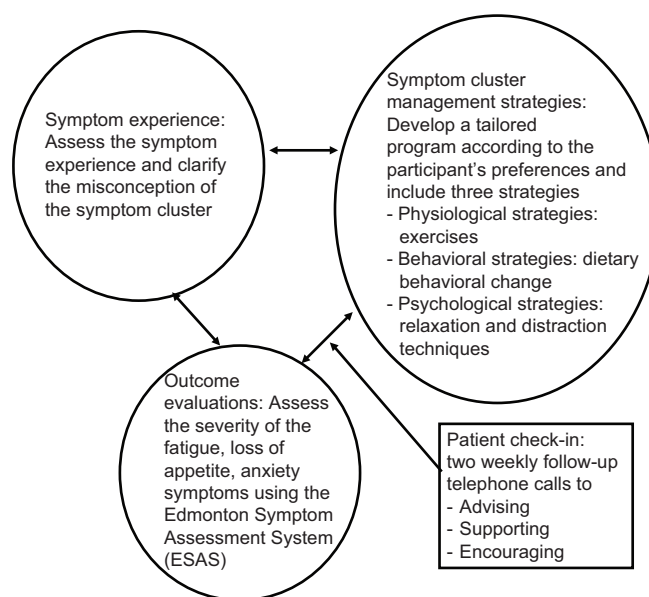


Figure 2: The conceptual model of the symptom cluster management intervention based on symptom management theory

symptom cluster management intervention was delivered by a licensed nurse with at least 3 years of experience in working with cancer patients. A PhD-level nurse researcher trained the nurse. Training included didactic instruction and role plays of treatment sessions detailed in manuals. Following the initial training, the nurse received weekly supervision from the researcher regarding adherence to the study protocol and feedbacks. The nurse was trained until she reported improvements in her confidence and the skills to provide the intervention. During the study period, if the nurse discovered participants who needed special support from a psychologist or social worker, the consultation was made in the outpatient unit.

Routine care

The outpatient unit directed participants to resources for health information and services. The nurse was the same as those for symptom management intervention. Instructions in symptom cluster management strategies did not occur in routine care, but each patient was handed an information booklet on day 28.

Measures

The study outcome was assessed with validated self-report measures used with cancer patients, the Edmonton Symptom Assessment System (ESAS). The ESAS was developed in 1991 by Hui and Bruera as a clinical tool to document the symptom burden in patients with advanced cancer admitted to a palliative care unit.^[23] It has been validated by multiple groups, translated into over twenty languages, and adopted in clinical practice and research to support symptom assessment in many hospitals worldwide. The ESAS has

evolved from horizontal 0 to 100 mm visual analog scales to 11-point numeric rating scales ranging from 0 (no symptom) to 10 (worst possible). ESAS scores of 0, 1–3, 4–6, and 7–10 are generally considered as none, mild, moderate, and severe in clinical practice.^[23] Nine components of symptoms experienced by cancer patients were assessed including pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath. This present study adopted three components: tiredness, appetite, and anxiety as the outcome measures. Studies reported ESAS to have good internal reliability, test-retest reliability, and convergent validity (exceeding 0.80).^[24-26] The ESAS was translated into Thai and tested for validity and reliability. Its internal reliability was good with a reported Cronbach alpha of 0.89.^[27]

Statistical analysis

A descriptive statistic was used to summarize the demographic and clinical characteristics of participants. Continuous variables were reported as means (standard deviations) and categorical variables as frequencies (percentages). Baseline comparisons (Chi-square, Fisher's exact tests, and *t*-tests) were performed to assess differences between the control and experimental groups. Repeated-measure ANOVA was analyzed to determine mean differences between groups across time. The assumptions of independent observations, normality, and sphericity were checked before running repeated-measures ANOVA. Because multiple comparisons on the same dependent variables (severity of tiredness, appetite, and anxiety as measured by ESAS) were carried out, Bonferroni correction was conducted to lessen the chance of committing a Type I error. A significant treatment effect was indicated by a significant time × study group. The effect size was calculated from the strength of eta-squared values and interpreted as low, moderate, and high if the value was 0.2, 0.5, or 0.8, respectively.^[22] The statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS) version 17.0 (IBM, Armonk, NY, US). All tests were two-tailed with $P < 0.05$ considered significant.

Results

During the study period, a total of eighty patients consented to participate and were followed through the study, resulting in a 0% attrition rate. The majority of patients were male (57.50%), married (81.25%), and had advanced-stage cancer (IV) (95.00%). Half of the patients had received a fourth cycle of chemotherapy (55.00%); the other had undergone the fifth cycle (45.00%). The majority of patients (35.00%) were treated with carboplatin and paclitaxel. All patients reported moderate fatigue, loss of appetite, and anxiety at the beginning of the study. There

were no significant differences between the control and experimental groups in terms of sociodemographic, clinical characteristics, and the severity of outcome symptom cluster at baseline [Table 1].

Results in Table 2 show the effects of the symptom cluster management intervention based on SMT on outcome measures in comparison to the control group. The significant effects of the interaction terms time × group ($P < 0.001$) for all symptoms within the cluster indicate the benefit of the intervention over time. Overall, anxiety decreased gradually on days 7, 14, and 28 ($P < 0.001$ for all time points) among the experimental group patients. Fatigue and loss of appetite also declined after days 14 ($P < 0.001$) and 28 ($P < 0.001$) compared to baseline. On the contrary, the control group reported a significant increase in the severity of fatigue, loss of appetite, and anxiety after days 7 ($P < 0.001$), 14 ($P < 0.001$), and 28 ($P < 0.001$). According to Cohen,^[22] the intervention effects were large for all symptoms (2.00 for fatigue, 1.74 for loss of appetite, and 1.69 for anxiety).

Discussion

Published research on managing symptom clusters in patients with cancer is growing. The present study aimed to examine the effectiveness of the symptom cluster management intervention based on SMT for relief of a symptom cluster involving fatigue, loss of appetite, and anxiety in patients with lung cancer undergoing chemotherapy, compared with a usual care control group. The pattern of change on the symptom cluster across the study period was found to be significantly different between the two study groups. Patients in the experimental group reported an improvement in fatigue, loss of appetite, and anxiety over time after receiving the intervention. The results suggested that the symptom cluster management intervention provided a promising approach for the simultaneous treatment of multiple symptoms within a cluster.

The current results are partially consistent with those of prior intervention studies with this population.^[18,19,28-31] For example, Quist *et al.*^[29] tested the effect of a physical exercise program comprising 12 weeks of supervised, structured aerobics, strength, and relaxation training twice weekly for patients with advanced inoperable lung cancer. They found a significant reduction in anxiety and depression and a significant increase in all muscle strength outcomes in the intervention group than in patients assigned to usual care. Conversely, another study examined the feasibility of a multicomponent intervention delivered over two intervention training sessions and a follow-up telephone call on lung cancer patients.^[19] The researchers found no significant differences in a respiratory distress symptom

Table 1: Comparison of the participant's characteristics between the control group and the experimental group

Characteristics	Control group (n=40), n (%)	Experimental group (n=40), n (%)	df	t/χ^2	P
Age, years, mean±SD	60.43±6.13	61.58±6.28	78	0.83 ^c	0.410
Gender					
Male	23 (57.50)	23 (57.50)	1	0.00 ^a	1.000
Female	17 (42.50)	17 (42.50)			
Marital status					
Married	34 (85.00)	31 (77.50)	1	0.74 ^a	0.390
Divorce/widowed/single	6 (15.00)	9 (22.50)			
Stage of disease					
III	2 (5.00)	2 (5.00)	-	-	1.000 ^b
IV	38 (95.00)	38 (95.00)			
Chemotherapy cycle					
4	22 (55.00)	22 (55.00)	1	0.00 ^a	1.000
5	18 (45.00)	18 (45.00)			
Chemotherapy protocol					
Carboplatin, paclitaxel	14 (35.00)	14 (35.00)	3	0.00 ^a	1.000
Carboplatin, gemcitabine	12 (30.00)	12 (30.00)			
Cisplatin, etoposide	7 (17.50)	7 (17.50)			
Cisplatin, gemcitabine	7 (17.50)	7 (17.50)			
Fatigue severity score (baseline), mean±SD	4.70±1.99	5.03±2.07	78	0.72 ^c	0.476
Loss of appetite severity score (baseline), mean±SD	6.36±2.09	5.45±2.23	78	1.86 ^c	0.067
Anxiety severity score (baseline), mean±SD	6.55±1.84	5.88±1.80	78	1.66 ^c	0.101

^aChi-square, ^bFisher's exact tests, ^cIndependent t-test. SD: Standard deviation, df: Degree of freedom

Table 2: The effects of the symptom cluster management intervention based on symptom management theory on outcome measures in comparison to the control group

Symptoms	Times (mean±SD)				Time, P	Group, P	Time × group interaction, P	Effect size Cohen'd
	Baseline ^a	Day 7	Day 14	Day 28				
Fatigue ^b								
Experimental	5.03±2.07	4.25±1.60	3.93±1.59**	3.58±1.63**	0.168	<0.001	<0.001*	2.00
Control	4.70±1.99	5.73±1.71**	6.53±1.41**	6.63±1.41**				
Loss of appetite ^b								
Experimental	5.45±2.23	4.50±1.85	4.00±1.85**	3.70±1.67**	0.009	<0.001	<0.001*	1.74
Control	6.35±2.09	6.63±1.82**	6.90±1.81**	6.83±1.92**				
Anxiety ^b								
Experimental	5.88±1.80	4.48±1.78**	3.75±2.01**	3.53±2.06**	<0.001	<0.001	<0.001*	1.69
Control	6.55±1.84	6.83±1.77**	6.88±1.83**	6.82±1.78**				

^aBaseline defined as prior to start CTX, ^bScores range from 0 (no symptom) to 10 (worst possible). *Post hoc* analysis time × group interaction: *Statistically significant difference between groups at <0.05 level, **Bonferroni's *post hoc* with $P<0.05$ compared to baseline. SD: Standard deviation, CTX: Chemotherapy treatment

cluster including dyspnea, cough, and fatigue between the intervention and usual care groups. Differences in findings across studies may be related to the characteristics of the sample, intervention and control groups, and assessments.

Several potential explanations for the current findings warrant consideration. First, the symptom cluster management intervention based on SMT provided an opportunity to clarify and discuss patients' inaccuracies and misconceptions about symptom clusters. A package of different techniques that patients could choose and the patients' preferences were also incorporated into the intervention, resulting in a tailored program for each participant. These preferences and flexibility regarding intervention content may accommodate patients with

significant symptoms and enhance the intervention acceptability. Furthermore, the follow-up telephone calls by the nurse to identify patients' concerns and provide emotional support may contribute to high retention and large intervention effects. A similar approach is reported to manage sleep, anxiety, breathlessness, and fatigue successfully in lung cancer patients.^[18,31] Thus, this present study contributes to growing evidence that nonpharmacologic interventions impact lung cancer patient outcomes.

Second, the researchers of the current study were interested in the short-term outcome of the intervention (the 28 days between the day after patients received chemotherapy and the day before they started the next cycle). Our ultimate goal

was to develop a program that can alleviate disease-related and treatment-related symptoms among patients with lung cancer undergoing chemotherapy. The findings of our study were contrary to most intervention studies that measured outcomes at 6–12 weeks and found no differences in outcomes between study conditions.^[19,30] Further work is needed to determine the intermediate and long-term outcome of the symptom cluster management intervention.

Finally, although the outcome measures of this current study (ESAS for tiredness, appetite, and anxiety components) were concise and did not overburden the poor health status of the subject, they may cause a Type I error as we conducted multiple comparisons with the same group of patients.^[32] The composite outcome should be developed to capture the totality of the effectiveness of the intervention. The total difference in symptom intensity between the intervention and control groups might go undetected if each dependent variables were to be examined separately.^[18]

The results of this study suggested that the symptom cluster management intervention based on SMT was found to be an acceptable and feasible intervention and appeared to cause no harmful effects to patients, even at advanced stages of the disease. It was performed in a hospital setting, reflecting a realistic implementation of the intervention into daily practice. Nevertheless, several limitations should be noted. The small sample size, the single study site, the lack of randomization, and the nature of the historical control may produce enrollment bias and control bias. Hence, the findings may not generalize to advanced lung cancer in other geographic regions. Data on Karnofsky, Eastern Cooperative Oncology Group scores, change in body weight, and chemical blood tests were not collected in this study. These parameters may influence some of the results. It is necessary to consider including these parameters in a future trial.

Based on our findings, we also recommend that future studies examine associations between specific intervention components and outcomes as these will allow researchers to develop more efficacious interventions. Notably, the understanding of mechanisms underlying the effects of interventions will advance symptom management science and push research from bench to bedside.

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Conflicts of interest

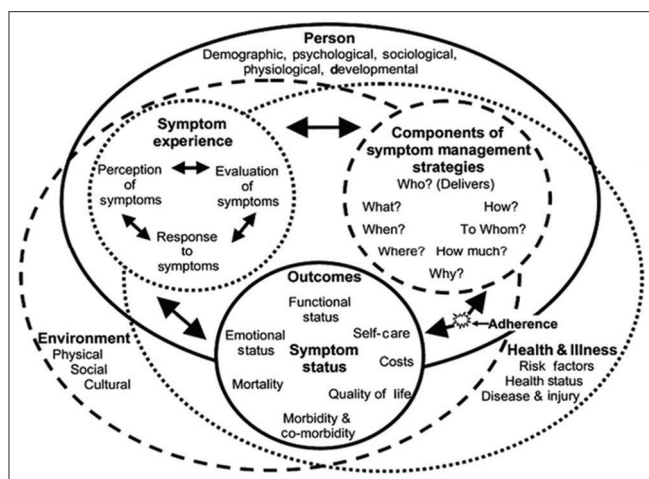
There are no conflicts of interest.

References

1. World Health Organization. Fact Sheet: Cancer. World Health Organization; 2020. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>. [Last accessed on 2020 Aug 01].
2. Russell J, Wong ML, Mackin L, Paul SM, Cooper BA, Hammer M, *et al*. Stability of symptom clusters in patients with lung cancer receiving chemotherapy. *J Pain Symptom Manage* 2019;57:909-22.
3. Choi S, Ryu E. Effects of symptom clusters and depression on the quality of life in patients with advanced lung cancer. *Eur J Cancer Care (Engl)* 2018;27:e12508.
4. Davis K, Yount S, Wagner L, Cella D. Measurement and management of health-related quality of life in lung cancer. *Clin Adv Hematol Oncol* 2004;2:533-40.
5. Karomprat A, Chaichan P, Santawesuk U, Sookprasert A. Symptoms, symptom management and outcome in cancer patients undergoing chemotherapy. *Srinagarind Med J* 2017;32:326-31.
6. Kim HJ, McGuire DB, Tulman L, Barsevick AM. Symptom clusters: Concept analysis and clinical implications for cancer nursing. *Cancer Nurs* 2005;28:270-82.
7. Molassiotis A, Wengström Y, Kearney N. Symptom cluster patterns during the first year after diagnosis with cancer. *J Pain Symptom Manage* 2010;39:847-58.
8. Reich RR, Lengacher CA, Alinat CB, Kip KE, Paterson C, Ramesar S, *et al*. Mindfulness-based stress reduction in post-treatment breast cancer patients: Immediate and sustained effects across multiple symptom clusters. *J Pain Symptom Manage* 2017;53:85-95.
9. Hsu HT, Lin KC, Wu LM, Juan CH, Hou MF, Hwang SL, *et al*. Symptom cluster trajectories during chemotherapy in breast cancer outpatients. *J Pain Symptom Manage* 2017;53:1017-25.
10. Chen E, Nguyen J, Cramarossa G, Khan L, Leung A, Lutz S, *et al*. Symptom clusters in patients with lung cancer: A literature review. *Expert Rev Pharmacoecon Outcomes Res* 2011;11:433-39.
11. Sanders SL, Bantum EO, Owen JE, Thornton AA, Stanton AL. Supportive care needs in patients with lung cancer. *Psychooncology* 2010;19:480-9.
12. Northouse LL, Katapodi MC, Song L, Zhang L, Mood DW. Interventions with family caregivers of cancer patients: Meta-analysis of randomized trials. *CA Cancer J Clin* 2010;60:317-39.
13. Rueda JR, Solà I, Pascual A, Subirana Casacuberta M. Non-invasive interventions for improving well-being and quality of life in patients with lung cancer. *Cochrane Database Syst Rev* 2011;9:CD004282.
14. Mosher CE, Ott MA, Hanna N, Jalal SI, Champion VL. Development of a symptom management intervention: qualitative feedback from advanced lung cancer patients and their family caregivers. *Cancer Nurs* 2017;40:66-75.
15. Kwekkeboom KL. Cancer symptom cluster management. *Semin Oncol Nurs* 2016;32:373-82.
16. Bender MA, Janson SL, Franck LS, Aldrich KL. Middle range theory for nursing. In: Smith MJ, Liehr PR, editors. *Theory of Symptom Management*. New York: Springer; 2018. p. 147-78.
17. Brant JM, Beck S, Miaskowski C. Building dynamic models and theories to advance the science of symptom management research. *J Adv Nurs* 2010;66:228-40.
18. Chan CW, Richardson A, Richardson J. Managing symptoms in patients with advanced lung cancer during radiotherapy:

- Results of a psychoeducational randomized controlled trial. *J Pain Symptom Manage* 2011;41:347-57.
19. Yorke J, Lloyd-Williams M, Smith J, Blackhall F, Harle A, Warden J, *et al.* Management of the respiratory distress symptom cluster in lung cancer: A randomised controlled feasibility trial. *Support Care Cancer* 2015;23:3373-84.
 20. Khamboon T, Pakanta I, Jitpewngam W, Wangteeraprasert K. A development of symptom clusters management model in lung cancer persons receiving chemotherapy. *J Nurs Health Sci* 2019;13:121-32.
 21. Jongkhetkit W, Saesia W, Mnasurakarn J. The effects of a gastrointestinal and fatigue symptom cluster management promoting program on symptom experiences in patients with breast cancer receiving chemotherapy. *South Coll Netw J Nurs Public Health* 2019;62:187-98.
 22. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. New York: Academic Press; 2013.
 23. Hui D, Bruera E. The Edmonton Symptom Assessment System 25 years later: Past, present, and future developments. *J Pain Symptom Manage* 2017;53:630-43.
 24. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. *Cancer* 2000;88:2164-71.
 25. Nelson JE, Meier DE, Oei EJ, Nierman DM, Senzel RS, Manfredi PL, *et al.* Self-reported symptom experience of critically ill cancer patients receiving intensive care. *Crit Care Med* 2001;29:277-82.
 26. Pautex S, Berger A, Chatelain C, Herrmann F, Zulian GB. Symptom assessment in elderly cancer patients receiving palliative care. *Crit Rev Oncol Hematol* 2003;47:281-6.
 27. Chinda M, Jaturapatporn D, Kirshen AJ, Udomsubpayakul U. Reliability and validity of a Thai version of the Edmonton Symptom Assessment Scale (ESAS-Thai). *J Pain Symptom Manage* 2011;42:954-60.
 28. Chen HM, Tsai CM, Wu YC, Lin KC, Lin CC. Randomised controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *Br J Cancer* 2015;112:438-45.
 29. Quist M, Langer SW, Lilledund C, Winther L, Laursen JH, Christensen KB, *et al.* Effects of an exercise intervention for patients with advanced inoperable lung cancer undergoing chemotherapy: A randomized clinical trial. *Lung Cancer* 2020;145:76-82.
 30. Mosher CE, Winger JG, Hanna N, Jalal SI, Einhorn LH, Birdas TJ, *et al.* Randomized pilot trial of a telephone symptom management intervention for symptomatic lung cancer patients and their family caregivers. *J Pain Symptom Manage* 2016;52:469-82.
 31. Chen HM, Cheung DST, Lin YY, Wu YC, Liu CY, Lin KC, *et al.* Relationships of exercise timing with sleep, fatigue and rest-activity rhythms of lung cancer patients in Taiwan: An exploratory study. *Eur J Cancer Care (Engl)* 2020;29:e13233.
 32. Armstrong RA. When to use the Bonferroni correction. *Ophthalmic Physiol Opt* 2014;34:502-8.

Appendixes



Appendix 1: Symptom management theory model and its components. Source: Dodd M, Janson S, Facione N, Faucett J, Froelicher ES, Humphreys J, *et al.* Advancing the science of symptom management. *J Adv Nurs* 2001;33:668-76

Appendix 2: A summary of the intervention components

Session	Activities	Duration (min)
Day 1: Session 1 Symptom experience	At the outpatient chemotherapy unit, the specially trained nurse introduced herself and implements the study protocol as follow Explains the purpose of the study and describes the summary of the intervention Hands out the diary to record participants' symptom and activities as well as the information booklet Assess the symptom experience and clarify the misconception of the symptom cluster Discusses the misconceptions and help participants to adjust the perception regarding their symptom experience	15
Day 1: Session 2 Symptom clusters management strategies	The specially trained nurse at the outpatient chemotherapy unit provided the information booklet including evidence-based instruction in physiological, behavioral, and psychological strategies to manage the symptom clusters. The instruction content consisted of Physiological strategies: appropriate exercises (such as walking, swinging arms, breathing exercise, etc.) Behavioral strategies: dietary behavioral change, meal planning Psychological strategies: relaxation and distraction techniques (such as meditation and praying, etc.) The nurse discussed the participant's needs, goals, beliefs, and preferences. Then, a tailored program for the participant was derived, and the measures to help participants adhere to the program were discussed The nurse helped train and coach self-management symptom cluster strategies regarding the participant's preferences by asking the participant to Demonstrate and repeat the discussed activities Explain how to record the activities and the symptom experience in the diary The nurse explained how to evaluate the patient's symptoms (the severity of fatigue, loss of appetite, and anxiety) using the Edmonton symptom assessment system Questions and answers	45
Day 7: Session 3 Patient check-in	The nurse made a follow-up telephone call to assess the adherence to the program. The patient's symptoms regarding the severity of fatigue, loss of appetite, and anxiety were discussed. The participant evaluated the feasibility of the program and suggested some modifications The nurse identified the patient's concerns and provided emotional support Questions and answers	10-15
Day 14: Session 3 Patient check-in	The activities from day 7 were reimplemented	10-15
Day 28: Session 4 Outcome evaluation	Participants were scheduled to visit the outpatient chemotherapy unit. The research assistant who was blind to the study condition collected the diaries	5-10