EFFECTS OF QIGONG ON SYMPTOM CLUSTER OF DYSPNOEA, FATIGUE, AND ANXIETY IN VIETNAMESE LUNG CANCER PATIENTS: A RANDOMISED CONTROLLED TRIAL

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PhD

The Hong Kong Polytechnic University

2019

The Hong Kong Polytechnic University

School of Nursing

Effects of Qigong on symptom cluster of dyspnoea, fatigue, and anxiety in Vietnamese lung cancer patients: A randomised controlled trial

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A thesis submitted in partial fulfilment of the requirements for the degree of

Doctor of Philosophy

January 2019

CERTIFICATE OF ORIGINALITY

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ABSTRACT

Background: Patients with lung cancer experience a variety of symptoms and most of them are at a moderate level of severity. Dyspnoea, fatigue, and anxiety are often the most problematic symptoms of lung cancer. Non-pharmacological approaches to manage symptoms among lung cancer patients showed either no or mild effects. Qigong is used by cancer patients, but its effects are not adequately evaluated, all past related trials focus on a single symptom, none have been done with lung cancer patients, and many trials have methodological limitations.

Objective: 1) To assess the effect of Qigong on managing dyspnoea, fatigue, and anxiety (as a symptom cluster) in lung cancer patients; 2) To explore the effect of Qigong on cough, which is another common symptom linked with dyspnoea, fatigue and quality of life, in lung cancer patients.

Methods: One hundred and fifty-six patients were recruited and randomly assigned to either the Qigong group (n = 78) or the wait-list control group (n = 78). A 6-week Qigong intervention program was conducted that comprised of 2 weeks training at hospital then home-based practice 30 min per day for 5 days per week, for 4 weeks. A DVD, a logbook and weekly phone calls were provided to the Qigong group. The primary outcome was a composite score of the Functional Assessment of Cancer Therapy-Fatigue (FACT-F), Cancer Dyspnoea Scale (CDS) and Depression Anxiety Stress Scales 21 subscale anxiety (DASS21-A), while the secondary outcomes included the three symptoms of the cluster individually, cough assessed with the Manchester Cough in Lung Cancer Scale (MCLCS), and quality of life assessed through the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (QLQ-C30), and Lung Cancer module (LC13). All outcomes were assessed at baseline, post-intervention, and post 6-weeks of follow-up.

Generalized estimating equation methods were used to analyze the effects of Qigong on primary and secondary outcomes.

Results: There was no improvement on the symptom cluster, fatigue or anxiety, between the two groups across time. However, the subjects in the Qigong group showed a trend towards an improvement in symptoms in within-group analysis in the fatigue, dyspnoea, and anxiety from baseline to 6^{th} week (p=0.004, 0.002, and 0.049, respectively). Between group statistically significant improvements from baseline to 12^{th} week were observed in cough (p = 0.001), dyspnoea (p= 0.014), global health status (p = 0.021), functional quality of life score (p = 0.001), and the symptom subscale of the quality of life scale (p = 0.002).

Conclusion: Qigong was not a promising treatment for relieving the symptom cluster. However, Qigong was effective and safe on the single symptom of dyspnoea and cough alongside core quality of life indicators. In addition, Qigong needed more than 6 weeks to improve dyspnoea and the intervention was more effective in managing respiratory symptoms in males more than in females. Qigong may be useful in managing respiratory symptoms rather than a symptom cluster that includes fatigue and anxiety. Symptom cluster research should carefully target appropriate symptom combinations in the future.

PUBLICATIONS AND PRESENTATION AT CONFERENCE ARISING FROM THE THESIS

Vu, D. V., Molassiotis, A., Ching, S. S. Y., & Le, T. T. (2017). Effects of Qigong on symptom management in cancer patients: A systematic review. *Complementary Therapies in Clinical Practice, 29*, 111-121.

Vu, D. V., Molassiotis, A., & Ching, S. S. Y. (2016, March 14–15). Effects of Qigong on symptom management in cancer patients: A systematic review. Poster presentation at The 19th East Asian Forum of Nursing Scholars, Chiba, Japan.

Vu, D. V., Molassiotis, A., & Ching, S. S. Y. (2019, January 18–19). Effects of Qigong on symptom cluster of dyspnoea, fatigue, and anxiety in Vietnamese lung cancer patients: A randomised controlled trial. Paper presented at The 22th East Asian Forum of Nursing Scholars, Singapore.

ACKNOWLEDGMENTS

First and foremost, I would like to send my sincere appreciation to my supervisors, Professor Alex MOLASSIOTIS and Dr. Shirley Ching, for their valuable advice, emotional support, and dedicated supervision throughout the whole process. Without their guidance, I would not have been able to complete this thesis in an effective manner.

I would like to express my deep thanks to all the study subjects for spending their time and energy participating in the doctoral research project.

I would also like to thank the hospital staff at the study sites for their kind support of my data collection.

Last, but not least, I would like to extend my deep appreciation and gratitude to my family - my wife, my parents, and my parents-in-law for their patience and unconditional support, which were truly, very important throughout my study.

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LIST OF ABBREVIATIONS

BDI	Beck Depression Inventory
BFI	Brief Fatigue Inventory
BMI	Body Mass Index
BSI	Brief Symptom Inventory
CCT	Clinical Control Trial
CDS	The Cancer Dyspnoea Scale
CES-D	Centre for Epidemiologic Studies Depression Scale
CFS	Cancer Fatigue Scale
CG	Control Group
CONSORT	Consolidated Standards of Reporting Trials
COPD	Chronic obstructive pulmonary disease
CQLQ	Cough-specific Quality of Life Questionnaire
DASS	Distress Alerting Satellite System
DASS21	Depression, Anxiety, and Stress Scale 21
DVD	Digital Video Disc
ECOG	Eastern Cooperative Oncology Group
EFS	Edmonton Frail Scale
EORTC	European Organization for Research and Treatment of Cancer
EORTC QLQ-C30	European Organization for Research and Treatment Quality of Life
FACT-B	Functional Assessment of Cancer Therapy-Breast
FACT-Cog	FACT-Cognitive Function

FACT-F	The Functional Assessment of Cancer Therapy-Fatigue Subscale
FACT-G	Functional Assessment of Cancer Therapy-General
FACT-H&N	For patients with Head & Neck cancer
FSI	Fatigue Symptom Inventory
FQ	Fatigue Questionnaire
GEE	Generalized Estimating Equations
GOG-NTX	Gynaecologic Oncology Group- Neurotoxicity
HADS-A	Hospital Anxiety and Depression
HTCG	Healthy Control Group
ID	Identification
LCQ	Leicester Cough Questionnaire
LFS	Lee Fatigue Scale
LOCF	Last Observation Carried Forward
MCLCS	Manchester Cough in Lung Cancer Scale
MFSI-SF	Multidimensional Fatigue Symptom Inventory–Short Form
MOH	Ministry of Health
MQ	Medical Qigong
NSCLC	Non-small cell lung cancer
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
QG	Qigong Group
QoL	Quality of Life
RCT	Randomised Controlled Trial
SCLC	Small cell lung cancer

SDS	Symptom Distress Scale
SPIRIT	Standard Protocol Items Recommendations for Interventional Trials
STAI	State-Trait Anxiety Inventory
TACE	Transcatheter arterial chemoembolization
TCM	Traditional Chinese Medicine
UNESCO	United Nations Educational, Scientific and Cultural Organization
VAS	Visual Analogue Scale
VSHSS	Verran and Snyder-Halpern Sleep Scale
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION

In this chapter, the researcher described the background significance and purpose, and specified research objectives; outlined the framework of the research study; defined the terms used; delineated the scope of study; and described the project contributions.

Background and significance of the study

Lung cancer is a very common and lethal malignant disease. Lung cancer causes more than 1.6 million deaths annually (Markaki, Tsamardinos, Langhammer, Lagani, Hveem, & Røe, 2018). It is known that lung cancer has been the most common cancer worldwide for several decades, resulting in nearly 20% of all deaths from cancer during that period (Ferlay, Shin, Bray, Forman, Mathers, & Parkin, 2010). The survival rate of patients with lung cancer in developing countries is only 9% (Parkin, Bray, Ferlay, & Pisani, 2005). Annually, there are 20,000 newly diagnosed cases and 17,000 deaths in Vietnam due to lung cancer (Phuong, 2013). According to the national survey in Vietnam, lung cancer is ranked as the 4^{th} highest cause of death in males and the 7^{th} highest cause in females (Nguyen, 2011).

Patients with lung cancer experience a variety of symptoms (Liao, Liao, Shun, Yu, Yang, & Lai, 2011). However, despite the fierce efforts of both nurse practitioners and researchers, the management of symptoms in lung cancer is still suboptimal. In a study of 100 lung cancer patients in America, 49% of lung cancer patients had to be hospitalised because of uncontrolled symptoms (Podnos, Borneman, Koczywas, Uman, & Ferrell, 2007). Boyes, Girgis, D'Este, and Zucca (2012) investigated the supportive care needs of 1323 patients in the sixth month after diagnosis with different types of cancer, including prostate, melanoma, breast, blood, colorectal, head and

neck, and lung. The results demonstrated that lung cancer patients reported the highest need for supportive care in comparison to all other types of patients. Nursing interventions often focus on single symptoms, such as fatigue, dyspnoea, pain, and anxiety, etc., rather than on multiple symptoms (Huhmann & Camporeale, 2012; Thompson, Sola, & Subirana, 2005; Zhao & Yates, 2008). Obviously, single symptom interventions would not be a suitable approach because they contrast with both the patients' real situation and the theoretical basis of symptom management. In particular, it is obvious that cancer patients suffer from multiple symptoms concurrently (Esper, 2010; Gift, Jablonski, Stommel, & Given, 2004).

Theoretically, concurrent symptoms are interactive and the presence of one symptom may be the catalyst for the occurrence of another (Lenz & Pugh, 2008). In the Theory of Symptom Management, Dodd, Janson, Facione, Faucett, Froelicher, Humphreys, Lee, Miaskowski, Puntillo, Rankin, and Taylor (2001) suggested that coexisting symptoms should be controlled simultaneously. It is hypothesised that the management of concurrent symptoms, instead of single symptoms, would enhance the effectiveness of interventions (Tsai, Wu, Chiu, & Chen, 2010; Xiao, 2010). Therefore, addressing only single symptoms could be one of the reasons why existing nursing interventions produce only a low-level effect. Systematic reviews pointed out that most non-pharmacological interventions used to manage single symptoms in lung cancer yield a small effect size (Yorke, Brettle, & Molassiotis, 2012; Zhao & Yates, 2008). Therefore, this proves that new nursing interventions that target multiple symptoms are needed.

However, since lung cancer is a highly lethal disease with a short life expectancy and high mortality, the integration of too many symptoms in a single intervention may be a burden to patients. Researchers have reported a very high

attrition rate from their experiments on lung cancer populations due to the severity of illness (Chan, 2011; Moore, Corner, Haviland, Wells, Salmon, Normand, Brada, & Smith, 2002). Thus, it is assumed that only the central and most distressing symptoms should be selected for new interventions.

Previous authors have identified a number of symptom clusters: Dyspnoea, fatigue, and anxiety that were associated with poor patient performance (Fox, 2006; Chan, Richardson, & Richardson, 2005). Breathlessness, cough, and fatigue are distressing symptoms for patients with lung cancer (Cheville et al., 2011; Molassiotis et al., 2011). Among that dyspnoea, fatigue, and anxiety were the most problematic symptoms in lung cancer (Chan, Richardson, & Richardson, 2005). Dyspnoea is described as "an uncomfortable awareness of breathing" (DiSalvo, Joyce, Tyson, Culkin, & Mackay, 2008: p.342). Several terms are also used to describe dyspnoea, such as shortness of breath, difficulty breathing, feeling out of breath, or not getting sufficient air (Quast & Williams, 2009). Fatigue is defined as "a subjective feeling of tiredness, weakness or lack of energy" (Radbruch, Strasser, Elsner, Gonçalves, Løge, Kaasa, Nauck, Stone, & Care, 2008: p.15). However, different from normal tiredness, cancer fatigue cannot be eased by usual interventions such as sleep, rest, food, or water (Olson & Morse, 2005). Anxiety is defined as "the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension" (American Psychiatric Association, 2005: p.138). Anxiety consists of both subjective responses and objective signs. Anxiety is a universal human experience and the most basic of emotions (Varcarolis, 2014). Anxiety at the mild and moderate levels are constructive, which help the sufferers deal with the situation (Whitley, 1992). However, at the severe and panic levels, anxiety is destructive; it diminishes the patients' physical and mental function, resulting in

exhaustion (Townsend, 2009).

Both quantitative and qualitative studies repeatedly describe the problematic presence of these three symptoms (dyspnoea, fatigue, and anxiety) in patients with lung malignancy (Brown & Kroenke, 2009; Koczywas, Williams, Cristea, Reckamp, Grannis, Tiep, Uman, & Ferrell, 2013; Lai, Chan, & Lopez, 2007). In Vietnam, Ngo (2003) demonstrated that nearly half (48.2%) of the lung cancer population were suffering from dyspnoea at the start of treatment. There is evidence that dyspnoea, fatigue, and anxiety significantly impact on lung cancer patients' quality of life (Alacacıoğlu, Öztop, & Yılmaz, 2012; Joyce, Schwartz, & Huhmann, 2008; Smith, Hann, Ahles, Furstenberg, Mitchell, Meyer, Maurer, Rigas, & Hammond, 2001), mortality (Cheville, Novotny, Sloan, Basford, Wampfler, Garces, Jatoi, & Yang, 2011), functional status (Cella, Eton, Hensing, Masters, & Parasuraman, 2008), the utilisation of healthcare services (Doyle, Lloyd, & Walker, 2008), and hospital readmission (Borneman, Ferrell, Sun, Piper, & Koczywas, 2008). Therefore, alleviating these symptoms could be a central task of oncology nursing when working with lung cancer patients.

It is also evident that dyspnoea, fatigue, and anxiety symptoms are related. Oh, Kim, Lee, and Kim (2004) asserted that 48.4% of the variance in overall fatigue was explained by dyspnoea and negative mood state. Another study investigated correlates of fatigue in 157 lung cancer patients. Data showed that symptoms of dyspnoea on walking and symptom distress were associated with fatigue (Okuyama, Tanaka, Akechi, Kugaya, Okamura, Nishiwaki, Hosaka, & Uchitomi, 2001). Long, Thanasilp, and Thato (2015) explored a causal model explaining fatigue in 246 lung cancer patients in Vietnam. The hypothesised model explained that dyspnoea had the largest total effect on fatigue, followed by anxiety. Qualitatively, patients described suffering

from fatigue after episodes of dyspnoea (Lai et al., 2007). Thus, it could be hypothesised that the control of one of these three symptoms may also help to ease the others and vice versa.

The selection of dyspnoea, fatigue, and anxiety as the target symptoms of a new intervention is derived from existing evidence, which points out that these symptoms compose a group of sentinel, or central, symptoms in lung cancer (Maguire, Stoddart, Flowers, McPhelim, & Kearney, 2014). From the viewpoint of symptom cluster researchers, within the cluster, there would be one, two, or several sentinel symptoms. These symptoms are the most important, all influencing the others as well as accounting for the stability of that cluster (Barsevick, 2006; Kirkova, Aktas, Walsh, Rybicki, & Davis, 2010; Molassiotis, Wengstrom, & Kearney, 2010). Barsevick (2006) extended the idea of sentinel symptoms within the cluster to the idea of sentinel clusters of patients' symptoms. It is asserted that the sentinel symptoms/cluster should be more prioritised in symptom management (Lacasse & Beck, 2007).

Findings from studies investigating symptom clusters in lung cancer seem to suggest that dyspnoea, fatigue, and anxiety are the sentinel symptoms (Chan et al., 2005), which are associated with many other symptoms. It is shown that these three symptoms can be clustered with coughs (Cheville et al., 2011; Molassiotis, Lowe, Blackhall, & Lorigan, 2011a), and pain and sleeplessness (Molassiotis et al., 2011a). Brown, Cooley, Chernecky, and Sarna (2011) explored symptom clusters in women with lung cancer; it was found that participants suffered from several clusters, which consisted of four to six concurrent symptoms. Although those clusters are different, dyspnoea, fatigue, and anxiety are essential parts of all. Therefore, dyspnoea, fatigue, and anxiety are symptoms that could be prioritised in symptom management research. Importantly, although little is known about the causal relationship between dyspnoea,

fatigue, anxiety, and other symptoms, the inherent associations between symptoms as proposed in the theory of unpleasant symptoms (Lenz & Pugh, 2008) may be the rationale for the assumption that interventions focusing on dyspnoea, fatigue, and anxiety may offer positive effects to other concurrent symptoms.

Two large systematic reviews demonstrated that most medications were not effective in reducing symptoms in cancer (Minton, Stone, Richardson, Sharpe, & Hotopf, 2008; Peuckmann, Elsner, Krumm, Trottenberg, & Radbruch, 2010). There are several non-pharmacological interventions for managing symptoms that could be applicable in lung cancer. They are acupuncture, qigong, counselling, exercise, relaxation, distraction, etc. (Cairns, 2012; Mitchell, Bethesda, & Berger, 2006; Puetz & Herring, 2012). Non-pharmacological approaches, such as education, counselling, cognitive therapy, or alternative medicine showed either no or mild effects (Finnegan, Molassiotis, Richardson, & Ream, 2013; Jacobsen, Donovan, Vadaparampil, & Small, 2007; Mitchell & Beck, 2009). A meta-analysis by Jacobsen et al. (2007) yielded small effect sizes of non-pharmacological interventions on fatigue both during and after treatments. The overall effect size of such interventions was only 0.09 (95% CI = 0.02 - 0.16). Only Qigong intervention is hypothesised to alleviate these adverse outcomes (Lee, Chen, & Yeh, 2006).

Particularly, Krishnasamy, Wilkie, and Haviland (2001), asserted that despite 50% of lung cancer patients demonstrating breathlessness, even at rest, only 15% of them received advice on how to live with this distressing symptom. Respondents in a qualitative study by Lai et al. (2007) mentioned that they received insufficient information about dyspnoea from nurses. Lung cancer patients assumed that when the health care worker did not offer any information, it means that there should be no solution for their problems. This was the reason why patients may not seek help to

control their symptoms (Steele & Fitch, 2008). A previous study tested the effectiveness of educational intervention on relieving a symptom cluster of dyspnoea, fatigue, and anxiety in lung cancer. Significant effects were found on the patterns of changes in breathlessness ($p = 0.002$), fatigue ($p = 0.011$), and anxiety ($p = 0.001$) (Chan, 2011). However, there are several shortcomings in this experiment. Firstly, although the authors claimed that they used randomisation, the study still failed to control the allocation of stages of disease between two participant groups. The experimental group consisted of more advanced stage patients than the control arm. Moreover, the attrition rate (due to death) of the experimental group was much higher than that of the control group, which were 42% and 11%, respectively. In addition, this study recruited only end-stage individuals.

A complementary and alternative modality of traditional Chinese medicine such as Qigong is often used by cancer patients to manage their symptoms (Chen, 2002). Qigong has been developed and used in cancer treatments (Lee et al., 2006). Qigong consists of a series of simple, performed in synchrony, repeated practices including body posture or/and movements, breathing practice, and meditation (Ernst, 2002). It consists mostly of gentle movements (with some vigorous and shaking movements in addition to quiet, stillness practice) designed to attain a deeply relaxed state.

A burgeoning literature has examined the effects of Qigong on supportive care outcomes in people with cancer including physical function, physical symptoms, psychological symptoms, and quality of life (QOL) (Chan, 2012). Many positive health-related impacts from the use of Qigong have been reported in the literature, such as improving depression, fatigue and anxiety (Shneerson, 2013), appetite, nausea and vomiting (Fong, 2015), and decreasing heart rate, blood pressure, lipid levels and

levels of circulating stress hormones, and improving immune function (Oh., 2012; Wang, Chan, Ho, Tsang, Chan, & Ng, 2013). Systematic reviews and meta-analyses have concluded that Qigong interventions during and after cancer therapies often result in meaningful and reliable improvements in several supportive care outcomes (Lee, 2007; Zeng, 2014). These benefits include observed changes in physiological measures, objective performance indicators, self-reported functioning and symptoms, psychological well-being and overall QOL. However, these studies did not include people with advanced lung cancer.

Qigong could be highly beneficial because cancer symptoms are chronic, thus requiring patients to have long-term self-management of their symptoms. Therefore, this approach seems to be suitable the Vietnamese context, in which the majority of cancer patients stay at home due to the overloading of oncology hospitals. Normally, Vietnamese cancer patients are only hospitalised for active treatments of the cancer. Most of the time, they stay in the community without or with very limited palliative care (Ministry of Health, 2008). The separation from healthcare facilities, as is happening in Vietnam, could be a risk for the insufficient control of symptoms. Dyspnoea is much worse in patients staying at home in comparison to those who are hospitalised because of the difficulty in implementing dyspnoea treatment at home compared to in the hospital (Leppert, Turska, Majkowicz, Dziegielewska, Pankiewicz, & Mess, 2012). Therefore, Qigong could be highly beneficial for lung cancer patients in the Vietnamese population.

In conclusion, lung cancer is common, and patients may experience many symptoms brought about by the disease and its treatments. Symptom management for lung cancer patients should be offered effectively because this population is suffering from a significant number of symptoms. However, symptom control among lung

cancer patients is still suboptimal. Dyspnoea, fatigue, and anxiety are distressing symptoms for patients with lung cancer. Usually, these symptoms are managed in isolation, yet they often occur simultaneously. Previous research has often addressed management of discrete symptoms rather than considering them to be a cluster. Existing interventions cannot produce appropriate effect sizes because they focus only on single symptoms. However, interventions targeting too many symptoms would be burdensome to patients. Theoretically, it is hypothesised that the integration of dyspnoea, fatigue, and anxiety, being the three central and most distressing lung cancer symptoms, would enhance the effectiveness of an intervention without bringing any burden to the participants. However, there is no empirical evidence about the effectiveness of such integrative interventions.

Moreover, the literature suggests that Qigong would be an appropriate approach to ease patients' symptoms. Several studies with Qigong interventions have been conducted to reduce cancer-related physical and psychological symptoms. The results are promising. However, the findings from those studies still require further affirmation due to their shortcomings in research designs such as small sample sizes, differences between control and experimental groups, and high attrition rates.

The literature indicates a need for the enhanced management of dyspnoea, fatigue, and anxiety in lung cancer patients. Therefore, this study is designed to examine the effects of Qigong on dyspnoea, fatigue, and anxiety in lung cancer patients as a symptom cluster. The findings from the study can be accumulated with the results of previous experiments to open up a new direction in symptom management in lung cancer. It would also be the response to the question raised by symptom management theorists about the efficacy of interventions focusing on a group of interrelated symptoms, or symptom clusters.

Aims of the study

The primary aim of this study is to assess the effect of Qigong on managing dyspnoea, fatigue, and anxiety (as a cluster) in lung cancer patients.

The secondary aim of this study is to explore the effect of Qigong on coughs, which are another common symptom linked with dyspnoea, fatigue, and anxiety as a cluster, and QOL in lung cancer patients.

Hypotheses of the study

The primary hypothesis of this study is that patients with lung cancer who receive Qigong training intervention will show greater improvement in dyspnoea, fatigue, and anxiety than those who receive usual care, as assessed immediately after completion of the Qigong intervention, and at the 6-week follow-up.

The secondary hypothesis of this study is that patients with lung cancer who receive Qigong training intervention will show greater improvement in QOL and cough than those who receive usual care, as assessed immediately after the completion of Qigong intervention, and at 6-weeks follow-up.

Operational definitions

Fatigue referred to the perception of Vietnamese lung cancer patients receiving medical treatment toward the subjective, persistent, and overwhelming feeling of tiredness or lack of energy, which is highly distressing and negatively interferes with the patients' ability to function normally. Fatigue was measured by The Functional Assessment of Cancer Therapy- Fatigue subscale (FACT-F) (Yellen, Cella, Webster, Blendowski, & Kaplan, 1997).

Dyspnoea referred to the subjective perception of breathing discomfort, as reported by Vietnamese lung cancer patients receiving medical treatments. Dyspnoea was measured by the Cancer Dyspnoea Scale (Tanaka, Akechi, Okuyama, Nishiwaki,

& Uchitomi, 2000)

Anxiety referred to the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension, as reported by Vietnamese lung cancer patients receiving medical treatment. Anxiety was measured by the Anxiety subscale of Depression, Anxiety, and Stress Scale (DASS 21 -A) (Tran, Tran, & Fisher, 2013).

Cough referred to a perception towards the severity and influence of violent expulsion of air from the lungs with a characteristic sound, as reported by Vietnamese lung cancer patients receiving medical treatment. Coughs were measured by the Manchester Cough in Lung Cancer Scale (Molassiotis, Ellis, Wagland, Williams, Bailey, Booton, Blackhall, Yorke, & Smith, 2012).

Quality of life referred to the perception of Vietnamese lung cancer patients receiving medical treatment towards to the symptom burden and severity in lung cancer. Loss of physical functioning, psychological events such as depression, and reduced overall QOL is associated with uncontrolled symptoms. QOL was measured by the European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire - Core (EORTC-QLQ-C30) (Fayers, Aaronson, Bjordal, Groenvold, Curran, & Bottomley, 2012) and Lung module (LC-13 subscale) (Bergman, Aaronson, Ahmedzai, Kaasa, & Sullivan, 1994) .

Qigong consists of two words: “Qi” and “Gong”. The word “Qi” means ‘breath’ or ‘vital essence’ or ‘energy’. The word “Gong” means ‘daily effort’ or ‘self-discipline’ or ‘mastery’ or ‘power’. Qigong in this study was founded by the Faculty of Nursing, Chulalongkorn University, Thailand (Thanasilp, 2013).

Scope of the study

This is a Randomised Controlled Trial to explore the effect of Qigong on the management of dyspnoea, fatigue, and anxiety (as a cluster) in lung cancer patients and the effect of Qigong on cough, which is another common symptom linked to dyspnoea, fatigue, and anxiety as a cluster, and QOL in lung cancer patients. This study was conducted in the Vietnamese population.

Significance of study

This study is expected to provide a contribution to nursing care in Vietnam and in other populations in the region. Firstly, this study aims to depict the Health Qigong for fatigue, dyspnoea, and anxiety in lung cancer patients. The effectiveness of existing interventions for fatigue, dyspnoea, and anxiety is currently modest, resulting in the need to design new interventions for these symptoms. The outcome of this research may reduce the occurrence of fatigue, dyspnoea, and anxiety in the studied population. It may be a new intervention to fatigue, dyspnoea, and anxiety, which are the most distressing and devastating symptoms in cancer patients. Thus, the findings of this study give some indications for symptom management not only for Vietnamese patients but also for patients in other countries. Secondly, this study was conducted in a Vietnamese population where qualified nursing care and nursing research are still in its infancy. Thus, the findings of this study would be a “pioneer” to open the door for subsequent study and practice.

CHAPTER TWO

LITERATURE REVIEW

The purpose of this study was to examine the effects of Qigong on dyspnoea, fatigue, and anxiety in lung cancer patients as a symptom cluster. This chapter presents the review of literature related to the study. Major issues addressed are: 1) lung cancer statistics in Vietnam, 2) symptom incidence in lung cancer, 3) fatigue in lung cancer, 4) dyspnoea in lung cancer, 5) anxiety in lung cancer, 6) cough in lung cancer, 7) health-related quality of life in lung cancer, 8) symptom clusters of dyspnoea, fatigue, and anxiety in lung cancer, 9) Qigong overview, 10) therapeutic effects of Qigong on symptom management in cancer populations, and 11) theories explaining symptom management.

2.1 Lung cancer statistics in Vietnam

Lung cancer is a malignant tumour in the tissue of one or both lungs. There are two types of lung cancer: Non-Small Cell Lung Cancer (NSCLC) is the most common and makes up approximately 80% of all lung cancers; while Small Cell Lung Cancer (SCLC) makes up about 20% of lung cancers. The three main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. The different types of lung cancer are classified according to the type of cell affected, as outlined in the following table (Sherief, Lau, Wu, Drake, Abbott, & Rice, 2014).

Type of lung cancer	Frequency	Other features
Non-small cell (NSCLC)	80-85%	The exact type of NSCLC needs to be diagnosed for optimal therapy.
Adenocarcinoma	35-40%	Most common type of lung cancer overall in women and in people who have never smoked.
Squamous cell carcinoma	25-30%	Highly associated with tobacco smoking.
Large cell carcinoma	15%	Can grow rapidly and spread more quickly than other forms of lung cancer.
Small cell (SCLC)	15-20%	These cancer cells multiply rapidly and form large tumours that can spread throughout the body. Current or former smoking is the usual cause.

Cancer is becoming the most problematic non-communicable disease in Vietnam (Vuong, Velasco, Lai, & Busse, 2009). Among the cancers, lung cancer has the highest incidence of 20,000 new cases every year. Most Vietnamese people are diagnosed with lung cancer after the age of 40 years (Bui, Le, & Nguyen, 2010). A study by Thang and Chuong (2012) reported that the most common age group for lung cancer is between 50 and 69 years of age (67. 9%). The male-to-female ratio is 2.8 to 1 (Nguyen & Tran, 2010). Most lung cancer patients in Vietnam are diagnosed in the hospital in advanced stages (65-80%) (Anh & Duc, 2002).

Interestingly, the Northern part of Vietnam showed a significantly higher proportion of lung cancer than the south (Anh & Duc, 2002). It is believed that the higher rate of smoking in the North than in the South is the main reason for this difference (Ngoan, 2006). Vietnam also showed a higher mortality from lung cancer than its neighbouring countries (21.5 per 100,000) (Kimman, Norman, Jan, Kingston, & Woodward, 2013). In addition, the treatment and care for lung cancer in Vietnam is limited (Phuong, 2013). Health sectors in Vietnam are classified into national, provincial, district, and community level. Currently, only several national hospitals can provide systematic cancer treatments (Hung, Minh, Dung, & Thinh, 2008). Therefore, most patients (80%) are referred to national hospitals for treatment.

Vietnamese patients suffer from various distressing symptoms, with fatigue, dyspnoea, and anxiety being the most prevalent. Palliative care is not readily available to the vast majority of Vietnamese cancer patients (Krakauer, Ngoc, Green, Van Kham, & Khue, 2007). The Ministry of Health explicitly stated that symptom relief is one of the five major goals in its national plan for cancer control (Phuong, 2014). The study by Tung (2010) demonstrated that, in comparison to all other cancers, lung cancer showed the highest need for palliative care.

2.2 Symptom incidence in lung cancer

Lung cancer is usually classified by histology as small cell or non-small cell cancer. Small cell lung cancer (SCLC) has an aggressive nature and poor response to treatment. It is primarily treated with frequent, intensive doses of chemotherapy. The median survival rate for people with localised SCLC is 14 months, or half that time for those with extensive disease (Murphy, Lawrence, & Lenhard, 1995). Surgery, radiation, and/or chemotherapy are used to treat the various types of non-small cell lung cancer (NSCLC). The median survival rate for people with NSCLC varies based

on the extent of disease and treatment modality. People with localised NSCLC treated with surgery and chemotherapy have a survival rate of approximately two years. The median length of survival for people with respectable tumours, treated with chemotherapy and radiation, is 20 months (Murphy et al., 1995).

The high mortality rates associated with lung cancer reflect the fact that the majority of patients are diagnosed when their lung cancer is at a relatively advanced stage. During the period of disease, patients may often undergo a range of invasive and/or toxin treatment potentially including surgical intervention, chemotherapy, and radiotherapy, along with supportive and palliative care. Patients' health also inevitably declines over this period because of both the illness trajectory and the side effects of treatment. A diagnosis of lung cancer and its treatment may also carry a variety of potentially adverse symptoms and psychological consequences for the patients and their families (Molassiotis & Lowe, 2010).

Patients with lung cancer reported having 1 to 27 symptoms (Gift, Stommel, Jablonski, & Given, 2003). The most commons symptoms in patients with lung cancer at any stage are characterised by symptoms of fatigue, cough, dyspnoea, anxiety, pain, loss of appetite, and insomnia (Chan et al., 2005; Chen, Nguyen, Cramarossa, Khan, Leung, Lutz, & Chow, 2011; Molassiotis et al., 2011a). A study of 152 patients showed that, on average, each lung cancer patient suffered from 10.4 ± 5.0 symptoms. The number of symptoms ranged from 7.8 to 13.2, and most of them were at a moderate level of severity (Liao et al., 2011). Therefore, patients with lung cancer are likely to experience multiple symptoms. Among those, fatigue, dyspnoea, and anxiety are the most severe and common symptoms (Chan, 2011).

2.3 Fatigue in lung cancer

Fatigue is the most common symptom of lung cancer. Surveys showed that nearly 90% of patients had fatigue in the past week (Lidstone, Butters, Seed, Sinnott, Beynon, & Richards, 2003). A large study (n = 1213) found that almost all patients with lung cancer (98%) reported fatigue (Iyer, Roughley, Rider, & Taylor, 2013). A longitudinal study shows that fatigue has always been considered one of the most common symptoms over 52 weeks, at a rate of 74.8% (Borneman, Ferrell, Koczywas, & Cristea, 2008). In Vietnam, a large cross-sectional study found that fatigue is the most common symptom of advanced cancer, including lung cancer (Vu, Hanh, Giang, & Hoang, 2010). Forty percent of advanced lung cancer patients reported moderate and 22% reported severe fatigue (Swanson, Dolce, Marsh, Summers, & Sheldon, 2008). According to Hung, Krebs, Coups, Feinstein, Park, Burkhalter, and Ostroff (2011), 41% of early stage lung cancer had mild fatigue and 16.8% had moderate or severe fatigue. A study in Vietnamese lung cancer patients receiving chemotherapy showed that fatigue is the most problematic symptom, with nearly 30% of patients reporting a severity score of fatigue higher than all other symptoms such as pain, difficulty breathing, coughing, or decreased appetite (Hung et al., 2008; Iyer, Taylor, & Roughley, 2013).

Phuong (2014) conducted a study in Vietnam to survey the effectiveness of supportive care (a combination of measures to relieve suffering and improve the quality of life of patients through the prevention, early detection, and treatment of physical and psychological symptoms, and to provide counselling and support to address social and spiritual problems that patients and their families are encountering) for cancer patients during and after anti-cancer treatments. A comparison of fatigue scores was made before and after receiving supportive care. Tiredness intensity was

statistically reduced from 70 to 62%. However, this change was not clinically significant because a difference should be referred to show a clinically meaningful improvement of the symptom (Maringwa et al., 2011). More significantly, the fatigue score after treatment in Vietnamese cancer patients is at an unacceptable level, which is still very high compared to its recommended reference mean value (Scott, Lasch, Barsevick, & Piault, 2011).

Fatigue negatively effects quality of life. Bozcuk, Dalmis, Samur, Ozdogan, Artac, and Savas (2006) found that fatigue was an important predictor of quality of life in advanced lung cancer patients with chemotherapy ($F = 7.92$, $p = 0.001$). Fatigue also hindered daily life activities (Swanson et al., 2008; Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2002), and impacted on patients' mental health (Tishelman, Petersson, Degner, & Sprangers, 2007). Additionally, fatigue could be linked to diminished survival (Scott, McMillan, Forrest, Brown, McArdle, & Milroy, 2002), the increased utilisation of healthcare services (Doyle et al., 2008), hospital readmissions (Borneman, Koczywas, Cristea, Reckamp, Sun, & Ferrell, 2008) or early referral to supportive care specialists (Reyes, Anderson, Shete, Bruera, & Yennurajalingam, 2012). Therefore, fatigue is a complex, multifactorial disorder with physical, mental, and psychological dimensions that have been associated with diminished QOL in patients with lung cancer.

2.4 Dyspnoea in lung cancer

"Dyspnoea is a subjective symptom with a sensory component of laboured breathing and an effective reaction expressed as distress" (Joyce et al., 2008). The American Thoracic Society (ATS) found many definitions of dyspnoea in the literature, including "difficult, laboured, uncomfortable breathing", "awareness of respiratory distress", "the sensation of feeling breathless or experiencing air hunger",

and “an uncomfortable sensation of breathing” (American Thoracic Society, 1999). In their own definition, ATS described dyspnoea as “a term used to characterise a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity”. Huhmann and Camporeale (2012) also defined dyspnoea as “a subjective experience of breathing discomfort”.

Dyspnoea is very prevalent symptom in lung cancer. Kathiresan, Clement, and Sankaranarayanan (2010) pointed out that the average prevalence reported by studies on dyspnoea in lung cancer was 70.5% with a range of 50% to 87%. In lung cancer, being dyspneic is frightening to both patients and caregivers (Williams, Grant, Tiep, Kim, & Hayter, 2012). Many factors can cause and exacerbate dyspnoea. Lung cancer, obstruction of pulmonary tissue, anaemia, hot weather, obesity, anxiety, and cancer treatments such as chemotherapy, biotherapy or radiotherapy are examples of those factors (Huhmann & Camporeale, 2012; Williams et al., 2012). Lai et al. (2007) mentioned that lung cancer patients received insufficient information about dyspnoea from nurses. They assumed that when the health care worker did not offer any information, it meant that there would be no solution for their problems.

Henoch, Bergman, Gustafsson, Gaston, and Danielson (2008) described the complexity of the dyspnoea experience, the influence of other variables on dyspnoea as well as the influence of dyspnoea on QOL in a sample of patients with lung cancer. The results showed that dyspnoea increased over time, with a significant deterioration in the sense of effort component, the relationship between QOL and dyspnoea was not consistent over time, and dyspnoea did not predict QOL in this group of patients. Thus, dyspnoea, a subjective, multidimensional experience of breathing discomfort commonly occurring in patients with lung cancer, influences all aspects of life in the lung cancer patients.

2.5 Anxiety in lung cancer

Anxiety is defined as "the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension" (American Psychiatric Association, 2005). A concept analysis by Whitley (1992) described that anxiety is a vague, uneasy feeling of discomfort or dread, stimulated by unknown or unspecific causes. Anxiety consists of both subjective responses and objective signs. Anxiety is a universal human experience and the most basic of emotions. Anxiety at the mild and moderate levels are constructive, which help the sufferers deal with the situation. However, at the severe and panic levels, anxiety is destructive and negative effected on quality of life. It diminishes patients' physical and mental function, resulting in exhaustion (Townsend, 2009).

Anxiety is common among psychological problems of lung cancer patients. It is presented in 40% of advanced lung cancer patients and the prevalence is not different between in and out-patient groups (Du, Wood, Burch, Grutsch, Gupta, Tyer, Lis, Levin, Quiton, Reynolds, & Hrushesky, 2010). Anxiety was reported by nearly every patient with early stage (IA or IB) disease in lung cancer (Hung et al., 2011). Pirl, Temel, Billings, Dahlin, Jackson, Prigerson, Greer, and Lynch (2008) conducted a study with a heterogeneous lung cancer stage sample and found that 32.6% of patient demonstrated anxiety (HAD-A $\geq$ 8).

Anxiety is also a long lasting problem in lung cancer. Feinstein, Krebs, Coups, Park, Steingart, Burkhalter, Logue, and Ostroff (2010) investigated 342 long-term lung cancer survivors and found that 20.2% of the respondents reported anxiety (HAD-A $\geq$8). The level of anxiety was mild (HADS score was around five) and did not change over 12 months (Henoch, Bergman, Gustafsson, Gaston, & Danielson, 2007). Anxiety in lung cancer is also characterised by its severity. Genç and Tan (2011) examined

lung cancer patients undergoing chemotherapy by used the Brief Symptom Inventory. The results showed that patients suffered from noticeable level of anxiety. While the maximum possible score was 10, the mean score of anxiety was 5.8 ± 2.38. Hopwood and Stephens (2000) demonstrated that 34% of lung cancer patients self-reported anxiety, of whom 18% were at the level of probable case and 17% were at the level of borderline severity. According to Henoch et al. (2007), QOL significantly correlated with anxiety over time. Therefore, the symptom of anxiety is common in patients with lung cancer and may have an impact on both health-related qualities of life and survival (Polanski, Jankowska, Rosinczuk, Chabowski, & Szymanska, 2016).

2.6 Cough in lung cancer

Fontana and Widdicombe (2007) defined cough as "a violent expulsion of air from the lungs with a characteristic sound". According to the Thoracic Society Cough Guideline Group, cough is "a forced expulsive manoeuvre, usually against a closed glottis and which is associated with a characteristic sound" (McGarvey & Morice, 2006; Pavord & Chung, 2008). Cough consists of three phases, including an initial inspiration, the closure of the glottis and a forced expiratory effort, and the opening of the glottis and vigorous expiration. Coughing may occur as a single event or may include several or many expiratory efforts in a single episode (Fontana & Widdicombe, 2007).

In general, coughing is a reflex which protects the airways by forcibly removing obstructive or harmful substances. However, in lung cancer, a cough appears as a common and distressing symptom. The prevalence of coughing is about 80% in patients with lung cancer (Harle, Blackhall, Smith, & Molassiotis, 2012). This symptom presents in all stages and types of lung cancer. It occurs regardless of treatment modalities, such as chemotherapy, radiation therapy, and palliative care

therapy (Chernecky, Sarna, Waller, & Brecht, 2004). Coughing is present in more than 65% of patients at diagnosis with lung cancer, and a productive cough is present in a one-quarter of patients (Kvale, 2006).

Various factors contribute to the occurrence of coughs in lung cancer. They are centrally located tumours, bleeding tumours, infection, COPD, smoking, or anti-cancer treatment (Harle et al., 2012). These factors trigger the receptors of nerve fibres, which are distributed throughout the ciliated epithelial cells of airways from the pharynx to the terminal bronchioles (Cotes, Chinn, & Miller, 2009). The greatest concentration of cough receptors is found in the larynx, carina, and at the bifurcation of medium- to large-sized bronchi (Simpson & Amin, 2006).

2.7 Health-related quality of life (QOL)

Most patients with lung cancer and mesothelioma experience multiple symptoms, the number and severity of which increase as the disease progresses (Cooley, 2000; Lutz, Norrell, Bertucio, Kachnic, Johnson, Arthur, Schwarz, & Palardy, 2001). These physical symptoms in combination with psychological distress have a negative impact on the patients' QOL. Thus, the goals of cancer care in patients with advanced disease are symptom control, psychosocial support and improved or maintained QOL, as well as increased short-term survival (Porzsolt & Tannock, 1993). There is no gold standard definition of QOL. In 1948, the World Health Organisation (WHO) defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". QOL represents the influence of an illness and its treatment on physical and psychological functioning, as perceived by the patient. It has been defined as "patients' appraisal of and satisfaction with their current level of functioning compared with what they perceived to be possible or ideal" (Cella & Tulsky, 2009). QOL is a multidimensional concept. Most investigators agree

that it includes four dominant dimensions: 1) physical/occupational function, 2) psychological state, 3) sociability, and 4) somatic comfort (Nicklasson, 2013). QOL is also a dynamic parameter and changes over time (Schipper, Clinch, & Olweny, 1996).

There is very little literature that comprehensively and systematically describes the relationship between dyspnoea, fatigue, and anxiety perceptions and life quality in cancer patients specifically, or in the smaller subset of patients with lung cancer (Smith, 1992). In older studies, Fernandez, Rosell, Abad, Monras, Moreno, Serichol, and Roviralta (1989) studied the effect of chemotherapy on illness-related symptoms in advanced stage lung cancer patients. Patients who experienced symptom relief also reported improved life quality. Kaasa and Mastekaasa (1988) also found a relationship between disease-related symptoms and psychosocial well-being. The most relevant study by Dales and colleagues investigated QOL and dyspnoea following thoracic surgery in patients who were suspected of having lung cancer (Dales, Bélanger, Shamji, Leech, Crépeau, & Sachs, 1994). Although these studies support a relationship between symptoms and life quality, they were not designed to investigate the relationship specifically between dyspnoea and QOL.

In summary, conclusions regarding an interrelationship between three symptoms (dyspnoea, fatigue, and anxiety), cough and QOL cannot be made based on the currently available research. In addition, no studies have empirically examined the impact of the above symptoms on QOL in lung cancer population. This information may be useful in designing interventions aimed at symptom relief and improved QOL for lung cancer patients.

2.8 Symptom clusters of dyspnoea, fatigue, and anxiety in lung cancer

The term ‘symptom cluster’ was first conceived by Dodd, Miaskowski, and Paul (2001) to describe this phenomenon. Dodd and colleagues characterised a cluster as involving three or more interrelated concurrent symptoms that may or may not share a common aetiology. Kim, McGuire, Tulman, and Barsevick (2005) later proposed that two or more related symptoms occurring together, but relatively independent of other symptoms, constitute a cluster. Despite discrepancies in the present definition of symptom clusters, consensus does prevail among many researchers regarding the inverse correlation between the number or severity of symptom clusters experienced and the functional status of patients (Barsevick, Dudley, & Beck, 2006; Xiao, 2010).

The most common symptoms of lung cancer include breathlessness, coughing, fatigue, pain, insomnia, weight loss and anxiety (Cooley, 2000). Studies by Cheville et al. (2011) and Molassiotis et al. (2011) have identified fatigue, dyspnoea and cough as a rather consistent symptom cluster in this cancer population. However, only fatigue and dyspnoea were associated with poor patient outcomes. Chan et al. (2005) conducted a study on lung cancer patients undergoing palliative radiation treatment and identified a cluster of breathlessness, fatigue, and anxiety. Individuals with lung cancer are known to experience more symptom distress when compared with patients diagnosed with any other type of cancer (Degner & Sloan, 1995). Brown et al. (2011) explored symptom clusters in women with lung cancer. It was found that the participants suffered from several clusters which consisted of four to six concurrent symptoms. Although these clusters were different, fatigue and dyspnoea were essential parts of all. A longitudinal study with 103 lung cancer patients investigated the change in symptoms over 52 weeks. It was reported that fatigue and dyspnoea are the most prevalent symptoms among lung cancer patients. Longitudinal assessments

showed that fatigue remained consistently as the highest ranked symptom, with a prevalence ranging from 74.8% to 90.3%. Similarly, dyspnoea was described as the third most common symptom at baseline, and the second most common symptom in all follow-up points (Koczywas et al., 2013).

Lai et al. (2007) conducted a qualitative study to explore the experience with dyspnoea in lung cancer patients who were diagnosed with the disease from 1 to 12 months previously. Respondents described a lot of suffering, while several patients mentioned that if they could choose, they would opt to suffer from pain rather than dyspnoea. Some patients even stated the desire to end their lives because of dyspnoea (Lai et al., 2007). Dyspnoea was significantly associated with fatigue (Chen, Antras, Duh, Neary, & O'Brien, 2008; Wang, Tsai, Chen, Lin, & Lin, 2008). Cough and dyspnoea were also associated ($r = 0.47$) (Kuo & Ma, 2002).

Cheville et al. (2011) indicated that fatigue, cough, and dyspnoea constituted a cluster with the factor loadings of 0.68, 0.5, and 0.67, respectively. Fatigue has an immediate impact from dyspnoea (Henoch, Bergman, & Danielson, 2008). Sleep disturbance and breathlessness result in the exacerbation of fatigue (Molassiotis et al., 2011a). Fatigue was associated with anxiety ($r = 0.46$), depression ($r = 0.48$), and confusion ($r = 0.49$). Brant, Beck, and Miaskowski (2010) indicated that patients with more advanced disease showed more intense fatigue. Xará, Amaral, and Parente (2011) found that patients who were classified as undernourished had greater fatigue ($r = 0.54$) and lower quality of life ($r = - 0.42$). Anxiety and insomnia were also associated ($r = 0.36$), and anxiety was related to fatigue ($r = 0.31$) (Liao et al., 2011). Stone, Richards, A'Hern, and Hardy (2000) showed that anxiety was significantly associated with fatigue ($r = 0.67$).

In conclusion, the concept of symptom clusters has been of more concern

recently, with most research focusing on heterogeneous populations of cancer patients. Several studies have been examining empirically derived symptom clusters in lung cancer patients. All studies used varying analytical methods, assessment tools, and follow-up intervals. Such decisions must be made in the context of the goals of the research as well as practical and ethical considerations. More research is needed to address the treatment of a target symptom and its effect on other symptoms. The results suggest the need for nursing interventions on symptom cluster management for better quality of life in lung cancer patients.

2.9 Qigong overview

The Complete Book of Contemporary Chinese Qigong counted 182 different Qigong groups and 161 types of Qigong. Qigong is typically understood as an emblematic, trans-historical carrier of an intangible Chinese national essence linked, tenuously, to key figures in Chinese history. It defines qigong as follows: Taking the strengthening of the harmony [xietiao xing] of humanity's organism as its primary goal, using the adjustment of mind [tiaoxin], breath [tiaoxi] and posture [tiaoxing] to cultivate heart and mind [shenxin], that is Qigong (Li, 1988).

Accordingly, Qigong is a process of self-consciously cultivating one's 'life activities', including breath, thought (siwei), and physical body, of which thought is the most important. These activities should be goal-oriented, conscious (yishi), and planned (jihua) and therefore completely different from the instincts of animals. They should first and foremost benefit the health of people, for example, by promoting physical vigour (yuan qi), fighting disease, promoting self-healing abilities and intelligence, and developing the human potential. Any such techniques that allow the practitioner to enter a 'Qigong state' (qigong tai) where 'body and mind are one' (shenxin ru yi) and one 'forgets both oneself and everything else' (wu wo liang wang)

can be called Qigong (Wang, Li, Liu, Luo, Ma, & Alraek, 2014).

"Qi" means vital energy and "gong" means discipline. According to Traditional Chinese Medicine theory, the concept of qi includes the air we breathe in, yuan qi (innate vital substance), jing qi (qi that flows in the meridians), and the qi derived from nature. Besides that, "gong" regarded the improved functions of internal organs through Qigong practice. Qigong is mainly composed of five elements: visualisation, meditation, relaxation, deep breathing, and target qi circulation. Qigong puts emphasis on the control of the mind-states, posture, and breath. There are different ways to classify Qigong; one is to categorise it according to the five key religious or theoretical backgrounds, including Confucianism, Buddhism, Taoism, medical, and martial arts. Each approach has its own aim, discipline, and application. Taoists aim at the preservation of the physical body, high virtue, and ultimately for longevity. The Buddhists emphasise the liberation of mind, tranquillity in meditation, and the obtainment of enlightening wisdom. The Confucians focus on attaining high moral character and intelligence (Chen, Liu, & Liu, 2010).

Qigong has long been regarded as a form of "mind-body" intervention in Traditional Chinese Medicine, which simultaneously exercises the "mind" and the "body" for treating many chronic diseases and promoting wellness. About a hundred million people are currently practicing Qigong in China (Chen, Meng, Milbury, Bei, Zhang, Thornton, Liao, Wei, Chen, & Guo, 2013). Qigong is now regarded as a form of self-practise mind-body exercise and recently relevant to sports activity, which is officially known as "Health Qigong". This is different from "Medical Qigong" which involves a TCM practitioner to emit "Qi" to heal the patients (Tsang, Mok, Au Yeung, & Chan, 2003).

The practice of Qigong is based on the principle of integrating and harmonising

the mind, breathing, posture, and movement. Qigong emphasises focusing attention by using visualisation and/or autosuggestion, coordinating breathing with movement, aligning proper posture, especially the spine, interlacing muscle contraction and relaxation in a rhythmic sequence, and recruiting movements or muscle activities that are not commonly used in daily activities and are distinct from other forms of aerobic and/or stretching exercise (Tsang, Cheung, & Lak, 2002).

Although the physical property of "Qi" is still a subject of debate in modern science, "Qi" might be a form of vibration energy derived from rhythmic body movements, and usually identified at acupressure points (Wang, Li, Liu, Luo, Ma, & Alraek, 2014). This form of vibration energy was proposed to work in resonance with the heartbeats for the promotion of blood circulation, which was an essential factor for good health. This also partially explained the close relationship between "Qi" and "blood" within the traditional Chinese medicine context (Ng, 2009). The two theories also provide guidance for the practice of Qigong. For example, movements are always balanced; "breathing in" representing "Yang" is balanced with "breathing out" representing "Yin", and "bending down" as "Yin" is balanced with "straightening up the body" as "Yang". Moreover, certain acupressure points along the meridians are the focus of attention during practice. For example, focusing on the Mingmen point at the lumbar region and Dazhui point at the cervical region serves to prompt people to properly align their spine. Focusing on the Dantian point serves to prompt people to breathe slowly and deeply (Chen et al., 2010).

A body organ becomes dysfunctional and gradually manifests as diseased when "Qi" is either in excess or in deficiency states due to obstruction or disruption of "Qi" flow within the channels and collaterals. The underlying causes may be related to extreme emotions, improper eating habits, lack of rest, overworking, lack of exercise,

mental exhaustion, and/or drugs. When sick, the channels and collaterals must be dredged through a certain kind of force. The movements and mental regulation in Qigong practice are believed to stimulate and maintain stretching to the channels and collaterals, thus exerting a force to dredge the blockage to facilitate the flow of "Qi". Patent "Qi" flow serves to regulate the Yin and Yang forces by redirecting "Qi" from excessive accumulation to areas of "Qi" deficiency, thereby restoring the body to a balanced state (Chen et al., 2010).

With regards to the effects of Qigong on organ functions, Qigong balances parasympathetic sympathetic action (Crampton, 1995), increases circulation and decreases blockage in various energy channels (Sancier & Hole, 2001), increases vital energy to distribute nourishing nutrients and oxygen supply to cells, tissues, and accelerate the extraction of waste from the body, increases concentration and relaxation of the body and increases alveolar ventilation by activating gas exchange. In addition, Qigong increases gastrointestinal juices, gastrointestinal absorption and waste excretion, increases red blood cells, improves and reinforces microcirculation (Crampton, 1995), increases circulatory function, which reduces collagen formation in bones and lactic acid in the muscles (Sancier & Hole, 2001), and increases skin temperature and regulates skin resistance (Crampton, 1995).

In summary, Qigong is a form of meditative movement. Qigong roughly means "to cultivate Qi", and Qi is considered to be the inherent functional, energetic essence of human beings in traditional Chinese medicine (Jahnke, 2010). Qigong consists of a series of simple, repeated practices including body posture/movement, breathing practice, and meditation performed in synchrony. It consists mostly of gentle movements designed to bring deeply relaxed states. Qigong is typically a repetitive practice that is simple and very easy to learn (Haak & Scott, 2008).

2.10 Therapeutic effects of Qigong on symptom management in cancer populations

A systematic review of the literature has been conducted with this topic by the candidate. In addition, part of it was published in the Journal of Complementary Therapies in Clinical Practice (Vu, Molassiotis, Ching, & Le, 2017). The following is a detailed summary of this systematic review.

The effects of Qigong have been investigated on various populations (including healthy older people, chronic disease and cancer). It is most consistently supported to improve or manage physiological and psychological symptoms such as cardiorespiratory, physical function, balance, falls prevention, symptoms distress (including fatigue), mood, bone health and quality of life (Jahnke, 2010).

Qigong for symptom management is common in cancer populations. Recently, many studies have found that there may be benefits of Qigong for cancer populations during and after the intervention, including reductions in tiredness, breathlessness, improved mood, cognitive and physical functions and also improve quality of life (Oh , 2010). Campo (2014) conducted a study which focused on prostate cancer survivors using health Qigong and found significant improvements in fatigue and emotional distress. A systematic review of many studies on Qigong and associated changes in biomarkers among cancer patients even suggested the potential for Qigong to prolong life (Lee, Oh, & Ernst, 2011; Oh, Butow, Mullan, Hale, Lee, Guo, & Clarke, 2011; Zeng, 2014).

However, some other reviews have indicated that the evidence is not convincing enough to suggest that Qigong is an effective supportive cancer treatment (Oh, 2012; Zeng, 2014). Many of these purported outcomes are vaguely defined and may overlap. There is also some concern over the safety aspects of Qigong (Oh, 2014),

particularly when used with conventional cancer treatments such as chemotherapy and radiotherapy. Moreover, all of the previous systematic reviews mentioned above explored the effectiveness of Qigong on a single symptom only or symptom distress in cancer patients. There is a lack of a review to examine the benefit of Qigong on a variety of symptoms in cancer patients and synthesise the broader picture of Qigong in the available evidence. In addition, several new studies have been published since the last published review (Zeng, 2014). Hence, a thorough systematic review of the evidence is necessary to provide healthcare professionals with the information on which to base clinical judgments.

The aim of the systematic review was to critically evaluate the effectiveness of Qigong on symptom management in cancer patients. The specific questions addressed were: (1) Does Qigong reduce physical symptoms? (2) Does Qigong reduce psychological symptoms? (3) Does Qigong improve the quality of life? (4) Does Qigong produce any unwanted side effects?

Inclusion criteria

(a) Randomised controlled trials (RCTs), clinical trials (quasi-experimental trials and trials where there was a comparison group but no mentioning of randomisation), and feasibility trials involving adult participants (with 18 years old and above) with a diagnosis of cancer and receiving care in any healthcare setting; (b) Eligible intervention: Trials that compare Qigong interventions with usual care, placebo or other interventions to manage symptoms in cancer patients. Trials which tested the Qigong intervention, which is initiated during or after cancer treatment; (c) Eligible outcomes were patient-reported physical symptoms (fatigue, pain, dyspnoea, and weakness, lack of energy, nausea, dry mouth, constipation, early satiety, vomiting, and anorexia) and/or psychological symptoms (depression, anxiety, and mood

disturbance) and quality of life (using reliable and valid assessment tools). All studies were required to report the above symptoms as a primary or secondary outcome and studies including outcome either measures of symptoms as continuous measures or as dichotomous outcomes were included.

Exclusion criteria

(a) Trials that involved people who were receiving hospice care or were at the end of their life; (b) Observational and other types of studies such as prospective and retrospective cohort studies, case-control studies, qualitative studies, and analytical cross-sectional studies.

Primary and secondary outcomes of the systematic review

Primary outcomes for this review were changes in physical symptoms (fatigue, pain, dyspnoea, weakness, lack of energy, nausea, dry mouth, constipation, early satiety, vomiting, and anorexia) or psychological symptoms (depression, anxiety, and mood disturbance) and quality of life related to cancer patients who had undertaken a Qigong intervention, compared to those who had not. Secondary outcomes for this review were adverse events, referring to any harm caused to participants from the Qigong intervention.

Search strategy

The search strategy aimed to find both published and unpublished studies. A three-step search strategy was utilised in this review. An initial limited search of MEDLINE and CINAHL was undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe an article. A second search using all identified keywords and index terms was undertaken across all included databases: Cochrane Library, PubMed, MEDLINE, CINAHL, PsycINFO, PEDRO. Thirdly, the reference lists of all identified reports and articles were searched

for additional studies. Studies published in The Chinese Clinical Trial Registry (http://www.chictr.org.cn) and trial registry of the US National Institutes of Health (http://clinicaltrials.gov) were considered for inclusion in this review. The databases were searched including electronic databases from their inception through December 2015.

Assessment of methodological quality

Research papers were selected for retrieval, based on assessment for inclusion, were assessed by two reviewers independently using the Cochrane Collaboration's Tool for Assessing Risk of Bias (The Cochrane Collaboration, 2011). This mainly consists of seven domains: (1) Random sequence generation (for checking potential selection bias); (2) Allocation concealment (for checking potential selection bias); (3) Blinding of participants and personnel (for checking potential performance bias); (4) Blinding of outcome assessment (for checking potential detection bias); (5) Incomplete outcome data (for checking potential attrition bias); (6) Selective reporting (for checking potential reporting bias); and (7) Other bias.

Any disagreement between the reviewers about the criteria or level of bias were discussed until a mutual decision was reached, or with the arbitration of a third reviewer. Where necessary the study authors were contacted to obtain more information that is detailed. Assessment of the reliability and validity of the assessment tools were based on the information provided in each report.

Quality appraisal

The strength of the evidence was evaluated for all included studies using the Oxford Centre for Evidence-based Medicine Levels of Evidence (Oxford Centre for Evidence-based Medicine, 2009). This mainly consists of ten domains: (1a) Systematic review (with homogeneity) of inception cohort studies; Clinical Decision Rule

validated in different populations; (1b) Individual inception cohort study with >80% follow-up; Clinical Decision Rule validated in a single population; (1c) All or none case-series; (2a) Systematic review (with homogeneity) of either retrospective cohort studies or untreated control groups in RCTs; (2b) Individual cohort study (including low-quality RCT; e.g., <80% follow-up);

(2c) "Outcomes" Research; Ecological studies; (3a) Systematic review (with homogeneity) of case-control studies; (3b) Individual Case-Control Study; (4) Case-series (and poor-quality prognostic cohort studies); and (5) Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles".

Data extraction

Data from included studies were extracted independently, discussed and collected by two reviewers using a data extraction form. For each eligible study, the following information were extracted and recorded: (1) Name of first author and country, (2) year of publication, (3) participants' characteristics, (4) sample size, (5) intervention and control group information, (6) duration of intervention, (7) primary and all other outcome measures, and (8) results.

Data synthesis

All results were subject to double data entry. Where statistical pooling was not possible, the findings were presented in a narrative form including tables and figures to aid in data presentation where appropriate. For continuous variables, weighted mean differences were calculated when outcomes were measured using the same scale, and the standardised mean differences were used, with corresponding 95% confidence intervals. The following source of heterogeneity among included studies was presumed: types of intervention (Qigong), types of cancer.

Results of the systematic review

The search of the literature retrieved 2082 citations, of which 1816 records were excluded on the basis of the title and abstract alone because of non-relevance (n = 1509) or duplication (n = 307). The full texts of the remaining 266 articles were retrieved for more detailed evaluation and 247 papers were excluded because: 1) they included herbs or another medicine (n =115); 2) Qigong was combined with other non-Qigong intervention (n =63); 3) no relevant outcomes (n =22); 4) Case study (n = 7); 5) insufficient information (n = 39); and 5) Duplicate publication contents (n = 1) [Two papers reported the same findings of the same study that may be duplicate publication (Loh & Lee, 2015; Loh, Lee, & Murray, 2014), and hence only one of these two papers was included in the analysis]. An additional three articles were gleaned from reference lists and incorporated, for a total of 22 studies included in this review.

Study characteristics

Included reports covered the period from 1995 to 2015 and were conducted in Hong Kong, China, Taiwan, Malaysia, South Korea, United States, Israel, and Australia. The trials comprised 1751 patients including breast cancer, prostate cancer, gynaecological cancer, nasopharyngeal cancer, unresectable hepatocellular carcinoma, metastatic colon cancer, non-Hodgkin's lymphoma, advanced lung cancer, and gastrointestinal cancer. Timing of interventions ranged from an early stage in the treatment through the recovery phase. The median intervention duration was six weeks (ranging from 3 weeks to 24 weeks). Supervised training frequency varied from one to three times per week (Table 1).

Risk of bias analysis

Each trial was evaluated in terms of its risk of bias. Sixteen (73%) of the reports had a high risk of bias, and six (27%) had low risks of bias. Major sources of risk of bias were a lack of blinding, allocation concealment, and incomplete outcome data. Of

the twenty-two studies, only twelve (55%) studies described the method of blinding and methods of allocation concealment. Less than half of the twenty-two reports provided specified numbers and reasons for dropouts by each subject group. No more than 30% of the twenty-two reports provided information on the method of randomisation used.

Effects of the Qigong on symptom management

Effects are described according to outcome measures: symptoms including fatigue (10/22), sleep disturbance (3/22), pain (3/22), depression (2/22), anxiety (2/22), dyspnoea (2/22), strength, appetite, diarrhoea or irregular defecation (2/22), mood disturbance (1/22), neuropathy symptoms and sexual function (1/22), and overall QOL (10/22 of the comparisons), other clinical outcomes involving vital capacity (3/22) and body mass index (BMI) (3/22) (Table 1).

Twenty-two studies including fourteen randomised trials and eight controlled clinical trials examined the efficacy of Qigong in symptom management among patients with various cancers. The results of these studies indicated that symptoms in the Qigong group were significantly improved at post-intervention compared with the control group or there was an observed positive trend from pre- to post- intervention scores for physical symptoms (fatigue, pain, dyspnoea, weakness, lack of energy, nausea, dry mouth, constipation, early satiety, vomiting, and anorexia) or psychological symptoms (depression, anxiety, and mood disturbance) and quality of life related to cancer patients as primary or secondary outcomes.

Physical symptoms: Fatigue was evaluated in ten reports involving 844 participants. Qigong significantly lowered fatigue in seven studies (Campo, 2014; Chen et al., 2013; Fu & Zou, 1995; Hong, 2003; Huang, Tseng, Chien, Tai, Chen, Hung, & Hsiung, 2016; Larkey, Roe, Weihs, Jahnke, Lopez, Rogers, Oh, & Guillen-

Rodriguez, 2015; Oh B, 2010). However, no significant effect was found in three studies (Fong, Ng, Luk, Chung, Wong, & Chung, 2014; Loh & Lee, 2015; Oh, Butow, Boyle, Beale, Costa, Pavlakis, Bell, Davis, Choi, & Lee, 2014). Four trials involving 357 patients evaluated Qigong on sleep level using the Pittsburgh Sleep Quality Index (PSQI) and Verran and Snyder-Halpern Sleep Scale (VSHSS) as an outcome measure. A significant effect was only observed in one study (Yeh, 2016). There was no significant effect for this symptom in two studies (Chen et al., 2013; Larkey et al., 2015).

Table 1. Clinical Studies of Qigong on symptom management in cancer population

Author, Year, and Country	Design	Diagnosis	Sample size	Intervention/ Duration/follow	Time intervention	Control Condition	Outcome measures	Results	Adverse effect	Level of evidence
Campo, 2014 USA	RCT	Prostate cancer	N = 40 QC: 20/16 CG: 20/13	Tai –chi Qigong 60 min/ session, 2 times per week 12 weeks	Cancer survivors	Nonaerobic Stretching	1) Fatigue (FACIT –F) 2) Distress (BSI – 18)	1) p = 0.02 2) p < 0.05	Safe and feasible	A (2b)
Chen, 2013 China	RCT	Breast cancer	N = 96 QG: 49 CG: 47	Guolin new Qigong 40 min/ session, 5 times per week 6 weeks	Receiving 5 to 6 weeks Radiotherapy	waiting-list with usual care	1) Depressive symptoms (CES-D) 2) Fatigue (BFI) 3) QOL (FACT-G) 4) Sleep disturbances (PSQI)	1) p = 0.04 2) p < 0.01 3) p < 0.05 4) No significant changes	No reports	A(1b)
Gamus, 2014 Israel	RCT	Gynecological cancer	N = 60 TC/QG: 30 CG: 30	Tai-chi/Qigong 45 min/section once a week for 10 weeks	Receiving first or second line of CT	Usual medical care	1) Overall QOL (FACT-G) 2) Fatigue (LFS)	1) p < 0.05 2) P < 0.05	No reports	A(2b)
Fong, 2013 Hong Kong	CCT	Breast cancer	N = 23 QG: 11 CG: 12 HT CG: 16	18 forms Tai-chi internal Qigong Unclear about duration 6 months	Cancer survivors	Usual medical care	1) Muscular strength 2) QOL (FACT-B)	1) Significantly improved 2) No significant changes	No reports	B(2b)
Fong, 2014 Hong Kong	CCT	Nasopharyngeal Cancer	N = 52 QC: 25 CG: 27	18 forms Tai-chi internal Qigong 90 min/section weekly 6 months	Completed all cancer treatments	Usual medical care	1) Fatigue 2)QOL (QLQ-C30 and QLQ-H&N35)	All with no significant changes	Safe and feasible	B(2b)
Fong, 2015 Hong Kong	RCT	Nasopharyngeal Cancer	N = 52 QC: 25 CG: 27	18 forms Tai-chi internal Qigong 90 min/section weekly 6 months	Completed all cancer treatments	Usual medical care	1) Flexion ROM 2) TMJ mobility 3) Sleep disturbance	1) p < 0.008 2) p = 0.70 3) p = 0.037	No reports	A (1b)

Fu and Zou, 1995 China	RCT	Gastric cancer	N = 20 QG: 10 CG: 10	Qigong exercise (3 times daily) 4 weeks	Unclear about time of intervention	Usual care	1) Physical function 2) Symptoms	1) Response rate: p = 0.54 between the two groups. 2) Symptoms improved significantly (p-value not reported): QG: 80% CG: 70%	No report	B (2b)
Fu and Wang, 1995 China	RCT	Late stage Stomach Cancer	N = 40 QG 22 CG18	Qigong plus herbal medicine Unclear about duration 3 months	Unclear about time of intervention	Herbal medicine	1) symptoms checklist & quality of life	1) $p < 0.05$	No report	B (2b)
Hong, 2003 South Korea	CCT	Advanced gastric cancer	N = 24 CQ: 12 CG: 12	Yudong Kong exercise plus chemotherapy 15-20 min, twice per day 8 weeks	Unclear about time of intervention	Usual care	1) Fatigue (Piper fatigue scale) 2) Physical functioning (PF, SF-36) 3) Chemotherapy side effects	1) $p<0.05$ after 4 weeks, $p< 0.01$ after 8 weeks 2) $p<0.01$ after 4 weeks, $p < 0.001$ after 8 weeks 3) Nausea and vomiting: $p<0.05$ after 4 weeks, $p> 0.05$ after 8 weeks Stomatitis: $p<0.001$ After 8 weeks	No report	B(2b)
Huang, 2016 Taiwan	Qua-si CCT	Breast cancer	N = 95 SQC: 31 NSQG: 33 CG: 31	Sporting Qigong 30 min/3 times/week 3 months	During Chemotherapy	Non-sporting Qigong Post-surgical excise	1) Frailty (EFS) 2) Physical component 3) QOL (SF36-T)	1) $p < 0.01$ 2) No Significant changes 3) $p < 0.01$	No report	B (2b)
Lam, 2004 China	RCT	Hepatocellular carcinoma	N = 58 QG 29/13 CG 29/14	Guolin Qigong exercise plus TACE (2-hour class, twice weekly for 6	Unclear about time of intervention	TACE only	1) Survival rate 2) Quality of life (SF-36)	1), 2) No Significant changes	No report	A(2b)

				weeks plus home-based exercise, daily), 24 weeks						
Larkey, 2015 USA	RCT	Breast cancer	N = 101 QC/TCE: 49/42 SQG: 52/45	Qigong/Tai Chi Easy (QG/TCE) 60min/section Meeting twice/week in first two weeks Practice 30min/day 5days/week 12 weeks	Completion of primary treatment	Sham Qigong (SQG)	1) Fatigue (FSI) 2) Depression (BDI) 3) Sleep disruption (PSQI)	1) 12 weeks (p = 0.005) 3 months (p = 0.024) 2) 12 weeks (p = 0.725) 3 months (p = 0.902) 3) 12 weeks (p = 0.136) 3 months (p = 0.239)	No report	A (1b)
Lee, 2006 Taiwan	CCT	Breast cancer	N = 67 QG: 32 CG: 35	Chan-Chuang Qigong (15-60 min daily) 3 weeks (21 days)	Doing chemotherapy	Usual care	1) Symptom distress (Pain, numbness, heartburn and dizziness) 2) Psychological distress	1) $p < 0.05$ after intervention 2) Overall severity of psychological distress not improved ($p>0.05$).	No report	B(2b)
Loh, 2015 Malaysia	RCT	Breast cancer	N = 197 Qigong: 66 Placebo: 65 CG: 66	Zhi Neng Qigong 90 min/section 8 weeks Follow -up12 months	Completed primary treatment	Placebo Usual care	1) QOL (FACT-B) 2) Distress (DASS) 3) Fatigue (FACIT-F)	1) QOL Qigong/Placebo p = 0.036 Qigong/Control p = 0.048 2) $p > 0.05$ 3) $p > 0.05$	No report	A (1b)
Oh, 2014 Australia	RCT	Metastatic Breast cancer	N = 27 MQ: 14 MC: 13 Follow-up < 80%	Medical Qigong 60 min/section 2 times/week 10 weeks	Unclear about time of intervention	Meditation	1) QOL (FACT-B) 2) Fatigue (FACT – F) 3) Stress (PSS)	1) QOL (p = .084) 2) Fatigue (p = 0.71) 3) Stress (p = 0.52) 4) Neuropathy symptoms	Safe and feasible	A (1b)

							4) Neuropathy symptoms (FACT/GOG-NTX) 5-7) Sexual function (SFQ)	(p = 0.014) 5) Sexual satisfaction (p= 0.55) 6) Sexual activities (p = 0.95) 7) Sexual relationship (p = 0.79)		
Oh, 2012 Australia	RCT	Various cancers	N = 81 QG: 37/23 CG: 44/31	Medical Qigong, 90-min/ session, twice per week 10 weeks	Unclear about time of intervention	Usual care	1) Cognitive function (FACT-Cog) 2) QOL (FACT-G)	1) p = 0. 014 2) p < 0.001	No report	A (1b)
Oh, 2010 Australia	RCT	Various cancers	N = 162 QG: 79/54 CQ: 83/54	Medical Qigong exercise 90 min/section twice per week 10 weeks	Unclear about time of intervention	Usual medical care	1) Overall QOL (FACT-G) 2) Fatigue (FACT-F) 3) Mood disturbance (PMS)	1) Overall QOL improved ($p < 0.001$) 2) Fatigue improved ($p < 0.001$) 3) Mood disturbance improved ($p = 0.021$)	Safe and feasible	A (1b)
Oh, 2008 Australia	RCT	Various cancer	N = 30 QG:15/8 CG:15/10	Medical Qigong exercise plus usual medical care (90 min, twice a week), 8 weeks	Unclear about time of intervention	Usual medical care	1) QOL (EORTC QLQ-C30), 2) Symptoms of the side effects of treatment	No significant difference between the two groups	No report	A (2b)
Sun, 1998 Taiwan	CCT	Advanced stage of various cancers	N = 127 QG: 97 CG: 30	Qigong (2 hour daily for 3 months), 3 months	Unclear about time of intervention	Usual medical care	1) Strength 2) Appetite 3) Diarrhea or defection	All with significant difference (no p value reported)	No report	B(2b)
Thongteratham, 2015 Thailand	RCT	Breast cancer	N = 30 QC: 15 CG: 15	18 forms Tai-chi 60 min/section 3 times/week	After treatment completion	Usual care	1) Fatigue 2) QOL	1) p = 0.002 2) p = 0.004	No report	A (1b)

				12 weeks						
Wang, 2002 China	CCT	Various cancers	N = 211 QG: 104 CG: 107	Qigong 2.5 – 3.5 months	Unclear about time of intervention	Usual medical care	1) Symptoms (strength, appetite, diarrhea or irregular defecation)	1) $p < 0.01$ between the two groups	No report	B(2b)
Wang, 2009 China	CCT	Various cancers	N = 80 QG: 40 CG: 40	Guo Lin Qigong 2.5 – 3.5 months	Unclear about time of intervention	Usual care	1) QOL 2) Depression	1) $p < 0.05$ 2) $p > 0.05$	No report	B(2b)
Yeh, 2016 Taiwan	RCT	Non-Hodgkin's Lymphoma	N = 108 QG: 54 CG: 54	Chan – Chuang Qigong 3 weeks	During Chemotherapy	Usual care	1) Fatigue 2) Sleep quality (VSHSS)	1) $p < 0.001$ 2) $p < 0.001$	No report	A (1b)

RCT: Randomised Controlled Trial; CCT: Clinical Control Trial; N: sample size; QG: Qigong Group; CG: Control Group; MQ: Medical Qigong; HTCG: Healthy Control Group; FACT-F: Functional Assessment of Cancer Therapy: Fatigue; BSI: Brief Symptom Inventory; CES-D: Centre for Epidemiologic Studies Depression Scale; BFI: Brief Fatigue Inventory; FACT-G: Functional Assessment of Cancer Therapy-General; PSQI: Pittsburgh Sleep Quality Index; LFS: Lee Fatigue Scale; FACT-B: Functional Assessment of Cancer Therapy-Breast; FACT-H&N: For patients with Head & Neck cancer; EORTC; European Organization for Research and Treatment of Cancer; SF-36: the MOS item short form health survey; EFS; Edmonton Frail Scale; FSI: Fatigue Symptom Inventory; BDI: Beck Depression Inventory; DASS: Distress Alerting Satellite System; PSS: Perceived Stress Scale; GOG-NTX: Gynecologic Oncology Group- Neurotoxicity; FACT-Cog: FACT-Cognitive Function; BMI: Body mass index; VSHSS: Verran and Snyder-Halpern Sleep Scale; TACE: Transcatheter arterial chemoembolization.

Level of evidence: A - Consistent level 1 studies; B - Consistent level 2 or 3 studies or extrapolations from level 1 studies; 1b = Individual RCT (with narrow Confidence interval), > 80% follow-up; 2b = Individual cohort study (including low quality RCT; e.g., <80% follow-up).

Two studies including 82 patients (Oh, Butow, Mullan, & Clarke, 2008; Fong et al., 2014) evaluated the impact of Qigong intervention on dyspnoea (both using general Qigong). There was no significant effect for dyspnoea symptom. There was also no significant effect of Qigong on pain in these two studies (Oh et al., 2008; Fong et al., 2014). However, a significant effect was found in another study (Lee et al., 2006). Qigong was found to be effective at improving strength, appetite, diarrhoea or irregular defecation in one study (Wang & Ye, 2002). In another study, there was no significant effect on diarrhoea or irregular defecation (Sun & Zhao, 1988).

Psychological symptoms: Qigong significantly lowered depression in one study (Chen et al., 2013). In another two studies, there was no significant effect on this symptom (Larkey et al., 2015; Wang, Zhu, Yuan, Lu, Gao, Fan, Wang, Rowland, Courneya, & Schneider, 2009). There was no significantly effect for anxiety in two other studies (Lee et al., 2006; Loh & Lee, 2015). However, a significant effect was observed in one study (Campo, 2014). Qigong significantly improved mood disturbance in only one study (Oh, 2010).

Quality of Life: Cancer-specific QOL was measured by the FACT-G, FACT-B, SF-36 or EORTC QLQ-30 in ten studies. Multiple studies confirm that Qigong significantly improves QOL (Chen et al., 2013; Fu & Wang, 1995; Loh & Lee, 2015; Oh, 2010; Oh, 2012; Wang et al., 2009). However, four studies showed that there was no significant effect on QOL (Oh et al., 2008; Fong et al., 2014; Lam, 2004; Oh et al., 2014). In addition, Guolin Qigong had no effect on QOL of hepatocellular cancer (Lam, 2004).

Safety and feasibility: Four studies (Campo, 2014, Fong et al., 2014, Oh et al., 2008, Oh et al., 2014) mentioned that Qigong intervention was safe, feasible and potentially

efficacious in improving symptoms and functioning. No unwanted side effects were reported in their studies.

Qigong protocols: Interventions varied among protocols. Specific styles or forms of Qigong intervention in included studies consisted of: Health Qigong (ten studies), Medical Qigong (four studies), Guolin Qigong (three studies), Chan-Chuang Qigong (two studies), Zhi Neng Qigong (one study), Yudong Kong Qigong (one study), and sport Qigong (one study). All seven protocols were found to be effective for one or more of the major outcomes studied.

The content of the Qigong protocol addressed exercises or techniques performed as Qigong therapy. All effective intervention protocols employed some variations of slow exercise described and practiced as gentle, integrated, repetitious, flowing, weight-bearing movements. Each referred to a specific stylised form. Meditation/mindfulness training was described in six of seven protocols. Training in breath regulation was described in five of seven protocols. Reference to energy cultivation was evident in four of seven protocols. Reference to relaxation or arousal state was made in three of seven protocols.

Logistic address delivery management. All studies engaged experienced instructors certified or trained in the specific styles or forms of Qigong therapy employed in the respective study protocols. Three protocols described the instructor as a Qigong master. Home practice was reported in six of seven protocols. The home practice aids, described as DVDs or compact discs, were distributed in four of seven protocols. Some portions of the exercises were practiced as seated or accommodation for seated exercises were provided in three of seven protocols. Qigong therapy protocol constructs identified in the analysis and their frequency of use are presented in Tables 2 and 3.

Table 2: Summary of the therapeutic outcomes based on different Qigong types.

Types of Qigong	No. of Studies	Outcome 1	Outcome 2	Outcome 3	Outcome 4
Health Qigong	10	4 (40%)	4 (40%)	1 (10%)	1 (10%)
Medical Qigong	4	2 (50%)	1 (25%)	1 (25%)	0 (0.0%)
Guolin Qigong	3	1 (33.33%)	1 (33.33%)	0 (0.0%)	1 (33.33%)
Chan-Chuang Qigong	2	1 (50%)	1 (50%)	0 (0.0%)	0 (0.0%)
Zhi Neng Qigong	1	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)
Yudong Kong Qigong	1	1 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sport Qigong	1	0 (0.0%)	1 (100%)	0 (0.0%)	0 (0.0%)
Total	22	9 (41%)	9 (41%)	2 (9%)	2 (9%)

Outcome 1: For studies reporting multiple main outcomes, at least one "++" were identified

Outcome 2: For studies reporting multiple main outcomes, at least one "+" were identified

Outcome 3: "0" for all main outcome(s)

Outcome 4: "–" or "– –" for all main outcome(s)

++: Two outcomes with significant difference ($p<0.05$)

+: One outcome with significant difference ($p<0.05$)

Table 3 Content and logistic constructs identified through constant-comparison analysis and frequency of use extracted from data reported in seven Qigong protocols

CONSTRUCTS	**Qigong types**						
Content	Health Qigong	Medical Qigong	Guolin Qigong	Chan-Chuang Qigong	Zhi Neng Qigong	Yudong Kong Qigong	Sport Qigong
Gentle/integrated/repetitious/ flowing/ weight-bearing exercises	X	X	X	X	X	X	X
Stylized exercises	X	X	X	X	X	X	X
Meditation/mindfulness	X	X	X	X		X	X
Breath regulation	X	X	X	X		X	
Energy cultivation	X	X	X	X			X
Relaxation	X	X				X	X
Self-massage			X				
Logistic							
Qualified instructor	X	X	X	X	X	X	X
Home practice	X	X	X	X	X	X	X
Home practice aid (Guidebook or DVD)	X	X	X	X	X		
Accommodation for seated exercises	X	X		X			

The Buddhists Qigong emphasise the liberation of mind, tranquillity in meditation and the obtainment of enlightening wisdom. Buddhist Qigong, also known as Health Qigong, is a self-practice, non-religious Qigong. It was founded in the Faculty of Nursing, Chulalongkorn University, Thailand. Thailand is a Buddhist country with 95% of population following Buddhism. Chulalongkorn University started giving Qigong lessons to cancer patients across Thailand, while kept studying and verifying the therapeutic effects of Buddhist Qigong. It has been reported that many patients achieved complete remission from cancer after practising this Qigong lesson.

Reamrhom (2008) investigated the therapeutic effects of Buddhist Qigong on anxiety and fatigue in breast cancer patients receiving chemotherapy (this full-text paper is in The Thai language; therefore, it was not included in the systematic review). The sample included 40 patients with breast cancer receiving chemotherapy. The major findings were as follows: (1) The post-test mean scores of anxieties of the experimental group was significantly lower than that of the control group ($t = -11.12$, $p < 0.05$); (2) The post-test mean scores of fatigue of the experimental group were significantly lower than those of the control group ($t = -6.48$, $p < 0.05$). Although Buddhist Qigong has minimum research evidence, studies in other fields such as heart failure (Phoophiw, 2011), caregiver (Chansungnoen, 2007; Rubleak, 2006), COPD patients (Siangphairoj, 2006). Buddhist Qigong was then recognised and proclaimed publicly as a conventional therapy based on submitting the therapeutic evidence to the Ministry of Health in Thailand (Phoophiw, 2011). Nowadays, Buddhist Qigong is practised not only in Thailand but also in other ASEAN countries (Prechawong, 2011).

In conclusions, the findings of the review showed that Qigong might bring to the care of cancer patients' recovery from symptom distress. The finding indicated that management of cancer patients' quality of life might be more effective if improvements in psychological, emotional and physical functioning are targeted as in the case of the Qigong intervention.

Median Qigong intervention duration of 6 weeks and the duration of interventions ranged from 3 weeks to 6 months. The results of these studies indicated that physical symptoms and psychological symptoms in the Qigong group were significantly improved at post-intervention compared with the control group or there was an observed positive trend from pre- to post-interventions scores.

Although these results are positive and promising, still there are some limitations such as a high risk of bias and low follow-up rate. Major sources of risk of bias were related to allocation concealment, blinding study subjects for research personnel, and random sequence generation. Only one study (Oh et al., 2010) described the method of randomisation, the quality and the dosage of qigong intervention in detail and addressed incomplete outcome data with intention-to-treat analysis. Despite the difficulties in blinding participants and intervention delivery, these trials attempted to blind the outcome assessors to minimise the potential methodological bias. Moreover, those studies investigated the short-term benefits of the qigong intervention but not the longer term. In addition, there are no published studies of Qigong that specifically address persistent dyspnoea, fatigue and anxiety in lung cancer population in Vietnam. Therefore, a further methodologically rigorous study with a larger sample size is needed to validate results and provide a stronger evidence base on Qigong that may assist patients with cancer and clinicians in providing improved comprehensive cancer care.

2.11 Theories explaining symptom management

There are four groups of theory addressing symptom management, which are 1) Symptom Management Theory (SMT) (Froelicher, Gortner, Halliburton, Janson, Miaskowski, Savedra, Stotts, Taylor, & Underwood, 1994), 2) Theory of Unpleasant Symptoms (TUS) (Lenz, Pugh, Milligan, Gift, & Suppe, 1997), 3) Symptoms Experience Model (SEM) (Armstrong, 2003), and 4) Symptoms Experience in Time (SET) (Brant et al., 2010).

Nurse scientists at the University of California, San Francisco through a literature review and application of nursing research developed the SMT; this is a deductive, middle range theory depicting symptom management as a multidimensional process occurring in the domains of nursing science. Although the model is based on programs of research working with adult patients, the model also is proposed to be applicable for children. This comprehensive theory depicts single or multiple symptoms expressed within an intervention framework (Froelicher, Gortner, Halliburton, Janson, Miaskowski, Savedra, Stotts, Taylor, & Underwood, 1994).

The TUS was generated through concept analysis, derivation, and synthesis at a single concept level (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Origins of the TUS focus on the authors' development of a description of fatigue and dyspnoea, and the beginning efforts to document regularities between these concepts. Fatigue, the initial concept, was synthesised from two separate perinatal phases (i.e. intrapartum and postpartum). Dyspnoea, a second concept, was analysed in patients with chronic obstructive pulmonary disease or asthma. Concepts were examined for commonalities in an evolutionary process that led to the development of a theory for multiple symptoms that could apply to different clinical populations.

The SEM was developed through a concept analysis, using historical and current literature sources of the symptoms experience. This theory demonstrated that symptoms experience is the perception of the frequency, intensity, distress, and meaning of symptoms as they are produced and expressed. Symptoms are multiplicative in nature and may act as catalysts for the occurrence of other symptoms. Antecedents to the symptoms experience include demographic, disease, and individual factors. Consequences include the impact on mood state, psychological status, functional status, quality of life, disease progression, and survival (Armstrong, 2003). No specific symptoms were analysed; rather, the symptom

experience was examined.

Researchers at the University of Minnesota developed the SET. This theory is proposed as a synthesis and extension of existing theories: the TUS, the SMT and the Chronotherapeutic Intervention Theory for Postsurgical Pain (CIPP). The SET theory conceives the symptom experience as a flow process that explicitly incorporates temporal dimensions. Four dimensions of time are recognised: clock-calendar, biologic-social, perceived, and transcendent time. The four temporal dimensions are placed against a backdrop of "meaning-in-time" that brings forth the potential for transformation in a symptom experience (Henly, Kallas, Klatt, & Swenson, 2003). Therefore, The SET theory extends previous work by incorporating multiple temporal dimensions that reflect the human experience of health and illness manifested in the expression and management of symptoms.

The selection of theory to guide this study

Among above theories, only the Theory of Unpleasant Symptoms (Lenz et al., 1997) has been used in studies examining causative factors of fatigue and dyspnoea that could apply to different clinical populations (Fig. 1).

The analysis of other theories explaining symptom management found several shortcomings. The TSM does not include an evaluation of multiple symptoms or a depiction of the interactive relationships among symptoms. For example, although the symptom experience dimension of the theory includes the perception, evaluation, and responses to symptoms, no illustration is provided of how multiple symptoms could interact (Brant et al., 2010). In addition, no direct relationships are considered between antecedents and consequences, and the model does not account for the temporal aspects of symptoms in the SEM (Walsh, Donnelly, & Rybicki, 2000). Finally, variables in the SET are not well-defined, the four temporal components are complex and abstract and are not depicted in the visual model, and the model does not consider symptom interactions and clusters (Brant et al., 2010).

Based on the analysis of existing models for symptom management, the TUS is selected as the theoretical framework to guide this study.

Theory of Unpleasant Symptoms

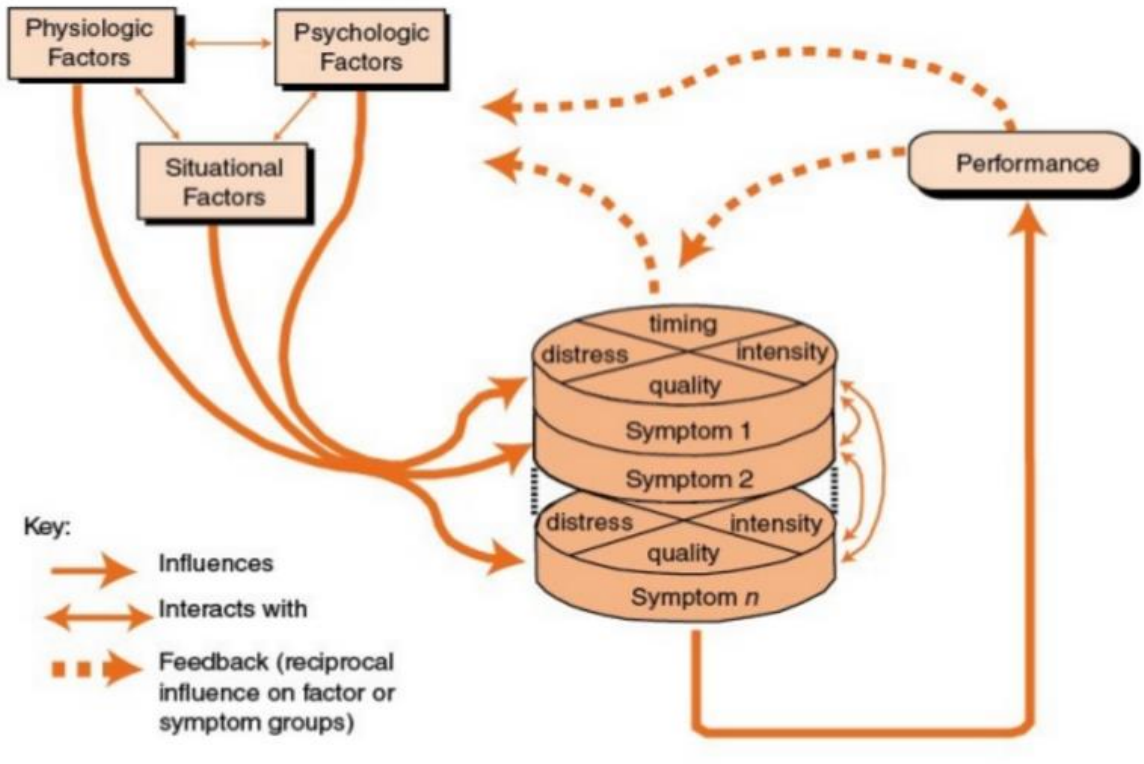

Fig. 1 Theory of Unpleasant Symptoms (Lenz et al., 1997).

In 1995, Lenz and colleagues proposed the TUS to explain symptom management in different clinical populations. According to Lenz et al. (1997), the original theory included only one symptom; the TUS was revised in 1997 to encompass multiple symptoms. The TUS was used to guide studies among patients with different type of disease such as breast cancer (Lee, 2005), cancer patients undergoing chemotherapy (Redeker, Lev, & Ruggiero, 2000), Alzheimer's disease (Hutchinson & Wilson, 1997), and COPD (Reishtein, 2005). In the TUS, physiological, psychological and situational factors are antecedents that influence the symptom experience. The symptom experience includes the distress, duration, intensity and

quality of each symptom. Specific outcomes include function, cognition, and physical performance.

Symptoms

According to the TUS, symptoms can occur alone or in combination and can interact with one another. Dyspnoea, for example, is often accompanied by fatigue. Each symptom is conceptualized to be a multidimensional experience, which can be conceptualized and measured separately or in combination with other symptoms. Although symptoms differ from one another, several dimensions are common across symptoms and clinical populations: intensity (strength or severity), timing (duration and frequency of occurrence), the level of distress perceived (degree of discomfort or bothersomeness), and quality. These dimensions are assumed to be separable but related to one another. For example, some of the indicators on the fatigue symptoms checklist are also indicators of high levels of dyspnoea or anxiety (e.g., feeling ill, difficulty thinking) (Lenz et al., 1997). Feedback loops are included to show that antecedents can influence one or more symptoms, symptoms can influence performance and performance can, in turn, affect both antecedents and further symptoms (Brant et al., 2010).

Influencing factors

In the TUS, three categories of variables are identified as influencing the occurrence, intensity, timing, distress level, and quality of symptoms: physiologic factors, psychological factors, and situational factors. Three categories relate to one another and may interact to influence the symptom experience (Lenz et al., 1997).

Examples of physiologic factors include normally functioning bodily systems; the existence of any pathology, including the occurrence of trauma; and the individual's level of energy (Lenz & Pugh, 2008). The psychological component of the model includes the individual's mental state or mood, affective reaction to illness, and degree of uncertainty and

knowledge about the symptoms and their possible meaning (Dales et al., 1994). Interventions aimed at altering psychological factors have been effective in reducing symptoms (Gift, Moore, & Soeken, 1992). Situational factors include aspects of the social and physical environment that may affect the individual's experience and the reporting of symptoms. Potentially relevant social situational considerations include employment status, marital and family status, social support, availability of and access to health care resources, and lifestyle behaviours such as diet and exercise (Lenz & Pugh, 2008). Fatigue tends to be more severe, for example, in people who engage in little regular exercise and is less severe in those with good social support (Winningham, 1995).

Consequences of the symptom experience

The final component of the TUS is performance, the "outcome" or "effect" of the symptom experience. Performance is conceptualised to include functional and cognitive activities. Functional performance is conceptualised broadly to include physical activity, activities of daily living, social activities and interaction, and role performance including work and other role-related tasks. Examples of cognitive activity include concentrating, thinking, and problem solving. It has been demonstrated with a variety of symptoms that people with more numerous or more severe symptoms tend to have lower functional health status, less effective role performance, lower cognitive functioning, lower quality of life, and lower physical performance capabilities (Lenz et al., 1997).

Application of TUS to create conceptual framework in this study

The antecedent categories of the TUS (physiological factors, psychological factors, and situational factors) are vastly and include several components (Brant et al., 2010). Meanwhile, Qigong is mainly composed of five elements: visualisation, meditation, relaxation, deep breathing, and target qi circulation. Qigong puts emphasis on the control of the mind-states, posture, and breath. The three main doctrines of qigong include tiao xin

(mind regulation), tiao shen (body regulation), and tiao xi (breath regulation). Qigong is a Chinese exercise for yang sheng (health preservation) and bao jian (health maintenance) (Tseng, Lin, & Yeh, 1995). In addition, Qigong is a system of self-practicing physical exercise which includes breathing regulation (modulation of autonomic nervous system and improving ventilatory function & oxygenation), mind regulation (possibly Synchronizing neural activities stabilising mood), and postural regulation (movement exercises). Those components are hypothesised that can apply to TUS flowing physiological factors, psychological factors, and situational factors.

Breathing retraining in pulmonary diseases aims to teach patients to breathe more efficiently, replacing rapid shallow breathing patterns that may worsen gas exchange with slower breathing patterns that improve chest wall mechanics, allow a complete expiration, and decrease air trapping. Conventional breathing retraining, such as diaphragmatic and pursed-lip breathing, may improve symptoms, increase tidal volume and total ventilation, decrease respiratory rate, and improve gas exchange (Gosselink, 2004). In addition, slow, deep breathing can also have beneficial effects on the autonomic nervous system which is increasingly recognised as highly relevant to respiratory diseases (Cahalin, Braga, Matsuo, & Hernandez, 2002).

A fundamental component of Qigong is the deliberate attention to bodily sensation, movement, breath, and emotion, which fosters acute self-awareness, both physically and emotionally. Participants learn, for example, to discriminate areas with or without strain or tension, stronger or weaker regions, movements that feel graceful or fearful, or aspects of breathing that feel laboured or unconstrained (Ries, Bauldoff, Carlin, Casaburi, Emery, Mahler, Make, Rochester, Zu, & Herrerias, 2007). This awareness may in turn complement other Qigong components that foster improved function (for example, improved posture, relaxation). Recent studies support that mindfulness training can impact interceptive

awareness of key COPD symptoms (such as dyspnoea and cough) which may lead to better symptom management in the lung cancer population (Pbert, Madison, Druker, Olendzki, Magner, Reed, Allison, & Carmody, 2012; Young, Brammer, Owen, Brown, Lowe, Johnson, Calam, Jones, Woodcock, & Smith, 2009). Inner awareness of moment-to-moment sensations also helps to develop focused attention, providing a tool to manage distracting thoughts (Daubenmier, Sze, Kerr, Kemeny, & Mehling, 2013).

Daubenmier et al. (2013) hypothesised that increased awareness of postures and breathing will allow participants to better anticipate and manage their symptoms, decreasing the risk of worsening dyspnoea and precipitating further breathing difficulty and anxiety. This heightened mindfulness and self-awareness of breathing, body shape, and emotion may be important in facilitating changes in lung cancer patients who have developed maladaptive physical and psychological patterns due to symptom distress over time, and lead to better symptom management. In addition, it is increasingly recognised that patients with lung cancer are at high risk of developing symptoms of fatigue, dyspnoea and anxiety (Chan, Chang, Leung, & Mak, 2007). Anxiety over dyspnoea-producing activities is common and may promote maladaptive sedentary lifestyles (Kirkova et al., 2010). Collectively, the mind-body approach of Qigong inherently addresses stress management that is an important component of lung cancer self-management. It may be necessary to compromise the optimal management of one cluster symptom (fatigue, dyspnoea, and anxiety) to achieve optimal management of another troubling symptom (such as cough) (Barsevick, 2006). In order to manage symptom distress and enhance quality of life, Qigong is selected as intervention in this current study. In addition, performance (the "outcome" or "effect" of the symptom experience) is the only outcome noted in the theory that are measured by symptoms outcome and QOL of lung cancer patients in this study (Fig. 2).

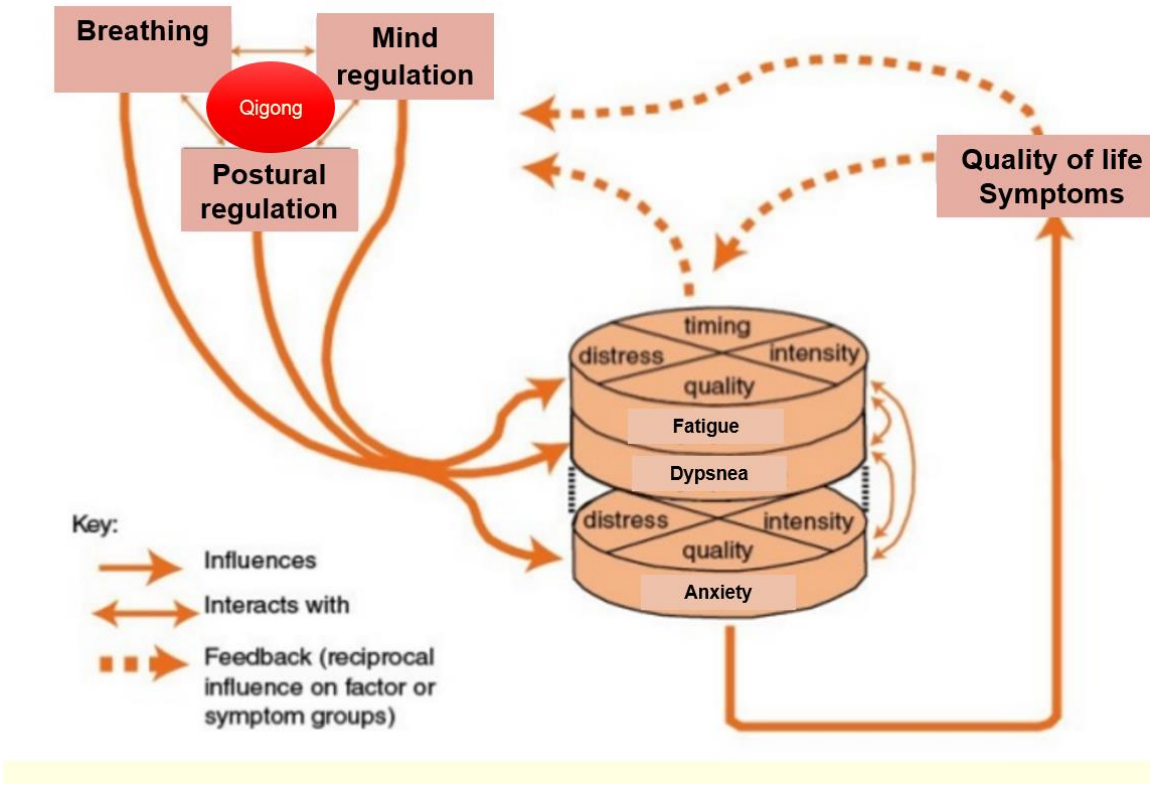

Fig. 2 Theoretical framework of this study

CHAPTER THREE

METHODOLOGY

This chapter will present the research methodology of this study, which includes eight major sections: 1) study design, 2) subjects and setting, 3) randomisation and blinding, 4) intervention method, 5) outcomes measurement, 6) data analysis, 7) quality assessment, and 8) ethic consideration.

3.1 Study design

The design of this study was a randomised controlled trial (RCT) with two parallel groups in a 1:1 allocation ratio, allocation concealment and assessor blinding. The design follows the Standard Protocol Items Recommendations for Interventional Trials (SPIRIT) (Chan et al., 2013) and the Consolidated Standards of Reporting Trials (CONSORT) (Schulz, Altman, & Moher, 2010). Participants from National Lung Hospital and Nam Dinh General Hospital were enrolled and randomised to the 6-week Qigong intervention or the 6-week wait-list control group to explore effects of Qigong (two weeks training followed by home-based practice for four weeks) with the intervention compared to wait-list control group. The lung cancer patients' dyspnoea, fatigue, and anxiety were measured as primary outcomes and cough, quality of life was evaluated as secondary outcomes. The intervention in this study was based on protocol that was enacted by Chulalongkorn University, Thailand (Thanasilp, 2013). All outcomes were measured at baseline before randomisation, at the 6^{th} week (at the end of intervention), and at the 12^{th} week (after 6-week follow-up period). The data collectors were blinded to the group assignments.

3.2 Subjects and setting

3.2.1 Study population

The study population included patients with a diagnosis of lung cancer at National Lung Hospital and Nam Dinh General Hospital, Vietnam, commencing from January 2017

to December 2017.

Eligibility criteria

The inclusion criteria of subjects were:

(a) Age 18 or above

(b) Diagnosis of invasive lung cancer [Non-small cell lung cancer (NSCLC) or Small cell lung cancer (SCLC)];

(c) Patients with NSCLC or SCLC who have completed treatment with chemotherapy and/or radiotherapy for a minimum of 4 weeks prior to commencing the study;

(d) Medically fit to participate in general well-being and activities of daily life, as two or smaller on a 0 - to 5-point numeric rating scale at the time of recruitment, as determined by The Eastern Cooperative Oncology Group (ECOG) score (Appendix 5);

(e) With no clinically confirmed recurrence or occurrence of other cancers; and

(f) Patients report all three symptoms (dyspnoea, fatigue, and anxiety) in the previous week and ranked the severity of at least two of the three symptoms as three or more on a 0 - to 10-point numeric rating scale at the time of recruitment, as determined by dyspnoea, fatigue, and anxiety intensity rating scales (Appendix 6).

Exclusion criteria

1) Known history of clinically diagnosed with major psychiatric illness;

2) Presenting with criteria associated with risk during physical activity: severe cachexia; frequent dizziness; bone pain; or severe nausea;

3) Having had past or current regular experience with mind-body practices that blend movement with meditative practices, such as Yoga, Tai Chi, or Qigong;

4) Life expectancy estimates to be less than 6 months (as determined by their physicians).

5) Visual problems or deafness.

3.2.2 Sample size

The sample size was calculated based on relevant published literature. Sample sizes for fatigue, dyspnoea, and anxiety variables were calculated on the basis of improvement in fatigue, dyspnoea, and anxiety scores in relevant research, with the highest sample number being chosen.

In a study managing symptoms among COPD patients (Ng, 2009), the effect size of Qigong intervention on fatigue and dyspnoea in COPD patients after the intervention between a Qigong and control group (t-test) was 0.30 and 0.32, respectively. A sample size of 71 and 62 subjects, respectively, was calculated with a type 1 error of 5% (α=0.05) and 80% power (β=0.20) by Gpower 3.1.9.2 software (http://www.gpower.hhu.de).

Fatigue scores (mean and its SD) in lung cancer patients after the intervention between a Tai Chi-Qigong and control group (t-test) are 53.3 ± 11.8 and 59.3 ± 12.2 according to relevant published literature (Zhang, Wang, Chen, & Yuan, 2016). A sample size of 102 participants has been calculated to be sufficient to detect the effect size of relevant study with a type 1 error of 5% (α=0.05) and 80% power (β=0.20) by Gpower 3.1.9.2 software (http://www.gpower.hhu.de).

Anxiety scores (mean and its SD) in breast cancer patients after the intervention between a Qigong and the control group (t-test) are 47.73 ± 5.6 and 50.3 ± 6.1 according to relevant published literature (Loh, 2015). A sample size of 130 participants has been calculated to be sufficient to detect the effect size of relevant study with a type 1 error of 5% (α=0.05) and 80% power (β=0.20) by Gpower 3.1.9.2 software (http://www.gpower.hhu.de).

Therefore, the sample size of 130 subjects is necessary for this study. Considering a 20% attrition rate, 156 subjects is necessary for total sample size, with 78 subjects in each group.

3.2.3 Withdrawal criteria and management

There were no subjects required to withdraw from the trial based on the following: (1) development of a serious disease or deteriorated health preventing continuation in the trial; (2) adverse events related to the Qigong intervention.

3.2.4 Settings and time frame

Vietnam is divided into three main parts: the north, the centre, and the south. The country's population is approximately 90 million people, with almost half of the population being found in the north (Who, 2010). Data collection was conducted in the north because this region demonstrated significant higher prevalence of lung cancer than other areas (Ngoan, Fukumitsu, Kaneko, & Yoshimura, 2001). The National Lung Hospital and Nam Dinh General Hospital are two hospitals in the north of Vietnam; on average, those hospitals have 180 to 200 lung cancer patients receiving treatment in inpatient and outpatient departments per day (Long et al., 2015). This study was conducted from January 2017 to December 2017 (Appendix 16).

3.2.5 Recruitment and screening

The researcher and research assistants from the National Lung Hospital and Nam Dinh General Hospital recruited participants (both inpatient patient and outpatient) by using posters, sending leaflets and brochures, and setting up a recruiting station at the corresponding hospitals. Research assistants with more than 5 years' experience, who hold a bachelor's degree in nursing science, and experience in the research process were involved. Two research assistants were required to support the researcher in the implementation of recruitment and screening, while two other research assistants were recruited for data collection. Potential participants were first screened based on the inclusion criteria to determine their eligibility (using review medical records and asking the patients). Eligible participants received information about this trial and had an informal discussion (asked and

answered questions that related to research project) with trained research assistants regarding the information provided. Written informed consent (Appendix 3) was obtained from those willing to participate. The results of the baseline assessment of outcomes were obtained.

3.3 Randomisation and blinding

3.3.1 Randomisation

To avoid the potential bias in the allocation of patients to receive Qigong intervention group or usual care group, neither the investigator, the patient themselves nor their physician could decide that a given person should receive the Qigong intervention or the standard usual care. Randomisation tends to balance two groups with respect to characteristics that could influence the development of an outcome. To randomise patients to receive Qigong intervention or another guaranteed that the two groups were well balanced and comparable with respect to all risk factors that could influence the outcome at study completion (Moher, Hopewell, Schulz, Montori, Gøtzsche, Devereaux, Elbourne, Egger, & Altman, 2010).

After the completion of baseline measurements, eligible patients were randomly assigned to either the Qigong group or wait-list control group following blocked randomisation procedures with a 1:1 allocation according to the computer-generated randomisation list based on ID assigned in the order of enrolment (www.sealedenvelope.com). The blocked randomisation refers to what the investigators decide to enrol participant into the study sequentially. The investigators were treated people who were being consecutively enrolled in a series called a block (Kim & Shin, 2014). Due to the research setting and patient's characteristics, the block size of six subjects (the next six subjects who are going to be enrolled in study) was used for this study. Blocks are best used in smaller increments as researchers can more easily control balance (Suresh, 2011). A randomisation scheme that constrains this block so that equal numbers of people are assigned to both the Qigong group and the wait-list guarantees balance within and between the blocks.

After a block size of six had been determined, all possible balanced combinations of assignment within the block (i.e., an equal number for all groups within the block) were calculated. The sample size of 156 was divided into 6 equal 26 blocks. Therefore, each group had 13 blocks. Blocks were then randomly chosen to determine the patients' assignment into the groups by a statistician expert from Nam Dinh University of Nursing.

Patients in the intervention groups received Qigong training and post-intervention data were collected at the end of completion of the 6 weeks of intervention, and again at the 6 weeks' follow-up. For the control group, the schedules for data collection and following up were the same as for the intervention group. Due to patients being recruited from the same hospital, patients receiving Qigong intervention were asked not to share information with other patients. Similarly, the Qigong Master was requested not to discuss the intervention with research assistants involved in different phases of the trial.

3.3.2 Blinding

Blinding is necessary for the control of bias in clinical trials. Blinding was defined as the process of concealing research design elements such as group assignment, treatment agent, and research hypotheses from participants, health care providers, or data collectors (Penson & Wei, 2006). Blinding allows the researcher to minimise threats to internal validity and construct validity, thereby strengthening the external validity and improving the generalisability of results (Portney & Watkins, 2009). In the current study, based on nature of intervention, blinding was not feasible with the researcher, statistician, or Qigong Master who were responsible for the recruitment of subjects, randomisation, and delivering the intervention, respectively. However, the investigators who collect the outcome information were blinded to the allocation sequence. Blinding of the data collectors to group assignment is necessary to ensure objectivity and avoid the risk that assessors record more responses that are favourable when treatment status is known or may assume that improved performance is

evidence of treatment status.

3.4 Intervention method

3.4.1 Control group

The wait-list control group received the usual care provided by the hospitals or caregivers and received Qigong training after the follow-up period. The usual care of this study comprised a mandatory individual briefing of the lung cancer care procedure (nursing care after completion of medical treatment) and about a five to a ten-minute individual discussion focusing on symptom management (such as using oxygen when patients have dyspnoea) by a staff nurse before discharge. Patients were also invited to attend an optional group talk given by a registered nurse and a medical social worker about general care before and/or after they returned to the community (Ministry of Health, 2012). Patients in both intervention and control groups were offered this usual care.

The general care before and/or after returning to the community included a range of simple steps that patients can take, such as complying with the treatment regime, eating well, and exercising to cope with the physical and emotional toll of the disease.

1) Good nutrition is important to recovering from treatment and dealing with cancer. Patients' nutritional needs will vary during treatment, in recovery, and post-treatment or when living with advanced cancer. A dietician can help patients in each stage.

2) During treatment, patients need to be especially careful about good food hygiene.

3) Physical activity can help patients deal with the symptoms of lung cancer as well as improve the recovery time from treatment.

4) If a patient is a smoker, the patient can improve their chances of responding to treatment if they quit. However, because smoking is an addiction, the patient is more likely to succeed with help.

5) Comply with prescribed medications and only take the prescribed amounts.

Knowing the active ingredient will help patients to always take the correct dosage and be able to identify alternatives when traveling.

6) Complementary therapies may help patients to cope better with symptoms of cancer. Always discuss using these therapies with patient's doctor or researcher to make sure they can be combined safely with conventional treatment.

7) Patients may find themselves-esteem knocked about by cancer treatment. However, there are practical ways to deal with physical changes resulting from treatment.

8) Address early on any changes in patients' emotions or feelings with patients' family and friends.

9) Patients' sexuality may be affected by cancer; it will help patients to understand and address any potential impact this has on patients' life. Patients also may have to use contraception at times during treatment (Ministry of Health, 2012).

3.4.2 Intervention group

Qigong training was delivered at the National Lung Hospital and Nam Dinh General Hospital to subjects in the intervention group. One professional coach, who had been engaged in teaching Qigong to clients at the UNESCO Centre for Supporting Community's Heath for at 12 years, was employed to guide the participants' training. The training scheme of Qigong was planned according to the 'Qigong Standard' enacted by the Chulalongkorn University, Thailand (Thanasilp, 2013), and consists of seven postures (Appendix 8). This Qigong protocol produced small-to-large effects on symptom management in various populations and medical conditions (Prechawong, 2011). Qigong is generally reported to be safe in the general population when practiced according to standard moderate principles and when learned under the guidance of a qualified teacher. However, Qigong should not delay the time of diagnosis or replace more established treatments (Thanasilp, 2013).

Subjects in the intervention group (6 patients in each Qigong training section)

received a 90 minutes' Qigong training (Appendix 8b), meeting twice a week for the first 2 weeks to intensify proper learning of the Qigong intervention. Thereafter, subjects were asked to practice at home for at least 30 min a day, 5 days per week, over 4 weeks and to keep a log of the frequency, minutes of practice, and level of skills. The home exercises were the same as those learned in the training sessions and an instructional DVD and guidebook were also given to subjects. The DVD was modified from original Thai version with the performances of Qigong master with music, and Vietnamese description in the background (Appendix 8a).

3.4.3 Follow-up

After the 6-week intervention period, all participants stopped practice Qigong and started an additional 6-week unsupervised follow-up practice. During the follow-up period, all participants were required to record their daily activity information at 8 and 12 weeks (Appendix 9).

3.4.4 Adherence measures

All subjects were advised not to seek any other regular exercise during the trial period. The researcher supervised the training to guarantee the quality of Qigong delivery. In order to observe any impact of the usual physical activity, the researcher required all subjects to record information about their usual daily physical activity at 3 and 6 weeks of the intervention period on a daily activity log (Appendix 9).

The researcher assessed the subjects' compliance with the home program by asking and testing them every week though phone calls to encourage participants to practice and ensure that the training dose is adequate by recording in a diary logbook. If a subject missed a phone call, the researcher made an additional phone call in an effort to prevent loss-to-follow-up. To incentivise completion of the data collection, a 50,000 VND gift cash was provided at the baseline collection, 150,000 VND gift cash at the post-intervention data

collection, and 150,000 VND gift cash at the 12-week follow-up data collection time point. Subjects were reminded that the gift would be given to them upon completion of data collection. All participants can stop practicing Qigong during the follow-up period. The wait-list control group received usual care during the first 12 weeks of the study and participants then received the same Qigong training after the follow-up period.

3.4.5 Safety assessment

There were no side effects from practising Qigong in the intervention group in this study.

3.5 Outcome measures

The variables in this trial consist of baseline characteristics, primary outcomes, and secondary outcomes (Appendix 1). The demographic characteristics and medical information were measured at baseline (1-2 weeks before randomisation). Primary and secondary outcomes were measured face-to-face when the patients went to hospitals for follow-up medical treatment at baseline [T0], the end of the intervention period (6 weeks after randomisation) [T1], and the end of the follow-up period (12 weeks after randomisation) [T2]. An investigator who is an experienced staff at the Nam Dinh University of Nursing, Vietnam, and was blinded to the allocation results of participants, assessed all primary and secondary outcomes.

Baseline characteristics

The investigator using the printed questionnaires collected participants' demographic characteristics (e.g., age, sex, education, marital status, and occupation) and history of the disease, disease status, and current treatments.

Primary outcomes

Fatigue

The selection of instrument for fatigue in this study was based on two systematic

reviews on the measurement of fatigue in cancer (Minton & Stone, 2009; Seyidova-Khoshknabi, Davis, & Walsh, 2011). Based on psychometric properties and clinical feasibility of the instrument, the two systematic reviews recommended totally six scales: (1) Fatigue subscale of EORTC-QLQ-C30; (2) Fatigue Questionnaire (FQ); (3) Functional Assessment of Cancer Therapy Fatigue (FACT-F); (4) Cancer Fatigue Scale (CFS); (5) Brief Fatigue Inventory (BFI); and (6) Multidimensional Fatigue Symptom Inventory–Short Form (MFSI-SF). The analysis of instruments for fatigue favours the FACT-F. The scale has good psychometric properties, a reasonable length, and has been used widely in cancer populations. Moreover, the scale has been translated into Vietnamese (Long et al., 2015). Thus, the FACT-F was used in this study.

Description: The FACT-F consists of 13 items measuring the intensity of fatigue (Appendix 10). The period assessed is the previous 7 days. Each item is rated on a 5-point Likert scale, ranging from 0 to 4.

Scoring and interpretation: Items are scored as follows: 0 = Not at all; 1 = A little bit; 2 = Somewhat; 3 = Quite a bit; 4 = Very Much, except items #7 and #8 which are reversed scored. Score ranged 0 to52. A score of less than 30 indicates severe fatigue (Appendix 10). The higher the score, the better the quality of life (Webster, 2003).

Psychometric Properties: Cronbach's alpha of the FACT-F ranged from 0.93 to 0.95 (Yellen et al., 1997). In another study, the internal consistency coefficient calculated from 470 cancer patients was of 0.94. The coefficient between items and the total score varied from 0.52 to 0.82 (Van Belle et al., 2005); it also demonstrated a good test–retest reliability with the coefficient of 0.90) (3-7-day interval). Data indicated that Fatigue subscale FACT-F has strong negative association with POMS Fatigue (r = - 0.83), Piper Fatigue Scales (r = -0.77), and positive association with POMS vigor (r = 0.61) (Yellen et al., 1997). The scale could also discriminate the level of Performance Status assessed by ECOG performance

status. It also showed strong association (r = 0.76) with measurements of quality of life (SF-36) (Ishikawa, Thuler, Giglio, Baldotto, de Andrade, & Derchain, 2010). The scale had been translated to Vietnamese and the translation version demonstrate well psychometric. The content validity index (CVI) of whole scale was 0.98 with item-CVI ranging from 0.8 to 1.0. The Cronbach's alpha coefficient of FACT-F was 0.94 (Long et al., 2015). Cronbach's alpha of the FACT-F in this study was 0.794.

Dyspnoea

The selection of instrument for dyspnoea in this study is based on a review by Kathiresan et al. (2010). There are several instruments for dyspnoea that have been used in lung cancer: (1) A single scale such as the visual analogue scale (VAS) or single item of general symptom scales (e.g. Thurstone Scale of Symptom Distress, Symptom Distress Scale, or Lung Cancer Symptom Scale); (2) the Cancer Dyspnoea Scale (CDS), which consists of 12 items assessing both sense of effort, sense of anxiety and sense of discomfort of dyspnoea experience. Good psychometric properties of the CDS in a lung cancer sample have been reported (Henoch, Bergman, & Gaston-Johansson, 2006; Tanaka et al., 2000; Uronis, Shelby, Currow, Ahmedzai, Bosworth, Coan, & Abernethy, 2012). The CDS is also practical since it requires only 2 minutes to complete (Uronis et al., 2012). The comparison among those scales gives, while the VAS is a single dimension (severity), the CDS evaluate multi-facets of dyspnoea, therefore, an obvious favour to CDS. Thus, this study used the CDS (Tanaka et al., 2000) to measure dyspnoea.

Description: The CDS consists of 12-items, divided into three subscales, which are 'sense of effort' (physical dyspnoea or dysfunction of ventilation with organic cause(s) worsened on exertion), 'sense of anxiety' (affected or amplified by psychological status), and 'sense of discomfort' (unpleasant and unrelaxed feeling at rest as well). Patients respond by rating in the 5-point linked scale from 1 "not at all" to 5 "very much" (Appendix 11).

Scoring and interpretation: The score for sense of effort subscale is calculated by the following formula (items 4 + 6 + 8 + 10 + 12) – 5, producing possible range from 0 to 20. The score for the sense of anxiety is obtained by the following formula (items 5 + 7 + 9 + 11) – 4, producing possible range from 0 to 16. In addition, the formula for the sense of discomfort subscale is 15 – (items 1 + 2 + 3), producing possible range from 0 to 12. The total dyspnoea score is the sum of the three subscale scores, ranging from 0 to 48. A higher score indicates the higher level of dyspnoea (Tanaka et al., 2000).

Psychometric Properties: Factor analysis has confirmed the CDS has three subscales. The mean value of inter-subscale correlation coefficients was 0.48. Cronbach's alpha of the total scale was 0.86 and of the subscales were 0.83 (sense of effort), 0.81 (sense of anxiety), and 0.94 (sense of discomfort). Test–retest coefficients (7-day interval) between the sense of effort, sense of anxiety, and sense of discomfort and the total score were 0.71, 0.69, and 0.58, respectively (Tanaka et al., 2000).

In lung cancer, the Cronbach's alpha of sense of effort, sense of anxiety, and sense of discomfort subscales were 0.84, 0.80, and 0.84, respectively. The CDS also significantly related to VAS (r = 0.82), Borg's scale (r = 0.87), HADS (r = 0.57), physical status (r = 0.44), and SpO2 (r = 0.29) (Uronis et al., 2012). The Cronbach's alpha coefficient of CDS Vietnamese version was 0.86, with regards to subscale, the coefficients of the sense of effort subscale was 0.86, of the sense of anxiety subscale was 0.74, and of the sense of discomfort was 0.70 (Long et al., 2015). In the current study, the Cronbach's alpha coefficient of CDS was 0.919.

Anxiety

Several anxiety scales have been used in the lung cancer population.

a) The anxiety items of general symptom questionnaires or self-developed item have been used in studies of Genç and Tan (2011) (Brief Symptom Inventory), Kuo and Ma (2002)

(Symptom Distress Scale) or Tsai et al. (2010) (single self-developed item). The items mainly focus on intensity of anxiety. However, those measurements are not specific for anxiety and could not offer a highly reliable and comprehensive information toward the patients' problem (Chan, 2011).

b) State-Trait Anxiety Inventory (STAI) is a well-validated questionnaire. It consists of two subscales measuring state anxiety (20 items) and strait anxiety (20 items). Researchers have used it to measure trait anxiety in lung cancer (Alacacıoğlu et al., 2012; Smith et al., 2001).

c) Anxiety subscale of the Hospital Anxiety and Depression (HADS-A) scale is the most commonly used to measure anxiety in lung cancer. This subscale consists of seven items, measuring intensity of anxiety. Its excellent psychometric properties are widely reported (Ostroff, Krebs, Coups, Burkhalter, Feinstein, Steingart, Logue, & Park, 2011; Pirl et al., 2008; Uronis et al., 2012; Vos, Putter, Houwelingen, & Haes, 2011).

d) The Anxiety subscale of the Depression, Anxiety, and Stress Scale 21 (DASS-21) has also been used in lung cancer populations (Sharp, Carsin, & Timmons, 2013). It consists of seven items and demonstrates good psychometric properties (Henry & Crawford, 2005; Norton, 2007; Szabó, 2010).

Although STAI, DASS 21-A, and HADS-A are all well validated scales, the STAI is not prioritised because it is the longest one. A small number of items would make other scales more practical than STAI in a clinical setting. The DASS 21-A and HADS-A are quite equivalent. However, the DASS 21-A has been validated in Vietnamese in terms of both reliability and construct validity (Tran et al., 2013). Therefore, the DASS 21-A is selected and its psychometric quality is presented in the next paragraphs (Appendix 12).

Description: The Depression Anxiety Stress Scales 21 (DASS-21) is a short form of a 42-item self-report questionnaire named DASS (Lovibond & Lovibond, 1995). The DASS

was originally developed for people aged 17 or older but to evaluate the severity of core symptoms of depression, anxiety and stress (or tension). DASS-21 is a self-report measure in which participants rate the frequency and severity of experiencing negative emotions over the previous week. Frequency/severity ratings are made on a series of 4-point scales (0 = Not at all, 1 = A little, 2 = Quite a Bit, and 3 = very much, or most of the time) (Norton, 2007). The DASS-21 consists of three subscales, namely Depression, Anxiety, and Stress subscale. The anxiety subscale has seven items, assessing symptoms of autonomic arousal, skeletal musculature effects, situational anxiety and subjective experience of anxious affect.

Scoring and interpretation: The anxiety score is obtained by totalling the score of all seven items, and then multiplying this by 2 to calculate the final score. A higher score indicates more intense anxiety (Tran et al., 2013).

Psychometric Properties: Henry and Crawford (2005) validated the DASS-21 in a sample of 1,794 members of the general adult UK population. Cronbach's alpha of the anxiety subscale was found to be 0.82. The internal consistency coefficients were found to be from 0.78 to 0.81 (Norton, 2007) or 0.79 (Szabó, 2010) in other studies. The construct validity of the DASS-21 was widely confirmed in various studies. Three subscales of the questionnaires have been validated by factor analysis (Henry & Crawford, 2005; Norton, 2007; Szabó, 2010).

Tran et al. (2013) conducted a study to validate the DASS 21 in Vietnamese. The Cronbach's alpha of the DASS 21 – Anxiety subscale was found to be 0.77. Exploratory Factor Analysis was performed to test the construct validity of the instrument. Twenty-one items of the DASS 21 constitute three factors. Seven items of the Anxiety subscale fit to one single factor, suggesting that they form an independent subscale. The loading factors of items ranged from 0.46 to 0.7. Correlation coefficients between DASS21-D and DASS21-A were 0.65, DASS21-D and DASS21-S were 0.63, and DASS21-S and DASS21-A were 0.72. In

comparison to the women without depression and anxiety, the patients with depression and anxiety [assessed by the Structured Clinical Interviews for DSM-IV Axis 1 Diagnoses (SCID) modules for depression (mild, moderate, and severe Major Depression or Dysthymia) and anxiety (Generalised Anxiety Disorder and Panic Disorder)] showed higher scores in all subscale of DASS-21, a suggesting the discriminant validity of the instrument. The Cronbach's alpha coefficient of DASS21-A in this study was 0.63.

Symptom cluster

The hypothesis is about examining the effect of the Qigong on the symptom cluster, referred to as a composite outcome comprising the vector of means on the transformed scores of fatigue, dyspnoea, and anxiety across time; therefore, the original scores of fatigue, dyspnoea, and anxiety were transformed out of 100 that able to see it at the single symptom outcome. To reduce the possibility of a Type I error, the original alpha level of 0.05 was divided by 3, giving a new alpha level of 0.017 (Pallant, 2013).

Secondary outcomes

Cough

The literature review identified three qualified scales assessing cough (Chung, 2006; Harle et al., 2012). They are the Leicester Cough Questionnaire (LCQ), the Cough-specific Quality of Life Questionnaire (CQLQ), and the Manchester Cough in Lung Cancer Scale. (1) LCQ consists of 19 items. The scale examines three domains of cough, including physical, psychological and social on a seven-point Likert scale. (2) CQLQ is a 28-item questionnaire. This scale measures cough in six domains, which are physical complaints, extreme physical complaints, psychosocial issues, emotional well-being, personal safety fears and functional abilities. (3) MCLCS consists of 10 items measuring an intensity of cough. This self-rated scale was developed for use in lung cancer. A review of Chung (2006) pointed out that the LCQ and CQLQ still require further validation and have been used mainly in non-cancer

populations. MCLCS (Molassiotis et al., 2012) is brief, clear, and demonstrates good psychometric quality. Therefore, this study used the current instrument to measure cough.

Description: The MCLCS included 10-item, unidimensional scale measures patients experience with cough in terms of its frequency, intensity, and bothersomeness. Patients respond by rating in the 5-point linked scale from 1 = never; 2 = some of the time; 3 = often; 4 = Most of the time; and 5 = All of the time (Appendix 13).

Scoring and interpretation: The score item 8 is reversed before calculating the total score. The total score is the sum score all 10 items. The possible range is 10 to 50. Ten indicates no cough and higher scores indicate more severe cough (Molassiotis et al., 2012).

Psychometric Properties: For reliability, the Cronbach's alpha was 0.86. Items also showed the high item to total correlations, ranging from 0.40 to 0.76 ($p < 0.001$). The test-retest (after a week) reliability was examined by Spearman's rho correlation coefficient ($r = 0.76$, $p < 0.001$). The Intra-Class Coefficient of average measure was 0.83 (95% confidence interval 0.74 - 0.90). In total, 18 patients and 25 healthcare professionals validated face validity of the scale. The Principal Component Analysis showed all items clustered around a single factor, suggesting a unidimensional scale (Molassiotis et al., 2012). The CVI of MCLCS Vietnamese version was 0.96 with the item-CIV ranging from 0.8 to 1.0. Cronbach's alpha coefficient of MCLCS was 0.91 (Long et al., 2015). In the current study, the Cronbach's alpha coefficient of MCLCS was 0.819.

Quality of life

Several instruments such as the Functional Living Index-Cancer (FLIC) (Morrow, Lindke, & Black, 1992), the Functional Assessment of Cancer Therapy scale (FACT) (Cella, Tulsky, Gray, Sarafian, Linn, Bonomi, Silberman, Yellen, Winicour, & Brannon, 1993) and the Lung Cancer Symptom Scale (LCSS) have been developed to assess QOL in patients with cancer in clinical trials (Hollen, Gralla, Kris, Cox, Belani, Grunberg, Crawford, &

Neidhart, 1994). The instrument most frequently used in cancer patients is the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (QLQ-C30), which was designed primarily for use in oncology clinical trials. It has previously been shown that EORTC-QLQ-C30 appears to yield a more reliable and comprehensive assessment of QOL in this population than could be achieved by other tools (Hollen & Gralla, 1996). Therefore, in this study, QOL was measured by the European Organisation for Research and Treatment of Cancer - Quality of life questionnaire - Core (EORTC-QLQ-C30) and Lung module (LC-13 subscale) (Fayers et al., 2012) (Appendix 14,15)

Description: The QLQ-C30, which is a "core questionnaire", comprises 30 items that measure aspects of functioning (physical, emotional, cognitive, social and role) and symptoms (fatigue, pain, dyspnoea, sleep problems, constipation, diarrhoea, appetite loss and nausea/vomiting) commonly reported by cancer patients, as well as financial problems and global health/quality of life. The EORTC of the QLQ-C30 was validated in 305 patients with non-resectable lung cancer. The results were published in 1993 and demonstrated good psychometric properties of the questionnaire (Aaronson, Ahmedzai, Bergman, Bullinger, Cull, Duez, Filiberti, Flechtner, Fleishman, & de Haes, 1993). In this study, the researcher used updated versions of the questionnaire (Bjordal, De Graeff, Fayers, Hammerlid, Pottelsberghe, Curran, Ahlner, Maher, Meyza, & Bredart, 2000; Osoba, Aaronson, Zee, Sprangers, & Velde, 1997). In addition to the core questionnaire, a number of diagnosis-specific questionnaires modules have been developed (Sprangers, Cull, Groenvold, Bjordal, Blazeby, & Aaronson, 1998), including a lung cancer specific module, the LC13, focus in lung cancer specific symptoms and side effects (dyspnoea, cough, site-specific pain, peripheral neuropathy, sore mouth, alopecia) (Bergman et al., 1994).

Scoring and interpretation: The QLQ-C30 is composed of both multi-item scales and

single-item measures. These include five functional scales, three symptom scales, a global health status/QOL scale, and six single items. Each of the multi-item scales includes a different set of items - no item occurs in more than one scale. The QLQ-C30 is assessed on a 4- level Likert scale with options ranging from 1 = “not at all”; 2 = “A little”; 3 = “Quite a Bit”; and 4 = “very much”. All of the scales and single-item measures range in score from 0 to 100. A high scale score represents a higher response level of QOL (Fayers et al., 2012). Thus, a high score for a functional scale represents a high/healthy level of functioning, a high score for the global health status/QOL represents a high QoL, but a high score for a symptom scale/item represents a high level of symptomatology/problems.

The principle for scoring these scales is the same in all cases: (1) Estimate the average of the items that contribute to the scale; this is the raw score; and (2) Use a linear transformation to standardise the raw score, so that scores range from 0 to 100; a higher score represents a higher (‘better”) level of functioning, or higher (“worse”) level of symptoms (Appendix 15).

The lung cancer module incorporates one multi-item scale to assess dyspnoea, and a series of single items assessing pain, coughing, sore mouth, dysphagia, peripheral neuropathy, alopecia, and haemoptysis. The scoring approach for the QLQ-LC13 is identical in principle to that for the symptom scales/single items of the QLQ-C30.

Psychometric Properties: The EORTC QLQ-C30 has been found to be reliable, valid and sensitive to change, and is widely used in clinical trials (Bjordal et al., 2000; Nicklasson, 2013). Reliability was assessed using Cronbach's alpha coefficient, all values of which were >0.7, with the exception of cognitive functioning, social functioning, and nausea and vomiting ($\alpha = 0.57$, $\alpha = 0.69$, and $\alpha = 0.68$, respectively) (Paiva, 2014). The lung cancer module is meant for use among a wide range of lung cancer patients varying in disease stage and treatment modality (Nicklasson, 2013). The Vietnamese version of both questionnaires

is variable (Bergman et al., 1994). The Cronbach's alpha coefficient of EORTC QLQ-C30 and QLQ-LC13 in this study were 0.83 and 0.75, respectively.

3.6 Data analysis

3.6.1 Data collection and management

Two research assistants collected data from January 2017 to December 2017. The research assistants were nurse practitioners at National Lung Hospital and Nam Dinh General Hospital, Vietnam. Before the data, collection took at two hospitals, obtained ethical approval from the two hospitals and The Hong Kong Polytechnic University before data collection. Two research assistants were trained about all issues related to the current research such as the objectives, research design, measuring instruments, ethical issues and data collection process steps by steps. They were required to data collection sessions, which conducted by only the researcher (role-play simulation), before fully involving in the process.

The responsibilities of two research assistants were:

a) Preparing data collection forms;

b) Working with patients, deliver consent form, questionnaires, pen for the respondents and signatures;

c) Recording contact information and contacting patients to arrange appointments for data collection;

d) Deliver questions form to patients (Patients read and fill out the questionnaires by themselves);

f) Collect questionnaires and recheck them to make sure all items were answered before finishing the data collection process.

The data were entered into the computer by the researcher. The data were stored in the computer at separate password-protected locations. The researcher was responsible for ensuring the integrity and accuracy of all data by means of checks on value ranges and logical checks.

3.6.2 Data cleaning

The datasets were checked against the paper recordings of raw data to ensure that the data coding was correct. The datasets were double-checked by the doctoral researcher and another Vietnamese doctoral candidate at School of Nursing. A further data cleaning process was conducted by the doctoral researcher and one of his academic supervisors. Categorical data (nominal and ordinal variables) were checked by generating frequency counts to identify the frequency of codes as well as possible missing values for each outcome variable (Portney & Watkins, 2009). Continuous data (interval variables) were checked by generating the corresponding descriptive statistics, such as the maximum value, minimum value, and mean score, to see whether the score range fell within the normal scope (Portney & Watkins, 2009).

3.6.3 Statistical analysis

Data analysis was performed according to the procedures of the SPSS version 23.

An intention to treat (ITT) analysis concepts, being in line with the CONSORT statement, was used to analyse primary and secondary outcomes, and multiple imputation methods was used to fill in missing items data. Six complete datasets for the primary and secondary outcome variables was created after imputation. Continuous variables were expressed as mean (SD) for normal distribution or median for non-normal distribution, and categorical variables were expressed as frequencies or percentages. Descriptive statistics was used to analyse the demographic data and disease characteristics as well fatigue, dyspnoea, anxiety, cough, and QOL. Baseline characteristics and comparison among groups were compared using one-way analysis of variance or the independent t-test for continuous variables and Pearson Chi-square test or The Mann-Whitney U test, Kruskal Wallis test for categorical variables. Non-incomparability appeared; therefore, non-inequality factors was treated as confounding variables in the final efficacy analysis.

For primary outcome: Generalised Estimating Equation (GEE) was performed to

examine the effect of Qigong on fatigue, dyspnoea, and anxiety across time, referred to as a composite outcome comprising the vector of means on the transformed score of fatigue, dyspnoea, and anxiety across time. GEE is a marginal model popularly applied for longitudinal/clustered data analysis in clinical trials or biomedical studies (Wang, 2014).

GEE form an extension of generalised linear models (GLMs) in that they allow to adjust for correlations between observations. A major strength of GEE is that they do not require the correct specification of the multivariate distribution but only of the mean structure. The GEE approach is becoming more and more popular in handling correlated response data, for example in longitudinal studies. For longitudinal data, the AR(1) working correlation should be preferred over banded, e.g., the 1-dependent working correlation structure (Wang & Carey, 2003).

Test of model effects: The original scores of dyspnoea, fatigue, and anxiety were transformed to 100 by transformations to achieve the best distribution of normality. The analyses of changes in outcome variables between T0 and T1 was the focus; data relating to changes between T0 and T2 were only assessed in an exploratory manner to examine longer-term effects. An interaction term (group difference x time) was added to each model to investigate the interactive effects of Qigong and time.

For the analysis of secondary outcomes, the effect of the Qigong on cough and QOL, the GEE was used to analyse the effect of the intervention. In each model, the independent variables are the group (Qigong group and wait-list control group), time (different measurement time points, such as baseline, post-intervention, and post-follow-up), confounding factors (e.g., age, gender) and any inequality factors among groups at the baseline assessment. All tests involved a two-sided significance level of $\alpha = 0.05$.

3.7 Quality assurance

The quality assurance (QA) is to ensure that all patients in the trial arms are treated comparably so the outcomes of this trial is valid (Karlberg & Speers, 2010). Therefore, the QA of this study is as follows: (1) Pre-trial QA regarded to protocol, investigator's brochure, feasibility, site assessment, training, contact, budget was reviewed by the ethic committee; (2) During trial: Consent form, amendments, adverse event reporting, progress reports, site monitoring, data management, and data queries was conducted following research protocol; and (3) Post-trial: Data management, data queries, data lock, statistical analysis, final report, publication, archiving was reported to the ethic committee, scientific committee of the Hong Kong Polytechnic University, and two hospitals in Vietnam.

3.8 Ethical issues

The principles of this study was following the declaration of Helsinki Principles that included: (1) Protection of life, health, dignity, integrity, right to self-determination, privacy, and confidentiality by using an individual code with each subject only known by the researcher; (2) Acceptable scientific principles; (3) Described in a protocol; (4) Protocol must be reviewed by an ethics committee; (5) Consideration of local laws and regulations; (6) Assessment of predictable risks, burdens, and importance; (7) appropriate training and qualifications of investigator; (8) Participation must be voluntary; and (9) Participants were give consent (World Medical Association, 2013). Therefore, the study information and consent form were approved by the Research Ethics committee of the Hong Kong Polytechnic University (Appendix 17), Hong Kong and the two hospitals in Vietnam (Appendix 18).

CHAPTER FOUR

RESULTS

The results are presented in four sections. The first section describes the participant characteristics and subject recruitment and attrition; the second section presents the descriptive statistics of baseline outcome data; the third section explores the effect of Qigong on the cluster symptom of fatigue, dyspnoea, and anxiety over time, while the fourth section presents data about the effect of Qigong on cough and quality of life.

4.1. Participant characteristics and subject recruitment and attrition

4.1.1 Participant characteristics

Participants were recruited from January 2017 to December 2017. The research student and his research assistants screened 1384 patients by posting posters, sending leaflets, and brochures. One hundred and sixty-seven eligible patients from the National Lung Hospital and Nam Dinh General Hospital were assessed for eligibility by using the "dyspnoea, fatigue, and anxiety intensity rating scale" (Appendix 6) to ensure finding the right subjects based on the inclusion and exclusion criteria. After face-to-face consultations during which the research protocols and objectives were explained to all patients at these two hospitals, 11 patients were excluded because they were uninterested or living too far away (distance from their home to hospital) to participate. As shown in Table 1, the sample comprised 156 patients (National Lung Hospital 127 patients and Nam Dinh General Hospital 29 patients); the majority of the sample were male (n= 116, 74.4%), while 25.6% (n = 40) were female, aged from 22–78 years, with a mean age of 56.84 ± 9.45 years. Most of the sample had general education (primary, secondary, and high school) (91%), patients were with secondary degree accounted for the highest prevalence (53.2%), and those with university or higher education were only 7.1%. Remarkably, 99% of patients reported no religion and were currently married.

In particular, more than four-fifths of the participants were unemployment (84%) at the time of data collection. More than 97% of patients were diagnosed with non-small lung cancer cell. About stage of disease, the most prevalent was stage IV (61.5%), followed by stage III (29.5%). Patients with stage I accounted for the smallest proportion (2.6%). There were 41% of patients treated with chemotherapy only, followed by chemotherapy plus radiotherapy (38.5%), and operation plus chemotherapy (20.5%). The number of chemotherapy cycles received by subjects varied from 4 to 14 cycles, and subjects with 4 cycles accounted for the highest prevalence (55.1%); those with 6 cycles and 12 cycles accounted for 26.9% and 11.5%, respectively. No statistically significant differences emerged in baseline demographic data and disease characteristics between the Qigong and wait-list control groups (Table 4).

4.1.2 Missing data and analysis

Measurements were recorded at three time points: the measurements for 78 (50%) participants (patients completing study) were recorded at all 3 times points, but for the other 78 participants, the measurements were recorded at one or two time points only, after which the patients dropped out. The patients who dropped out were older (mean age of 57.94 *vs.* 55.74 years, $p = 0.04$); more male dropped out than female ($p = 0.02$); exhibited more severe baseline fatigue (26.42 *vs.* 28.44 with $p = 0.036$); and higher baseline anxiety score (13.35 *vs*. 11.94, $p = 0.034$) than the non-dropout patients (Table 5). The total attrition rate was 50%, and the reasons for dropping out are presented in Figure 3. Overall, 47 (60.2%) and 31 (39.7%) participants dropped out in the Qigong and wait-list control groups, respectively.

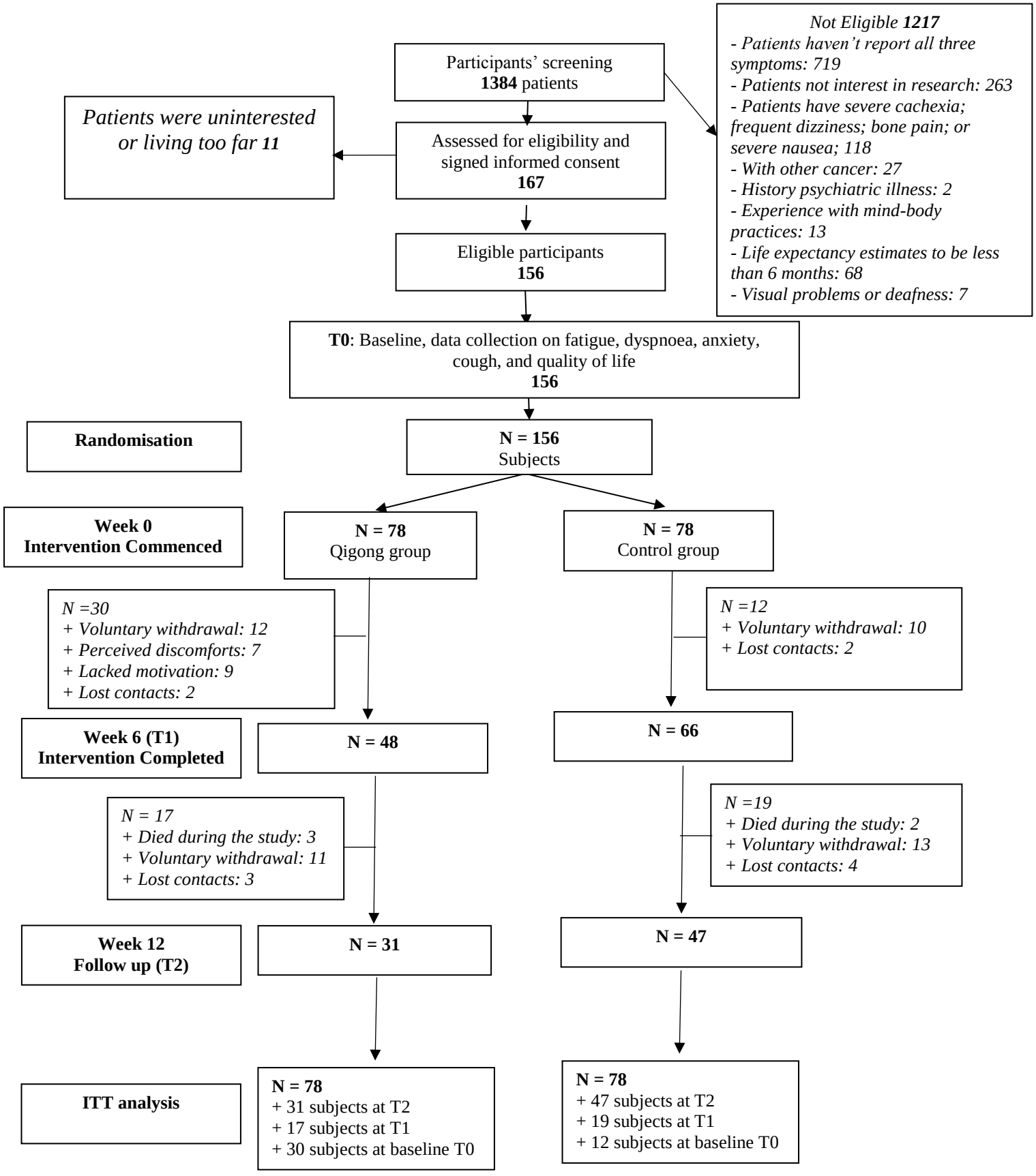

Figure 3. CONSORT Flow Diagram showing the number of participants

Table 4. Demographic data and disease characteristics for all participants in Qigong and control groups (n = 156)

Variables	All N = 156	Qigong groups n = 78	Control group n = 78	*p-value*[*]
Age (years)				
Mean (SD)	56.84(9.45)	57.62 (9.63)	56.06 (9.25)	0.429
Gender (n, %)				
Male	116(74.4)	59 (75.6)	57 (73.1)	0.714
Female	40 (25.6)	19 (24.4)	21 (26.9)	
Cancer type (n, %)				
NSLCC	152 (97.4)	78 (100)	74 (94.9)	0.43
SLCC	4 (2.6)	0 (0)	4 (5.1)	
Stage (n, %)				
I	4 (2.6)	4 (5.1)	0 (0)	0.28
II	10 (6.4)	4 (5.1)	6 (7.7)	
III	46 (29.5)	23 (29.5)	23 (29.5)	
IV	96 (61.5)	47 (60.3)	49 (62.8)	
Current treatment (n, %)				
Chemotherapy	64 (41)	31 (39.7)	33 (42.3)	0.73
Chemotherapy & Radiotherapy	60 (38.5)	29 (37.2)	31 (39.7)	
Chemotherapy & Operation	32 (20.5)	18 (23.1)	14 (17.9)	
Number of Chemotherapy Cycles				
Mean (SD)	5.67 (2.62)	5.33 (2.46)	6.01(2.73)	0.636
Education (n, %)				
Primary	16 (10.3)	10 (12.8)	6 (7.7)	0.508
Secondary	83 (53.2)	42 (53.8)	41 (52.5)	
High school	43 (27.6)	18 (23.1)	25 (32.1)	
Vocational school	3 (1.9)	1 (1.3)	2 (2.6)	
University and higher	11 (7.1)	7 (9.0)	4 (5.1)	
Religion (n, %)				
Non-religion	154 (98.7)	78 (100)	76 (97.4)	0.363
Buddhism	1 (0.65)	0	1 (1.3)	
Christian	1 (0.65)	0	1 (1.3)	
Employment (n, %)				
Current worker	25 (16)	16 (20)	9 (11.5)	0.095
Unemployment	131 (84)	62 (80)	69 (88.5)	
Marital status (n, %)				
Married	154 (98.7)	78 (100)	76 (97.4)	0.115
Single	2 (1.3)	0	2 (2.6)	

([*] The p-value are based on χ^2 analysis for categorical variables and t-tests for continuous variables)

NSLCC: Non-Small Cell Lung Cancer

SLCC: Small Cell Lung Cancer

4.1.3 Protocol adherence

For the attendance of Qigong group subjects, all 78 patients received 60 minutes of Qigong training, meeting twice a week for the first two weeks to intensify proper learning of the Qigong intervention over the research period. The majority demonstrated high attention and interest in the intervention. Patients in the Qigong group were asked to complete logbooks of their Qigong practice at home for the calculation of overall practice adherence. Adherence to the protocol was determined by self-reports on the logbooks. This checklist was completed at two weeks, and six weeks. Approximately 53% of participants (n = 41/78) self-reported practice of ≥ 3 h per week at two weeks, which corresponds to 30 minutes per day. Unfortunately, the completion of logbooks was so poor at 6 weeks that these data could not be used (due to patients forgetting to report at their home). Based on face-to-face meetings during follow-up at hospitals and telephone check-ups, on average, subjects reported practicing four to five sessions of Qigong/week and most of the subjects both read the Qigong book and listened to the DVD. Therefore, subject calculated adherence according to the reporting of practice during the reminder phone call face-to-face meeting until the end of intervention assessment point (T1). Of the 78 patients in the Qigong group, 48 (61.5%) completed the 6-week intervention program, and 66 (84.6%) completed at least half of the 6-week intervention. The practice adherence rate was 61.5%. The participants did not complete the intervention because they either voluntarily withdrew (n = 12), experienced discomfort (n = 7), lacked motivation (n = 9), or lost contact (n = 2). No related adverse effects were observed (none of the patients reported to research team) in the Qigong group during the study period (Figure 3).

Table 5. Description of patients' symptoms at baseline between those who dropped out and completed the study (i.e. active) in both intervention and control groups

Variables	Drop-out n = 78	Active n = 78	All subjects	*p-value**
Age (years)				
Mean (SD)	57.94 (7.21)	55.74 (11.19)	56.84 (9.45)	**0.004***
Gender (n, %)				
Male	67 (85.9)	49 (62.8)	116 (74.4)	**0.002***
Female	11 (14.1)	29 (37.2)	40 (25.6)	
Cancer type (n, %)				
NSLCC	77 (98.7)	75 (96.1)	152 (97.4)	0.620
SLCC	1 (1.3)	3 (3.9)	4 (2.6)	
Stage (n, %)				
I	2 (2.5)	2 (2.5)	4 (2.5)	0.226
II	2 (2.5)	8 (10.3)	10 (6.4)	
III	22 (28.3)	24 (30.8)	46 (29.5)	
IV	52 (66.7)	44 (56.4)	96 (61.6)	
Current treatment (n, %)				
Chemotherapy	35 (44.9)	29 (37.2)	64 (41)	0.138
Chemotherapy & Radiotherapy	32 (41)	28 (35.9)	60 (38.5)	
Chemotherapy & Operation	11 (14.1)	21 (26.9)	32 (20.5)	
Number of Cycles				
Mean (SD)	5.6 (2.65)	6.18 (3.04)	5.89 (2.86)	0.216
Education (n, %)				
Primary	11 (14.1)	5 (6.4)	16 (10.3)	0.394
Secondary	43 (55.1)	40 (51.3)	83 (53.2)	
High school	19 (24.4)	24 (30.8)	43 (27.6)	
Vocational school	1 (1.3)	2 (2.6)	3 (1.9)	
University and higher	4 (5.1)	7 (8.9)	11 (7)	
Religion (n, %)				
Non-religion	78 (100)	76 (97.4)	154 (98.7)	0.363
Buddhism	0	1 (1.3)	1 (0.65)	
Christian	0	1 (1.3)	1 (0.65)	
Employment (n, %)				
Current worker	9 (11.5)	21 (26.9)	30 (19.2)	**0.024***
Non-current worker	69 (88.5)	57 (73.1)	126 (80.8)	
Marital status (n, %)				
Married	78 (100)	76 (97.4)	154 (98.7)	0.497
Single	0	2 (2.6)	2 (1.3)	
Symptom outcomes				
Fatigue	28.44 (5.87)	26.42 (6.08)	27.25(5.9)	**0.036***
Dyspnoea	17.05 (3.53)	16.93 (2.88)	17.28(3.46)	0.525
Anxiety	13.35 (5.17)	11.94 (6.34)	13.5(5.43)	**0.034***
Cough	20.39 (5.23)	20.37 (6.12)	21.06 (5.23)	0.080

* $p \leq 0.05$

4.2. Descriptive data relating to the baseline outcome data

There were significant between-group differences at baseline in fatigue (Qigong 26.78 and control 27.71; $p = 0.039$) and diarrhoea (Qigong 6.41 and control 9.4; $p = 0.024$), as depicted in Table 6. At baseline, patients in both groups reported similar levels of QOL in most domains. There were no clinically relevant differences (MD) ≥10 points. Small differences of 5–10 points were encountered in dyspnoea, peripheral neuropathy LC13, and alopecia LC13 (MD – 7.29; -5.13; and -5.37 respectively), (Table 6).

The mean fatigue scores at baseline were 26.78 (SD = 6.58) and 27.71 (SD = 5.13) in the Qigong and control groups, respectively; a significant intergroup difference was observed (t = 0.981, p = 0.039) (Table 6). The mean dyspnoea scores at baseline were 17.26 (SD = 3.50) and 17.29 (SD = 3.44) in the Qigong and waitlist control groups, respectively. No significant intergroup differences were observed (t = 0.046, p = 0.723). At baseline, the mean anxiety scores were 13.31 (SD = 5.27) and 13.39 (SD = 5.21) for the Qigong and waitlist control groups, respectively. No significant intergroup differences were observed (t = -0.249, p = 0.658).

Table 6. Description of studied variables at baseline (N = 156)

	Mean (SD)			***p***
	All (n = 156)	Control (n = 78)	Qigong (n = 78)	
Primary outcome				
Fatigue (range 6 -42)	27.25(5.9)	27.71(5.13)	26.78(6.58)	**0.039***
Dyspnoea (range 9 -30)	17.28(3.46)	17.29(3.44)	17.26(3.5)	0.723
Anxiety (range 4 - 36)	13.5(5.43)	13.39(5.21)	13.31(5.68)	0.658
Secondary outcome				
Cough (range 12 -39)	21.06 (5.23)	20.71(5.36)	21.41(5.10)	0.870
Quality of life				
Global health status	48.39(13.12)	46.79(12.75)	50.00(13.36)	0.803
Physical functioning	63.37(14.81)	63.68(13.99)	63.07(15.66)	0.388
Role functioning	56.62(18.51)	57.05(17.71)	56.19(19.38)	0.520
Emotional functioning	66.44 (12.94)	64.42(12.43)	68.47(13.19)	0.567
Cognitive functioning	61.08(21.18)	57.88(20.22)	64.29(21.75)	0.781
Social functioning	48.29(19.59)	47.22(18.49)	49.35(20.70)	0.647
Fatigue	44.23 (14.95)	44.30(13.57)	44.17(16.30)	0.080
Nausea and vomiting	14.31(20.16)	15.17(19.95)	13.46(20.46)	0.888
Pain	31.10(20.40)	28.66(19.35)	33.54(21.23)	0.847
Dyspnoea	31.39(15.72)	35.04(15.09)	27.75(15.57)	0.082
Insomnia	45.29(28.32)	43.58(29.08)	47.00(27.62)	0.641
Appetite lose	44.87(25.01)	46.15(24.75)	43.58(25.37)	0.671
Constipation	10.25(17.60)	11.53(18.47)	8.97(16.70)	0.111
Diarrhoea	7.90(15.66)	9.40(16.90)	6.41(14.27)	**0.024***
Financial difficulties	55.12(27.21)	56.83(25.82)	53.41(28.59)	0.179

Table 6. Description of studied variables at baseline (N = 156) (Cont.)

	Mean (SD)			***p***
	All (n = 156)	Control (n = 78)	Qigong (n = 78)	
Secondary outcome				
Quality of life – LC13				
Dyspnoea	40.01(15.49)	40.00(14.37)	40.02(16.63)	0.363
Coughing	40.38(15.61)	40.59(16.68)	40.17(14.57)	0.594
Haemoptysis	5.15(13.19)	5.18(12.09)	5.12(14.29)	0.859
Sore mouth	14.23(23.02)	14.79(23.72)	13.67(22.43)	0.548
Dysphagia	30.55(26.22)	29.91(25.53)	31.19(27.04)	0.746
Peripheral neuropathy	35.89(28.97)	38.46(27.43)	33.33(30.38)	0.452
Alopecia	48.83(31.51)	51.52(30.17)	46.15(32.77)	0.133
Pain in chest	28.63(25.24)	29.48(24.60)	27.77(25.99)	0.176
Pain in arm or shoulder	25.85(26.38)	27.35(26.17)	24.35(26.68)	0.346
Pain in other parts	21.97(25.88)	20.04(24.59)	23.89(27.13)	0.405

** $p \leq 0.05$*

4.3. Primary outcome

4.3.1 Effect of Qigong on fatigue

There was no improvement in the between-groups analysis of the two groups, which means that Qigong did not improve fatigue. However, there were within-group significant changes in the Qigong group, and this suggests there were some variations in the effect of the intervention (Table 7a, 7b and Figure 4). There was also a trend in improvement within-group of the Qigong group, with the mean fatigue scores of the Qigong group being improved by 2.25 points between the baseline and the sixth week ($p = 0.004$), and then remained similar until the 12^{th} week by 2.71 points from baseline ($p = 0.021$). In contrast, the mean fatigue score of the control group changed little with a mean difference of 0.82 and 0.04 at the 6^{th} week and 12^{th} week, respectively, this change was not significant.

Table 7a. Description of studied variables at baseline (N = 156)

	Mean (Std. Error)		**Group*Time**		
	Qigong	**Control**	β	**95% CI**	*p- value*
Baseline	26.79(0.74)	27.72(0.58)			
6 weeks	29.04(0.67)	28.54(0.58)	1.426	-0.81; 3.66	0.062
12 weeks	29.49(1.15)	27.68(0.76)	2.745	-0.14; 5.63	0.211

Fatigue score range from 6 to 42 *(Higher score indicates less fatigue)*

Table 7b. Pairwise Comparisons on fatigue (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**2.25 (0.71; 0.78)**	**0.004***	**2.71 (0.42; 4.99)**	**0.021***	0.46 (-1.98; 2.90)	0.712
Control	0.82 (-0.81; 2.45)	0.323	0.04 (-1.79;1.71)	0.966	-0.86 (-2.45; 0.73)	0.290
Qigong & Control	0.93 (-0.91; 2.77)	0.323	-0.50 (-2.24; 1.24)	0.573	-1.82 (-4.51; 0.87)	0.185
	Baseline		**6th week**		**12th week**	

** $p \leq 0.05$*

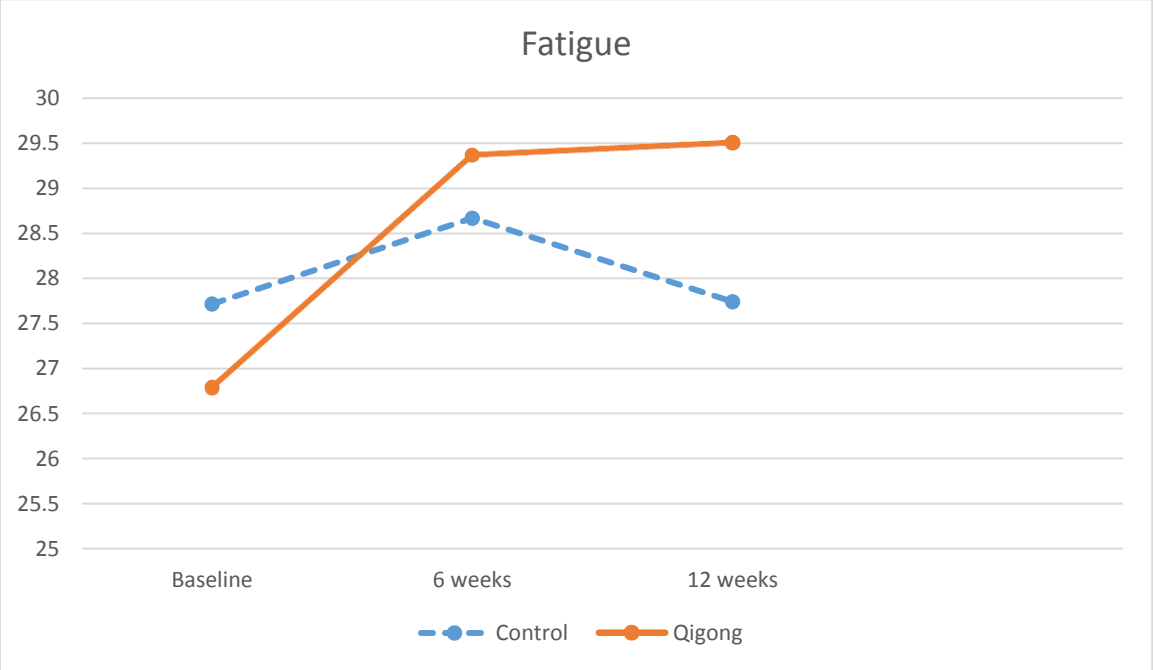

Figure 4. Changes in fatigue scores across time

4.3.2 Effect of Qigong on dyspnoea

A significant difference was observed at the 6th week and 12th week between-groups of the Qigong and waitlist control groups with a mean difference of 1.15 ($p = 0.014$) and mean difference of 1.50 ($p = 0.025$), respectively (Table 8a, 8b and Figure 5). Furthermore, the mean dyspnoea scores within group of the Qigong group declined from baseline to the 6th week with a mean difference of -1.43 ($p = 0.002$) and then marginally increased at the 12th week; these changes revealed no statistical significance in these scores. In contrast, the mean dyspnoea scores within group of waitlist control group gradually changed at the 6th week and then increased slightly at the 12th week, although these changes revealed no statistical significance in these scores. As indicated by statistically significant within-group changes, there was variation in Qigong group in the first 6 weeks and Qigong needed more than 6 weeks to improve dyspnoea.

Table 8a. Results of generalized estimating equations on dyspnoea (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	β	**95% CI**	*p- value*
Baseline	17.27(0.39)	17.29(0.39)			
6 weeks	15.84(0.33)	16.99(0.33)	-1.122	(-2.45;0.20)	0.097
12 weeks	16.04(0.55)	17.54(0.38)	-1.472	(-3.19;0.25)	0.094

Dyspnoea score range from 9 to 30 (*higher score indicates more dyspnoea*)

Table 8b. Pairwise Comparisons on dyspnoea (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**-1.43 (-2.35; -0.51)**	**0.002***	-1.23 (-2.67; 0.16)	0.082	0.20 (-1.05; 1.45)	0.752
Control	-0.31 (-0.78; 1.26)	0.525	0.24 (-0.78; 1.26)	0.640	0.55 (-0.47; 1.58)	0.290
Qigong & Control	0.03 (-1.06; 1.11)	0.963	**1.15 (0.24; 2.06)**	**0.014***	**1.50 (0.19; 2.80)**	**0.025***
	Baseline		**6th week**		**12th week**	

*$p \leq 0.05$

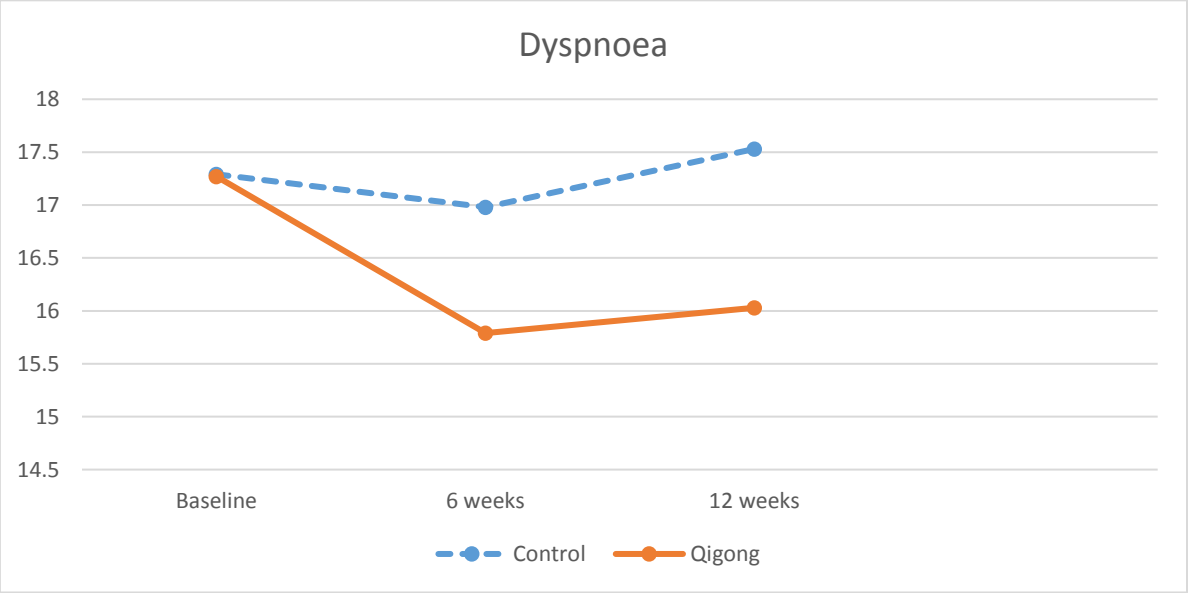

Figure 5. Changes in dyspnoea scores across time

4.3.3 Effect of Qigong on anxiety

There was no between-groups improvement in the two groups, which mean Qigong did not improve anxiety. However, there was the trend improvements within the Qigong group; the mean anxiety scores of Qigong group improved by 1.69 points between the baseline and the 6^{th} week ($p = 0.049$), and then remained similar until the 12^{th} week by 3.01 points from baseline ($p = 0.025$). Furthermore, no significant interaction term (group x time) of anxiety across time was observed. These results indicated that there were some variations in the Qigong group across time and need to explore more about the related confounding variables (Table 9a, 9b and Figure 6).

Table 9a. Results of generalized estimating equations on anxiety (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	13.62(0.64)	13.40(0.59)			
6 weeks	11.92(0.74)	12.03(0.72)	-0.322	-2.74; 2.10	0.794
12 weeks	10.61(1.31)	12.46(0.77)	-2.065	-5.21; 1.08	0.198

Anxiety score range from 4 to 36 *(Higher score indicates more anxiety)*

Table 9b. Pairwise Comparisons on anxiety (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**-1.69 (-3.38; -0.01)**	**0.049***	**-3.01 (-5.63; -0.38)**	**0.025***	-1.31 (-3.95; 1.32)	0.329
Control	-1.37 (-3.10; 0.36)	0.121	-0.94 (-2.67; 0.79)	0.286	0.43 (-1.36; 2.23)	0.638
Qigong & Control	-0.22 (-1.92; 1.48)	0.802	0.11 (-1.92; 2.13)	0.920	1.85 (-1.13; 4.83)	0.225
	Baseline		**6th week**		**12th week**	

* $p \leq 0.05$

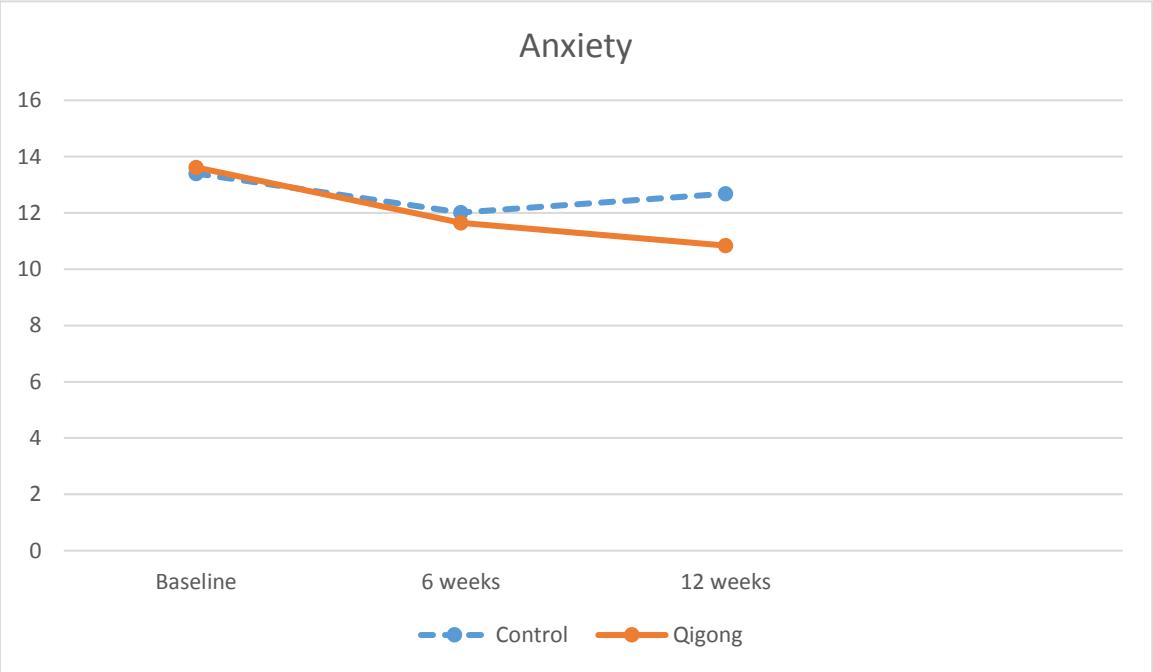

Figure 6. Changes in anxiety scores across time

4.3.4 Effect of Qigong on symptoms cluster of fatigue, dyspnoea, and anxiety

There was no improvement in the between-groups analysis of the two groups, which means Qigong did not improve the symptom cluster. However, there were within-group significant changes in the Qigong group, which suggests that there were some variations in the effect of the intervention (Table 10, 10b and Figure 7). There was also a trend in improvement within-group of the Qigong group, with the mean symptom cluster scores of Qigong group being improved by 3.78 points between the baseline and the 6^{th} week ($p = 0.002$), and then remaining similar until the 12^{th} week by 5.1 points from baseline ($p = 0.015$). In contrast, the mean symptom cluster score of the control group changed little, with a mean difference of 1.85 and 0.52 at the 6^{th} week and 12^{th} week, respectively; this change was not significant.

Table 10a. Results of generalized estimating equations on symptom cluster of fatigue, dyspnoea, anxiety (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	41.36 (1.11)	40.61(0.90)			
6 weeks	37.58(1.06)	38.76(0.97)	-1.926	-5.31; 1.46	0.264
12 weeks	36.26(2.04)	40.10(1.20)	-4.584	-9.46; 0.30	0.066

Higher score indicates more problems

Table 10b. Pairwise Comparisons on symptom cluster (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**- 3.78 (-6.16, -1.40)**	**0.002***	**-5.10 (-9.20, -0.99)**	**0.015***	-1.31 (-5.40, 2.77)	0.528
Control	-1.85 (-4.25, 0.54)	0.129	-0.52 (-3.15, 2.12)	0.702	1.34 (-1.33, 4.01)	0.327
Qigong & Control	-0.74 (-3.54, 2.05)	0.601	1.18 (-1.63, 3.99)	0.411	3.83 (-0.79, 8.46)	0.104
	Baseline		**6th week**		**12th week**	

** $p \leq 0.05$*

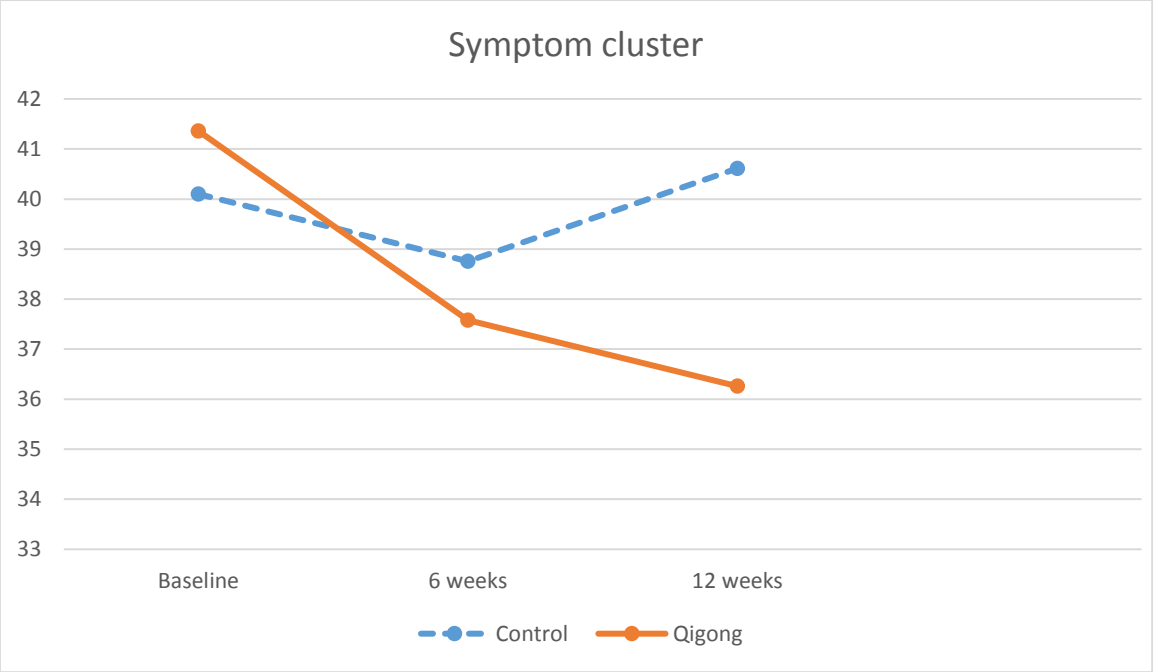

Figure 7. Changes in symptom cluster of fatigue, dyspnoea, and anxiety scores across time

As mentioned in the reports of the results of the primary outcomes, there were factors affecting the subjects in the Qigong group. The research students analysed additional factors related to demographics and pathology related to symptoms such as age, gender, occupation, types of lung cancer, stage, type of treatment, and the number of cycles. The results from GEE showed that the only gender was a factor influencing the effectiveness of the Qigong intervention, while other factors had no effect on primary outcomes (Table 10c). A further analysis of the difference between male and female in the Qigong group was made. There was a significant difference between males and females for dyspnoea, anxiety and symptom cluster. Qigong had more improved symptoms in male compare to female in the intervention group (Table 10d).

Table 10c. Results of generalized estimating equations on primary outcomes with gender as covariance (N = 156)

	Mean (Std. Error)		**Group*Time*gender**		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Fatigue					
Baseline	26.79(0.74)	27.72(0.58)			
6 weeks	29.04(0.67)	28.54(0.58)	1.33	-1.56; 4.22	0.367
12 weeks	29.50(1.15)	27.68(0.76)	-7.08	-11.62; -2.54	**0.002***
Dyspnoea					
Baseline	17.269(0.395)	17.295(0.388)			
6 weeks	15.84(0.33)	16.99(0.33)	0.85	-0.31; 2.02	0.152
12 weeks	16.04(0.55)	17.54(0.38)	3.46	0.91; 6.01	**0.008***
Anxiety					
Baseline	13.615(0.640)	13.398(0.587)			
6 weeks	11.92(0.74)	12.03(0.72)	0.79	-2.30; 3.89	0.616
12 weeks	10.61(1.31)	12.46(0.77)	7.98	1.77; 14.18	**0.012***
Symptom cluster					
Baseline	41.358 (1.107)	40.612(0.901)			
6 weeks	37.58(1.06)	38.76(0.97)	0.72	-3.51; 4.94	0.739
12 weeks	36.26(2.04)	40.10(1.20)	13.79	4.23; 23.35	**0.005***

** $p \leq 0.05$*

Table 10d. Results of primary outcomes between male and female within Qigong group

	Baseline (n = 78)			**6-week (n = 48)**			**12-week (n =31)**		
	Mean	SD	p	Mean	SD	p	Mean	SD	p
Fatigue									
Male	27.16	6.28	0.573	29.04	5.13	0.102	31.57	5.00	0.051
Female	25.63	7.51		30.24	4.08		25.16	7.53	
Dyspnoea									
Male	17.14	3.46	0.962	15.51	2.54	**0.032***	15.14	2.26	**0.038***
Female	17.68	3.71		16.54	1.51		17.90	3.900	
Anxiety									
Male	12.94	4.07	0.138	11.34	5.72	0.130	8.86	5.71	**0.018***
Female	15.68	7.24		12.46	3.92		15.00	9.39	
Symptom Cluster									
Male	40.47	9.08	0.272	36.64	8.44	**0.030***	32.74	7.77	**0.002***
Female	44.08	11.74		37.62	5.26		44.02	15.02	

* $p \leq 0.05$

4.4 Secondary outcomes

4.4.1 Effect of Qigong on cough across time

Qigong improved cough symptoms in this population, a significant interaction term (group x time) of the cough across time was observed with p = 0.001 and p = 0.017 at the 6th and 12th week, respectively; the results of GEE on cough were presented in Table 11a. The mean cough scores within group of the Qigong group declined from baseline to the 6th week with a mean difference of -4.25 (p = 0.000) and then marginally declined at the 12th week; these changes revealed statistical significance in these scores by -2.73 points from baseline (p = 0.018). In addition, significant difference was observed at the 6th and 12th week between-groups of the Qigong and waitlist control groups with a mean difference of 3.07 (p = 0.001) and 2.82 (p = 0.039), respectively. The changes of 4.2 in this score from baseline to the 6th week in Qigong group was close to the minimal clinically meaningful differences of 4.4 units for this scale (Table 11b and Figure 8).

Table 11a. Results of generalized estimating equations on cough (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	21.41(0.57)	20.72(0.60)			
6 weeks	17.21(0.67)	20.28(0.69)	-3.766	-5.962; -1.569	**0.001**
12 weeks	18.68(1.07)	21.51(0.85)	-3.519	-6.409; -0.629	**0.017**

Cough score range from 11 to 39 *(Higher score indicates more severe cough)*

Table 11b. Pairwise Comparisons on cough (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**-4.25 (-5.87; -2.54)**	**0.000***	**-2.73 (-4.99; -0.47)**	**0.018***	1.48 (-0.92; 3.87)	0.227
Control	-0.48 (-1.88; 1.00)	0.550	0.79 (-1.01; 2.59)	0.389	1.23 (-0.74; 3.19)	0.221
Qigong & Control	-0.70 (-2.33; 0.94)	0.404	**3.07 (1.18; 4.96)**	**0.001***	**2.82 (0.14; 5.51)**	**0.039***
	Baseline		**6th week**		**12th week**	

** $p \leq 0.05$*

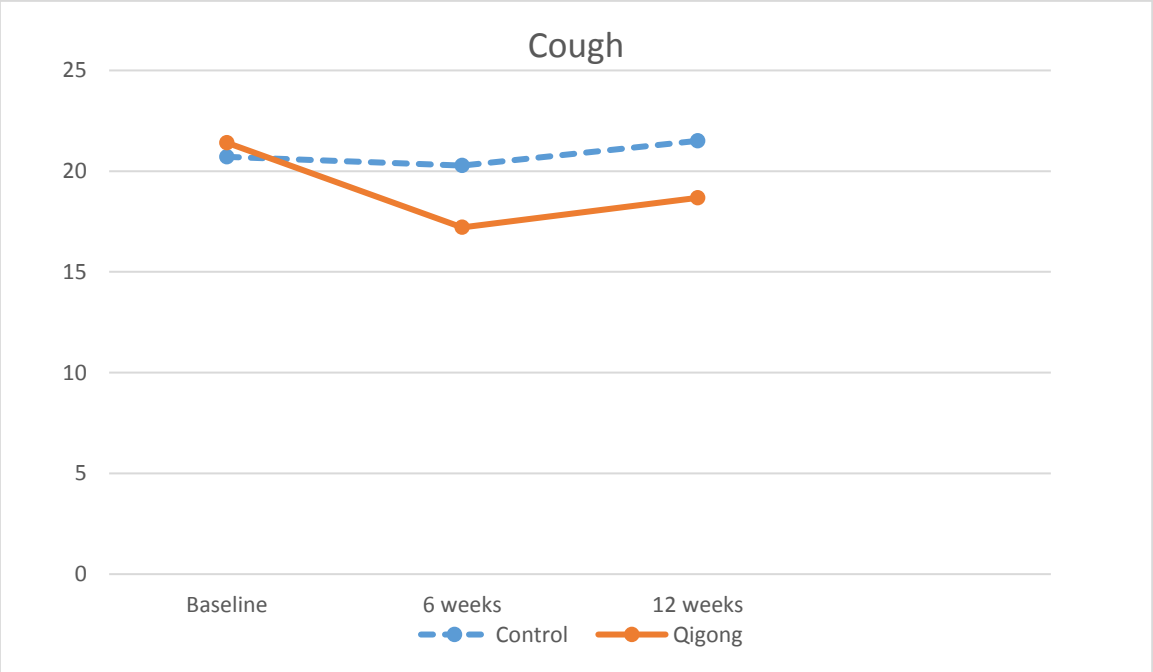

Figure 8. Changes in cough scores across time

4.4.2 Quality of life – global health status domain

A significant difference was observed at the 6th week between-groups of the Qigong and waitlist control groups with a mean difference of -5.69 (p = 0.021) (Table 12a, 12b and Figure 9). Furthermore, the mean global health status scores within group of the Qigong group increased from baseline to the 6th week with a mean difference of 5.29 (p = 0.010). In contrast, the mean global health status scores within group of waitlist control group gradually changed at the 6th week and then decreased slightly at 12th week although these changes revealed no statistical significance in scores. As indicated by statistically significant within-group changes, there was variation in the Qigong group in the first 6 weeks that need further exploration.

Table 12a. Results of GEE on global health status of QOL (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	50.00(1.50)	46.79(1.44)			
6 weeks	55.29(1.89)	49.61(1.57)	2.481	-2.94; 7.90	0.369
12 weeks	51.76(3.21)	45.80(2.28)	2.754	-5.55; 11.06	0.516

Global health status score ranges from 0 to 83.33 *(Higher score indicates better QOL)*

Table 12b. Pairwise Comparisons on global health status (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**5.29 (1.26; 9.32)**	**0.010***	1.76 (-5.15; 8.67)	0.618	-3.53 (-9.27; 2.20)	0.128
Control	2.81 (-0.81; 6.44)	0.128	0.99 (-5.60; 3.62)	0.673	-3.81 (-8.63; 1.02)	0.122
Qigong & Control	-3.21 (-7.28; 0.87)	0.123	**-5.69 (-10.50; -0.87)**	**0.021***	-5.96 (-13.67; 1.75)	0.130
	Baseline		**6th week**		**12th week**	

** $p \leq 0.05$*

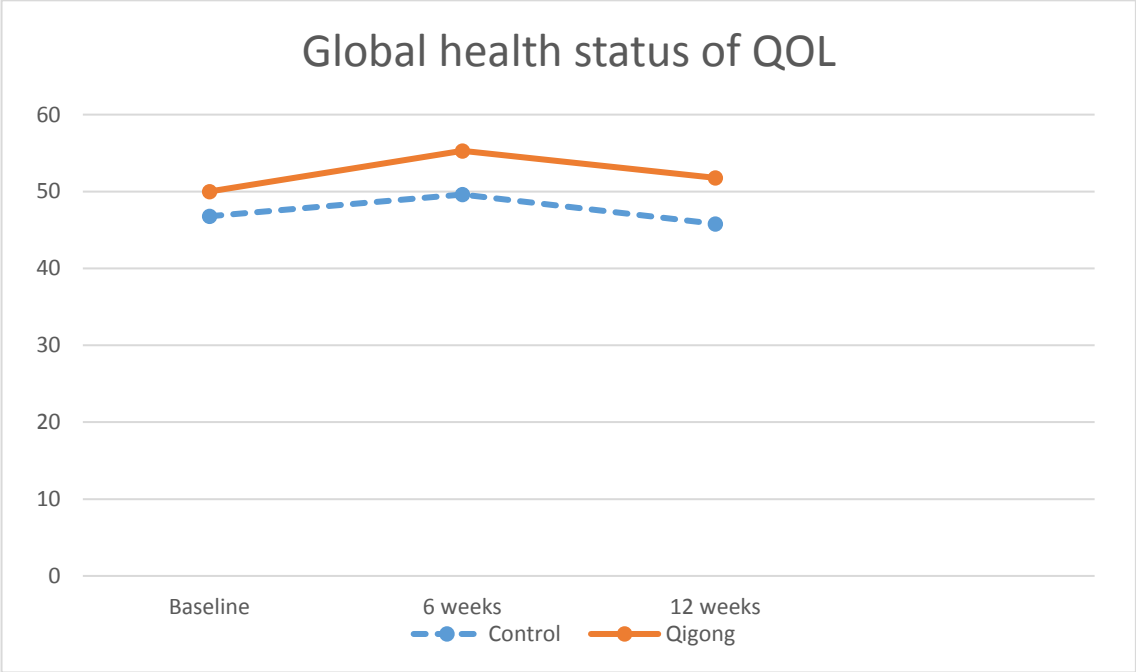

Figure 9. Changes in global health status scores across time

4.4.3 Quality of life - functional scales

The functional scales were the scoring of physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning. A significant difference was only observed at the 6th week between-groups of the Qigong and waitlist control groups with a mean difference of –6.02 ($p = 0.001$) (Table 13b). Furthermore, there were no significant differences in mean functional scores within both the Qigong and control groups. This means that Qigong did not improve functional scores across time (Table 13a and Figure 10).

Table 13a. Results of generalized estimating equations on functional score of QOL

(N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	60.28(1.42)	58.05(1.14)			
6 weeks	62.08(1.36)	56.06(1.22)	3.788	-0.52; 8.10	0.085
12 weeks	59.42(2.21)	55.49(1.71)	1.701	-4.38; 7.78	0.583

Functional score ranges from 18.33 to 92.33 *(Higher score indicates better function)*

Table 13b. Pairwise Comparisons on functional score (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	1.80 (-1.48; 5.08)	0.283	-0.86 (-5.82; 4.10)	0.733	-2.66 (-6.92; 1.60)	0.221
Control	-1.99 (-4.79; 0.81)	0.163	-2.56 (-6.08; 0.95)	0.153	-0.57 (-4.27; 3.13)	0.762
Qigong & Control	-2.23 (-5.80; 1.35)	0.222	**-6.02 (-9.60; -2.44)**	**0.001***	-3.93 (-9.41; 1.55)	0.160
	Baseline		**6th week**		**12th week**	

*$p \leq 0.05$

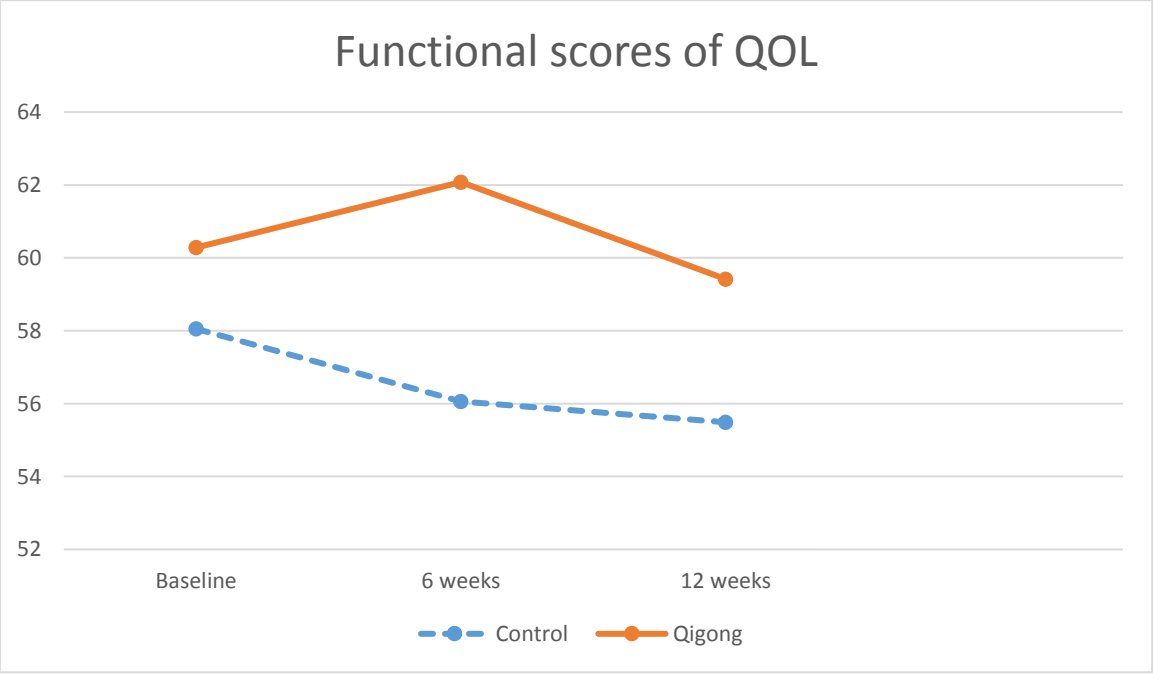

Figure 10. Changes in functional scores across time

4.4.4 Quality of life - symptom scales

The symptom scales were the scoring of fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties. A significant difference was observed at the 6th week and 12th week between-groups of the Qigong and waitlist control groups with a mean difference of 5.81 ($p = 0.002$) and 5.54 ($p = 0.034$), respectively (Table 14a, 14b and Figure 11). Furthermore, the mean symptom scores within group of the Qigong group declined from baseline to the 6th week, with a mean difference of -3.45 ($p = 0.035$), and then marginally increased at the 12th week; these changes revealed no statistical significance in these scores. In contrast, the mean symptom scores within the waitlist control group gradually changed at the 6th week and then increased slightly at the 12th week, although these changes revealed no statistical significance in these scores. As indicated by statistically significant within-group changes, there was variation in the Qigong group in the first 6 weeks and Qigong needed more than 6 weeks to improve symptom scores.

Table 14a. Results of generalized estimating equations on symptom scales of QOL (N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	30.93(1.36)	32.30(1.20)			
6 weeks	27.48(1.42)	33.29(1.20)	-4.440	-8.63; -0.25	**0.038***
12 weeks	29.54(2.15)	35.08(1.49)	-4.164	-9.87; 1.55	0.153

Symptom scales score range from 2.47 to 75.31 *(Higher score indicates more severe the symptoms)*

Table 14b. Pairwise Comparisons on symptom scales (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	**-3.45 (-6.65; -0.24)**	**0.035***	-1.39 (-6.15; 3.38)	0.569	2.06 (-2.20; 6.32)	0.343
Control	0.99 (-1.71; 3.70)	0.471	2.78 (-0.37; 5.93)	0.083	1.79 (-1.39; 4.96)	0.270
Qigong & Control	1.37 (-2.17; 4.92)	0.448	**5.81 (2.18; 9.45)**	**0.002***	**5.54 (0.41; 10.67)**	**0.034***
	Baseline		**6th week**		**12th week**	

* $p \leq 0.05$

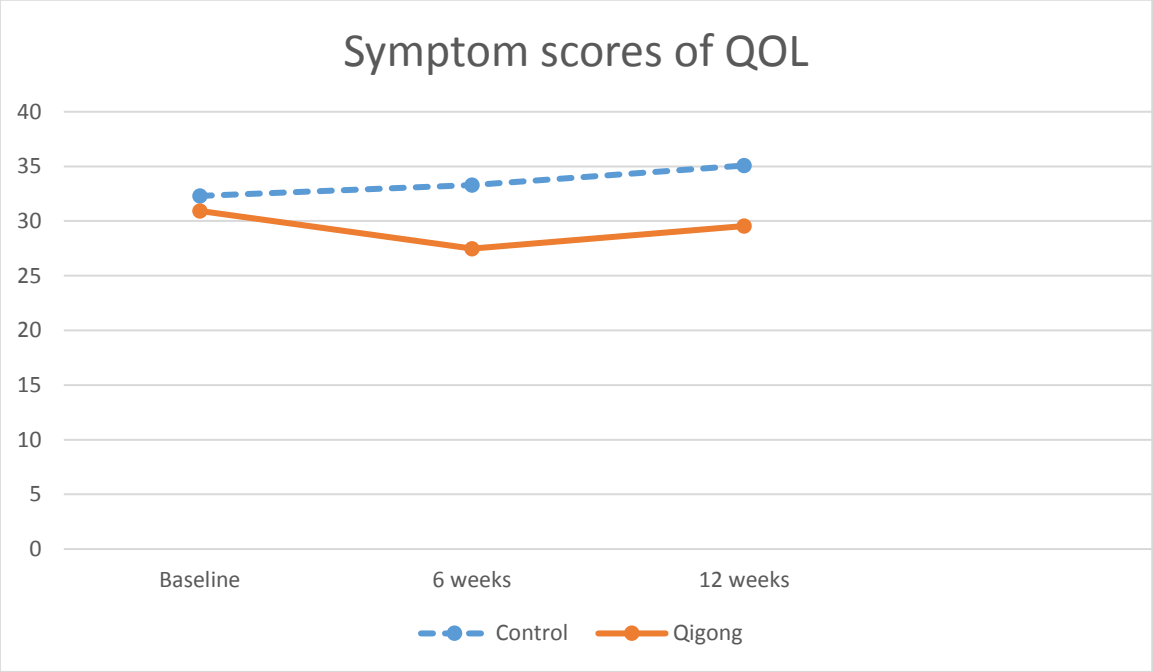

Figure 11. Changes in symptom scores across time

4.4.5 Quality of life – LC13 scales

The mean LC13 total scores of the Qigong group marginally increased from baseline to the 6th week with a mean difference of 1.16 (p = 0.448) and then increased at the 12th week with a mean difference of 7.23 (p = 0.001); these changes across time revealed statistical significance in these scores. The mean LC13 total scores of control group gradually increased at the 6th week with a mean difference of 3.27 (p = 0.024) and then continue increased at 12th week, these changes revealed statistical significance in these scores with a mean difference of 7.83 (p = 0.000). In addition, no significant differences were observed at the 6th week and 12th week between the Qigong and waitlist control groups. Furthermore, there was no significant interaction (group x time) of the model across time (Table 15a, 15b and Figure 12).

Table 15a. Results of generalized estimating equations on LC13 total score of QOL

(N = 156)

	Mean (Std. Error)		Group*Time		
	Qigong	**Control**	**β**	**95% CI**	*p- value*
Baseline	28.57(1.38)	29.74(1.24)			
6 weeks	29.73(1.55)	33.01(1.28)	-2.114	-6.23; 2.00	0.314
12 weeks	35.80(2.05)	40.83(1.58)	-3.868	-9.34; 1.60	0.166

LC13 total score range from 2.22 to 63.33 *(Higher score indicates more severe the symptoms)*

Table 15b. Pairwise Comparisons on LC13 total score (N = 156)

	Baseline – 6th week		**Baseline – 12th week**		**6th week - 12th week**	
	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*	Mean difference (95%CI)	*p-value*
Qigong	1.16 (-1.83; 4.14)	0.448	**7.23 (2.91; 11.55)**	**0.001***	**6.07 (1.86; 10.29)**	**0.005***
Control	**3.27 (0.44; 6.10)**	**0.024***	**11.10 (7.74; 14.45)**	**0.000***	**7.83 (4.63; 11.02)**	**0.000***
Qigong & Control	1.17 (-2.47; 4.80)	0.530	3.28 (-0.67; 7.23)	0.104	5.03 (-0.03; 10.10)	0.051
	Baseline		**6th week**		**12th week**	

** $p \leq 0.05$*

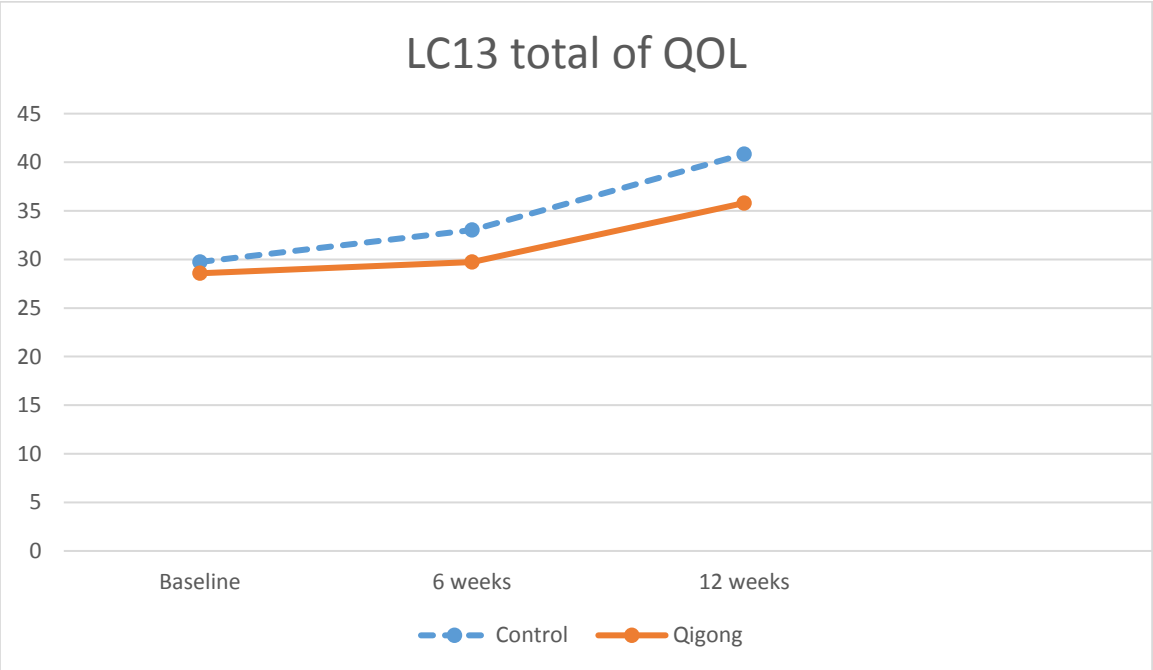

Figure 12. Changes in LC13 total scores across time

4.5 Summary of results chapter

This chapter reported the results of the current RCT. The sample included 156 Vietnamese lung cancer patients from the National Lung Hospital and Nam Dinh General Hospital. The majority of the sample was male (74.4%) and the mean age was 56.84 ± 9.45 years. Majority of the subjects completed secondary school (53.2%). The mean duration of treatment with lung cancer was 5.67 ± 2.62 cycles, majority of the subjects with 4 cycles of the chemotherapy (55.1%). The majority of the sample was at stage IV (61.5%) and III (29.5%). The mean score of fatigue at baseline was 27.25 ± 5.9 with a range from 6 to 42; dyspnoea was 17.28 ± 3.46 with a range from 9 to 30, and anxiety was 13.5 ± 5.43 with a range from 4 to 36.

There was no improvement in the between-groups analysis on fatigue, anxiety, and symptom cluster (fatigue, dyspnoea, and anxiety) of the two groups across time, which means that Qigong did not improve those symptoms. However, analysis of the primary outcome reported that the subjects in the Qigong groups showed a trend towards an improvement in symptoms which was not present for those in the waitlist control group, with the within-group difference in the fatigue, dyspnoea, and anxiety reaching statistical significance from baseline to 6^{th} week with p = 0.004, 0.002, and 0.049, respectively. In terms of the symptom cluster, the subjects in the Qigong group had a trend of improvement of the symptom cluster from 6^{th} week to 12^{th} week with the significant difference within group found of p = 0.002, but this was not observed in the waitlist control group. Moreover, no significant group*time interaction across time was observed. Gender was considered as a covariance.

Statistically significant among-group differences were identified on cough and significant interaction of group*time across time was observed. However, there was no significant interaction term (group x time) of the GEE model across time in global health status, functional scales, and symptom scales of QOL questionnaire. In addition, the declining health based on LC13 scales was significantly lower in the Qigong group than in the waitlist

control group, but no statistically significant differences were found interact group*time across time was observed.

The results provided reliable evidence in terms of the effects of Qigong treatment protocol in lung cancer patients with both primary and secondary outcomes. The study findings from the current RCT not only support the Qigong treatment protocol for using in Vietnamese lung cancer patients but also highlights the need for further implementation of the management of symptom clusters in cancer patients and palliative setting. Details of the study's findings and limitations, as well as implications for future research and practice, will be discussed in the next chapter.

CHAPTER FIVE

DISCUSSION AND CONCLUSIONS

This chapter will present the discussion and the challenges of this doctoral study. Eight sections are included in this chapter: (1) Summary of findings; (2) Interpretation and implementations the results; (3) Recommendations for relevant research and practice implications; (4) Methodological issues; (5) The experience of conducting an RCT in Vietnam; (6) The unique value of this doctoral research project; (7) The limitations of the current study; and (8) The conclusions of this doctoral research project.

5.1. Summary of the study findings

The aim of this study was to 1) assess the effect of Qigong on managing symptoms cluster of dyspnoea, fatigue, and anxiety in lung cancer patients; and 2) explore the effect of Qigong on cough which is another common symptom linked with dyspnoea, fatigue, and anxiety as a cluster, and QOL in lung cancer patients. To achieve the study's aim, the theory of unpleasant symptom management was utilised to guide the intervention of this study. The subject was recruited by purposive sampling into intervention and control groups followed by randomisation assignment of subjects were conducted through in Nation Lung Hospital and Nam Dinh General Hospital in North of Vietnam. The sample consisted of 156 lung cancer patients. The collection of data was conducted at three time points: baseline, 6^{th} week, and 12^{th} week for the two groups from January 2017 to December 2017. The attrition rate in the Qigong group at the end of the intervention and at the end of the follow-up was 38.5% and 60%, respectively. The attrition rate in the control group at the end of the intervention and the end of the follow-up were 15% and 40%, respectively. There were 78 subjects (50% of the sample) who completed the study in both groups.

The effects of Qigong on the symptom cluster, cough, and QOL were investigated in the RCT. Qigong did not improve the overall symptom cluster across time between the two

groups. However, there was a trend in improvement within the group of the Qigong intervention on symptom cluster and QOL. Particularly for cough, Qigong had a significant improvement across time compared with the waitlist control group. The improvement in LC13 of the Qigong group was also better than that of the control group. The study findings from the RCT provided initial evidence supporting the use of Qigong for cancer symptom management, especially to manage respiratory symptoms; male patients and a number of implications were also retrieved for future research and practice.

5.2 Interpretation and implications of the results

5.2.1 Characteristic of the subjects

The mean age of the patients was 56.84 ± 9.45. This finding is similar to other studies (Long et al., 2015; Nguyen, Alexander, & Yates, 2018), in that most lung cancer patients are diagnosed at a late adult age. The majority (74.4 %) of patients were male. The high prevalence of lung cancer in Vietnamese males may be "associated with their smoking behaviour-one of the most important causes of lung cancer" (Long et al., 2015). It was reported that smoking is highly prevalent in Vietnam, with 56.7% of males aged from 25-44 years, and 59.5% of males aged from 45-64 years being smokers (Khue, 2011).

With regard to stage of cancer, the most prevalent was stage IV (61.5%), followed by stage III (29.5%). Patients with stage I accounted for the smallest proportion of the sample (2.6%). These findings reflect the fact that most patients were diagnosed in advanced stages. Many patients came to hospital for treatments when the tumour had grown and spread widely (Nguyen, Tran, & Le, 2009). Most of the lung cancer patients in Vietnam (65-80%) are diagnosed in the hospital in advanced stages (Anh & Duc, 2002). The reason for this situation is the poor knowledge and awareness of the public and general practitioners at the community levels of the Vietnamese healthcare system (Long et al., 2015). The number of chemotherapy cycles received for the treatment of lung cancer among subjects varied from 4 to 14 cycles

(equally 4 to 20 months) with the mean of 5.67 ± 2.62 cycles; subjects with 4 cycles accounted for the highest prevalence (55.1%). It can be said that the subject of the current study was at the middle steps of the treatments as well as their lives with the cancer.

5.2.2 Characteristics of studied variables

Subjects in this study experienced fatigue (FACT-F) with a range from 6 to 43. The mean score of fatigue was 27.25 ± 5.9 in all groups. It should be noted that the possible range of fatigue score could be 0 – 52 when this study sample reported a score range from 6 – 43 with mean of 27.25, suggesting that patients were suffered from remarkable fatigue intensity. Previous studies which used the FACT-F scale also found high intently of fatigue in lung cancer patients. The study of Long et al. (2015) found that the mean score of fatigue (FACT-F) in Vietnamese lung cancer patients (n = 246) was 27.69 ± 11.12. Lou, Yates, Carthy, and Wang (2013) studied 171 Chinese cancer patients on chemotherapy and found the mean score of fatigue to be 29.90 ± 1.73. However, Peddle, Bell, Fenton, McCargar, and Courneya (2012) recruited 15 lung cancer survivors to conduct an intervention study controlling fatigue, with a baseline FACT-F score of 45.6 ± 5.2. The results of this study are similar to those in Vietnam and China but are different from the results of Peddle et al. (2013). This can be explained by the fact that they have a small sample size and theirs subjects were survivors. These above findings also strongly highlight the need to manage lung cancer patients' fatigue efficiently worldwide.

Subjects in the current study showed a high level of dyspnoea at the baseline, with the mean total score of 17.28 ± 3.46. In the literature, dyspnoea in lung cancer patients were commonly reported. Long et al. (2015) found that the mean scores of dyspnoea in 246 Vietnamese lung cancer patients was 11.97 ± 6.93. The subjects in Long's study were less dyspnoea because those patients started chemotherapy in the first and second cycles. Moreover, in this study subjects were patients with all three symptoms of dyspnoea, fatigue,

and anxiety. Theoretically, tumor in the upper or lower respiratory system and the muscle weakness of advanced disease may lead to shortness of breath (Molassiotis & Lowe, 2010). It is important to note that, although the previous studies reported that severe dyspnoea among cancer patients, the problem appears to be more problematic in the current study, patients were classified as severe dyspnoea both in CDS scale and dyspnoea subscale in QLQ C30-LC13 (40.01 ± 15.49). This fact called for the urgent and appropriate management of dyspnoeic problems in lung cancer, especially in Vietnamese population.

The mean of anxiety score of all subjects at baseline was 13.5 ± 5.43, ranging from 4 to 36 (the possible range of anxiety score could be from 0 to 42). It could be seen that the mean anxiety score in this study is lower than that of the previous study. Dean, Finnell, Scribner, Wang, Steinbrenner, and Gooneratne (2010) studied lung cancer patients on chemotherapy and reported that only 15% of participants were classified as possible case of anxiety (HADS scores between 8 and 10) while 10% were anxious cases (HADS scores ≥ 11). Long et al. (2015) used DASS-21 to measure anxiety of 216 Vietnamese lung cancer patients; the results show that the mean anxiety score was 6.26 ± 3.7 and there was a range of from 0 to 15. Seemingly, the diagnosis of cancer could be a focal factor causing the patient anxious. However, patients in this study was at the cycle 5.67 ± 2.62 of treatment, which may long enough for the patients lessen their anxiety and focus on treatment. Moreover, during the conversation and discussion with the subjects, the research student found that most of the patients were following Buddhist's perfective, so they felt calm in the face of their present condition, with the thought of "ready for death at any moment without fear or regret". According to Buddhism, there is a process of being reincarnated or born again. This has also been described in many studies conducted previously in Thailand (Pudtong, Aungsuroch, & Jitpanya, 2014). This could be one of reasons why the participants in this study were not severely anxious.

5.2.3 Effects of Qigong on fatigue, dyspnoea, and anxiety

The finding of the current study supports the beneficial effect of 6 weeks Qigong exercise program in patients with lung cancer to improve fatigue within group. Although most subjects exhibited an improving trend for fatigue over intervention time, the mean fatigue scores of the Qigong group increased by 2.25 points between the baseline and the 6^{th} week ($p = 0.004$), and then remained stable until the 12^{th} week; this shows that Qigong did not improve fatigue. Based on the TUS model, fatigue can be developed by two processes: physiological and psychological tracts; consistently, fatigue in patients with lung cancer can be caused by the cancer itself, treatment, and psychological distress (Lenz & Pugh, 2008). Moreover, patients with lung cancer live with a maladaptive state of energy sources such as low nutrition, sedentary life-style, and stressful minds, and they then experience worse fatigue (Chen et al., 2011).

Regarding the decreasing of fatigue but no significant difference in terms of group*time, this may be developed by increasing physical activity, doing exercise regularly, and psychological relaxation; therefore, an improving trend was found in the Qigong group only. There was a significant difference within Qigong group with a mean difference of 2.71. However, for fatigue, the FACIT-F was used which has a published MCID of 3 to 4 U (Yost & Eton, 2005). It could say that the change was closed to the clinical impact on fatigue in the current study. Throughout Qigong exercise every day for 6 weeks, the Qigong subjects experienced fatigue, similar to the case in related studies. Oh, Butow, Mullan, Clarke, Beale, Pavlakis, Kothe, Lam, and Rosenthal (2010) reported that compared with routine care, a 10-week medical Qigong program reduced fatigue in breast, lung, prostate, and other cancer patients. Campo (2014) pointed out a 12 weeks qigong intervention improve the fatigue level and distress in prostate cancer survivors with chronic fatigue. Yeh and Chung (2016) demonstrated that in non-Hodgkin’s lymphoma patients who were undergoing

chemotherapy, the average fatigue intensity significantly decreased over time in the Qigong group who exercise 20-min twice daily for 21 days.

This finding of the current study also supports that Qigong significantly improved dyspnoea at the 6th week and the 12th week between the Qigong and waitlist control groups with a mean difference of 1.15 ($p = 0.014$) and mean difference of 1.50 ($p = 0.025$), respectively; this is not consistent with the findings of other controlled studies. For example, Fong et al. (2014) investigated the effects of qigong intervention on cancer-related symptoms in 52 survivors of nasopharyngeal cancer. The experimental group underwent a weekly 1.5-hour Qigong training program and an identical home program (three times/week) for six months. Qigong training resulted in no apparent improvement in dyspnoea. In addition, Oh (2008) reported no significant difference in symptoms of the side effects (included dyspnoea) in cancer patients who participated in a Medical Qigong program for 8 weeks. The result of the current study can be explained by the anatomical structure that the injury organ in lung cancer is the lung. Therefore, when practicing Qigong, the chest will expand both horizontally and vertically rhythmic, it will have a direct effect on the lung functions, leading to certain comfort and hence the patient will feel more comfortable breathing.

The result indicated that the Qigong programme did not improve anxiety. To date, only very few studies (Campo, 2014; Lee et al., 2006; Loh & Lee, 2015) have examined the effect of Qigong exercise on anxiety symptoms; however, the findings were inconsistent, probably due to a diversity of participants or sample size, variability in the severity of comorbidities or anxiety symptoms, and heterogeneity in outcome measures. Our results supported the conclusive statement of two recent systematic reviews that the limited existing evidence did not support the effect of Qigong exercise on anxiety symptoms (Vu, Molassiotis, Ching, & Le, 2017; Wang et al., 2013).

Regarding symptom cluster management, the results did not support the hypothesis

that patients with lung cancer who receive Qigong training intervention will show greater improvements in fatigue, dyspnoea, and anxiety as a symptom cluster across time than those who receive usual care, under the condition that the patients in Qigong group complied with the protocol. The mean symptom cluster scores within group of the Qigong group declined from baseline to the 6^{th} week, with a mean difference of -3.78 ($p = 0.002$), and then continues to marginally decline at the 12^{th} week; these changes reveal a statistical significance in these scores ($p = 0.015$).

In addition, published research on managing symptom clusters in patients with cancer are scant. The current study does not support the management of fatigue, dyspnoea, and anxiety together as a symptom cluster, which rejects the hypothesis. The results suggest that Qigong provides a promising approach for the simultaneous treatment of respiratory symptoms within a cluster. Systematic reviews and meta-analyses of previous trials of Qigong in cancer patients report effect sizes ranging from small to moderate, depending on the symptom under investigation and the type of intervention (Vu et al., 2017; Wayne, Lee, Novakowski, Osypiuk, Ligibel, Carlson, & Song, 2017).

5.2.4 Effects of Qigong on cough

In the current study, the mean cough score was 21.06 ± 5.23, ranging from 11 to 39. It could be noted that all patients in this study have high intensity/severity of cough. Cough is defined as the forceful movement of air through the glottis or an autonomic reaction to remove foreign from the airway (Molassiotis, Lowe, Ellis, Wagland, Bailey, Williams, Tishelman, & Smith, 2011b). These findings align with other studies in Vietnam, which asserted that 100% of patients has cough (even haemoptysis) at diagnosis. It is one of the major symptoms bringing patients to hospitals (Cu, To, & Nguyen, 2000; Long et al., 2015; Nguyen & Tran, 2010; Phạm, 2010). The findings of this study, therefore, reflect the typical characteristics of Vietnamese lung cancer patients.

A significant difference was observed at 6th week and 12th week between the Qigong and waitlist control groups with a mean difference of 3.07 (p = 0.001) and 2.824 (p = 0.039), respectively. Remarkably, a significant interaction term (group x time) of the model across time was observed. Moreover, the mean change scores from baseline to post intervention in cough score over the 6 weeks were 4.25. A 4.4-point difference on the MCLC scale of a cough is considered to reflect a clinically important difference in lung cancer conditions (Yorke, Lloyd, Smith, Blackhall, Harle, Warden, Ellis, Pilling, Haines, Luker, & Alex, 2015). According to Molassiotis, Bryan, Caress, Bailey, and Smith (2010), non-pharmacological trials are scarce, with only three trials identified, and only two (speech pathology training and use of SMS messages to monitor symptoms) showing positive results. It can be said that there was a statistically significant effect of Qigong on cough across time in Vietnamese lung cancer patients with a close to clinically significant difference.

The results indicated that Qigong intervention helped manage respiratory symptoms such as dyspnoea and cough more than cluster symptoms. Qigong practice usually involves performing Qigong (movements with breathing exercises and visualisation), plus positive expectations. All these could have beneficial effects to psychological well-being, and so all these are encouraged in Qigong practice. It is acknowledged that the outcomes of the current study will not provide the answer to whether Qigong (movements with breathing exercise and visualisation) alone is beneficial to psychological well-being. Positive expectations may add to effects related to the Qigong intervention, to form a multi-component mind-body practice instead of a single (Qigong) intervention (Wang, 2013).

Qigong can be categorised into three groups based on the different applications and intensities: medical Qigong, meditative Qigong such as Daoism and Buddhism meditation and martial arts Qigong such as Xing Yi, Tai Chi, and Palm. The word Qigong is an integration of two elements. Qi is the vital energy of the body and breathing, and the gong is

the skills of generating stimuli to work on and with qi. Therefore, it is crucial to understand how the stimuli are generated by qigong skills in order to understand how and why Qigong produces changes on qi (Chen et al., 2010).

Qigong consists of three modalities: mindfulness training, breathing manipulation, and body posture. The Qi of Qigong is the vital energy of the body, and gong is the training skill of generating stimuli to work on and with qi. Therefore, this results in the hypothesis that the integrative skill of mindfulness-led breathing with accordant body postures (a critical component) generates mechanical stimuli (mediators) to produce changes on qi and the body-wide meridian network (biological mechanisms) in addition to emotional regulation (Chen et al., 2010). Traditional Chinese medicine is a holistic system for promoting health and healing including several physical therapies such as acupuncture, cupping, Qigong and so forth.

One of the primary underlying theories of traditional Chinese medicine is based on balancing qi-blood according to the theory of yin-yang, which has been used for more than 3000 years. In practice, the flow of qi is regulated, and blockage of the flow of qi is dredged by physical therapies with obvious mechanical stimuli to balance qi-blood circulation. The therapy may provide insights into that appreciation of the skill for generating mechanical stimuli to work on and with qi is the path toward predictable and improved treatment of Qigong. The critical components (Mindfulness-led breathing with accordant body posture), mediators (Pressure gradients body-wide and Mechanical forces body-wide) and biological mechanisms (Balancing of qi-blood body-wide and Lengthening of meridian network) of Qigong show the characteristics of Chinese physical therapies and linkages discussed

In addition, Gallen described the distribution of respiratory muscles and the “nerves that transmit the power of the mind from the brain to these muscles” (Furley & Wilkie, 2014). He also noted that not all muscles were actuated during normal breathing (eupnoeic breathing), and instead were recruited only during “forced” breathing. Thus, respiratory

muscles are classified into primary muscles (involved during normal breathing) and accessory respiratory muscles (recruited during conditions involving increased respiratory drive or voluntary breathing) such as genioglossus, trapezius, latissimus dorsi and erector spine and so on (Hudson, Gandevia, & Butler, 2011; Lane, 2011). This description is consistent with the integrative skill of Qigong that mindfulness-led breathing generates mechanical stimuli to activate respiratory muscles body-wide (Chen et al., 2010). Mindfulness detects the interceptions, a distinct cortical image, of all sensations of the physiological condition of the entire body (Craig & Craig, 2009). The brain impulses then purposely manipulate spinal respiratory motoneurons in order to actuate the spinal respiratory nerves to recruit both primary and accessory muscles (Hudson et al., 2011).

It is of note that mindfulness-led breathing contracted respiratory muscles (yin) and extending body postures (yang) coincide with the yin-yang theory constructing tensional forces bringing on the distending of joints and lengthening of meridians at the whole body level (Chen et al., 2010). The aforementioned evidence provides clues to support the hypothesis that mechanical stimuli of qigong are crucial for the enhancement of the lymphatic drainage of extracellular fluid for balancing of qi-blood and lengthening of meridians to regulate the homeostasis of meridian network, contributing to reduce cough, enhance health and well-being. Therefore, the result from this study would be providing concrete evidence for the management of this common and distressing symptom. Thus, it will give hints to symptom management of not only for Vietnamese patients but also for patients in other countries.

In conclusion, this result can explain the integration of the modalities of Qigong with modern theories of lymphatic biology and mechanobiology to put forth the efficacy of Qigong. Traditionally, Qigong as a holistic discipline comprises mindfulness-led breathing with accordant body posture generating mechanical stimuli affecting the body-wide meridian

network. The development of the formulated training of holistic components appears to be strongly associated with the quality of the beneficial effects. The beneficial mechanisms of Qigong target on the integrity of physical through the balancing of qi-blood and mechanical manipulation of a meridian network on top of emotional regulation. Discovering the science of mind-body interactions is a research area of top concern with great prospects and will likely lead to beneficial achievements and contributions in terms of symptom management.

5.2.5 Effects of Qigong on quality of life

The results from this study suggested that Qigong has a positive influence on QOL of lung cancer patients. Qigong intervention improved while the control group had little improvement or even a reduction of QOL. There was a significant difference within and between groups on global health status at the 6^{th} week with $p = 0.01$ and $p = 0.021$, respectively. There was also a significant difference between groups on function score at the 12^{th} week with $p = 0.01$. With regard to symptom scales, there was a significance difference within, between groups at the 6^{th} week, and across time with $p = 0.035$; $p = 0.002$; and $p = 0.038$, respectively. The results of this study are consistent with those of other studies. Multiple studies confirm that Qigong significantly improves QOL (Chen et al., 2013; Fu & Wang, 1995; Loh & Lee, 2015; Oh, 2010; Oh, 2012; Wang et al., 2009). In addition, Oh et al. (2008) found that the Qigong intervention group reported clinically significant improved global QOL scores pre- and post-intervention. Another similar study of a Tai Chi intervention reported improvement in health-related QOL of patients with breast cancer (Mustian, Katula, Gill, Roscoe, Lang, & Murphy, 2004).

Regarding minimal clinically important differences, changes to global health status in the Qigong group at post-intervention was 5.29. This finding provides estimates of MCIDs for lung cancer patients when using the EORTC QLQ-C30. The estimates generally agree with the estimates of 5–10 units of the QLQ-C30 scales we considered and as proposed by

Osoba, Rodrigues, Myles, Zee, and Pater (1998) and King, Bell, Costa, Butow, and Oh (2014). This change can be useful for clinicians to determine the proportion of patients benefiting from Qigong treatment. The change could also be used as guidance for classification of patients by changes in HRQoL and symptoms over time. Furthermore, the estimates may be useful in sample size determination and design for future clinical trials.

Regarding typical symptoms of lung cancer symptom related to QOL, there were LC13 scores increased in both the Qigong and control groups. There was no statistically significant difference between the two groups for this increase. However, symptoms in the control group increased more and heavier than those of the Qigong group. At the 6^{th} week, mean difference of LC13 score of control and Qigong group were 11.10 and 7.23, respectively. It can be said that Qigong does not directly reduce the typical symptoms of lung cancer related to QOL, but Qigong had helped to slow the severity of the characteristic symptoms. This result is consistent with the conclusions of the previously published systematic review (Montazeri, Gillis, & McEwen, 1998; Vu et al., 2017).

According to Anant, Guleria, Pathak, Bhutani, Pal, Charu, and Kochupillai (2005), several factors such as age, associated co-morbidities, and quality of medical and palliative care provided to the patients influence many aspects of QOL. In addition, the short-term survival of lung cancer, rapid deterioration of performance status, and dropouts due to treatment-related side effects may cause difficulty in collecting data and following-up the patients for a long period of time. This problem of "missing data" causes difficulties in making accurate assessments and drawing conclusions from many studies. It has been suggested that comparative analysis of QOL should be stopped when less than 30% of the data is available (Ranson, Davidson, Nicolson, Falk, Carmichael, Lopez, Anderson, Gustafson, Jeynes, & Gallant, 2000). In the current study, over 50% of the data are available, therefore, the results can provide meaningful information to clinicians in addition to the

clinical diagnosis (e.g. the history, the physical examination and other diagnostic and laboratory test) and it may also influence clinical decision making as well as improving QOL of patients (Osoba, Bezjak, Brundage, Zee, Tu, & Pater, 2005).

The repeated QOL assessment may train patients, thus influencing their scores, which could weaken the effects of the study intervention. Furthermore, the use of semi-structured interviews contributes meaning to individual patient scores (McCabe, Begley, Collier, & McCann, 2008) and adds information about perceived problems (Larsson, Ljung, & Johansson, 2012). In the course of the disease, patients´ perception of their health status usually changes due to deterioration as a tumour progresses, but also because of adaptation, as patients often adopt new internal standards. This phenomenon is known as response shift and is not easily observed by physicians (Huebner, Rosé, Geissler, Gleiter, Prott, Muenstedt, Micke, Muecke, Buentzel, & Bottomley, 2014; Sprangers & Schwartz, 1999).

5.3 Recommendations for research

The outcomes in the current study include suggesting certain lessons that are useful for the design of an RCT; having a realistic timeline, defining clear objectives and precise endpoints, and balancing the study with correct randomisation; these are key elements that help us to ensure a strong study validity. If we aim to obtain RCT strengthening evidence for clinical practice, we must build them on strong hinges that allow us to influence the scientific literature and change the clinical decision-making activity of doctors involved in lung cancer and symptoms management.

The lesson that we learned from our work on this study should prompt researchers to consider carefully the challenges of conducting research on lung cancer patients with high dropout rate. Our experiences may guide investigators who plan future implementation trials or other trials among lung cancer patients. To ensure clinical trials can achieve high participation, low attrition rates among eligible subjects, future study should focus on these expressed challenges, and solutions are proactively sought to overcome to minimise

challenges. Knowledge-based information should be conveyed to the patient to increase their interest to participate in a physical activity based clinical trials. Greater attention should be given to the challenges faced to ensure higher successful the rate of recruitment and completion of a trial.

5.3.1 Recommendations for nursing practice

The current study is one of the few Qigong studies conducted in an ASEAN population with cancer. As evidenced by the patients' lack of previous experience in using alternative interventions, and conclusions are drawn from previous reviews (Loh & Lee, 2015; Thongteratham, Pongthavornkamol, Olson, Ratanawichitrasin, Nityasuddhi, & Wattanakitkrilert, 2015), the application of Qigong in this context can be considered novel. The low attendance at the Qigong subjects indicates the need for a change in the current service and its delivery model. Qigong was found to be an acceptable and feasible intervention and appeared to cause no harmful effects to patients, even at their advanced stage of the disease. Future developments may consider incorporating Qigong as a usual component of practice and evaluating its clinical effects through the implementation phase.

The findings of the current study have demonstrated that Qigong could improve symptoms and QOL perceived by lung cancer patients. Given that a complementary and alternative medicine management is usually administered based on the orientations of non-invasiveness, integration of body, mind and soul, and economic efficiency (Keegan, 1998), Qigong is obviously suitable to serve as a clinical nursing intervention and desirable for promotion. For the administration of Qigong, however, nursing professionals should understand basic knowledge of Chinese medicine, so that they can provide patients with correct instruction and increase patients' willingness to accept. For introducing Qigong to health care settings, a promotion project on clinical continuous education is required.

The contribution of cluster symptoms and QOL assessment to patient-physician communication. Thus, and to the best of our knowledge, this study is the first to demonstrate that the assessment of patients´ self-reported cluster symptoms, QOL and the presentation of the results to the doctors increase the probability that perceived psychosocial problems and general symptoms would be captured during patient-physician conversations in a Vietnamese context. The positive effects of cluster symptoms and QOL assessment on patient-physician communication can be considered sufficient evidence of the value of the intervention in routine cancer care, as increased patient involvement in the care process is a goal of healthcare policy (Greenhalgh, Long, & Flynn, 2005).

Regarding the clinical significance of changes in QOL over time, overall, patients in the current study experienced positive improvements in global health status, emotional, and functioning over time. These improvements might also have been clinically significant, even though several were of a magnitude of less than 10 points. While a change of 10 points on a scale of 0-100 has been stated to be clinically meaningful, Maringwa et al. (2011) demonstrated in their study of MID from EORTC QLQ C30 scores in patients with lung cancer that meaningful improvement requires a smaller degree of change compared to meaningful deterioration. The symptom alleviation experienced by patients in the current study may be explained by Qigong treatment along with chemotherapy, while improvements in emotional functioning can be a result of gradually increased acceptance of the disease over time.

5.3.2 Recommendations for nursing education

Findings in the current study could be used in nursing education. Firstly, the study pointed out the concepts that Vietnamese nurses could use to develop new intervention for cluster symptom in cancer population. Secondly, this study provided preliminary descriptive information regarding several common health problems of lung cancer population, which are

fatigue, dyspnoea, anxiety, and cough being a cluster of symptoms. Vietnamese nurse educators can integrate such information in their curriculum. Equally important, instructors can revise their curriculum, emphasise their teaching content on severe and important problems in Vietnamese lung cancer patients, such as cluster symptom of fatigue, dyspnoea, and anxiety. It is believing that the use this study finding in nursing education would help student nurses be aware of, and concern to those problems in their future practices.

5.3.3 Recommendations for nursing research

5.3.3.1 Research design

The current study was a randomised controlled trial. The findings estimated effects of Qigong on cluster symptom and QOL among lung cancer population. Thus, it may help nurses foresee the possible outcomes if a certain variable is selected for their interventions. However, due to the challenges of its research design, the findings itself cannot be generated as the approval of the causality among studied outcomes. Therefore, trial testing the long-term outcomes of interventions, which use the placebo suggested from this study, are recommended.

5.3.3.2 Sample and sampling

This study was conducted at two hospitals in the north of Vietnam. It is believed that the findings could represent more comprehensive picture about the effect of Qigong intervention in Vietnamese lung cancer patients if the sample was larger and recruited throughout the country. Thus, future studies recruited patients from various centres nationwide are recommended.

5.3.3.3 Measurement and data collection

In the current study, several patients reported a zero score on fatigue, dyspnoea, and anxiety. The zero scores indicated that the patients did not experience those problems at the time of data collection. It is impossible to ensure that those zero scores reflected the true

experience of patients or due to any confounding factors. Nevertheless, during the data collection, it was noticed that social desirability could be the issue that future researchers should be cautious about. Some participants, especially those diagnosed with the disease and having finished several cycles of treatments, wished to “let go”. They appeared to not want to express their problems, which may suggest the severity of the disease or the impacts of the treatment. Researchers in the future should consider solving this issue in their studies. A replication of this study with larger samples is needed prior to making conclusions regarding the effects of Qigong on reducing symptom cluster and enhancing the quality of life. A double-blinded design might increase the validity and reliability of the findings. More sophisticated measurements of qi supplemented with qualitative analysis and increased follow-up checkpoints can possibly help us to understand qigong in a more comprehensive way. Recruitment of subjects should be extended to the other setting include more subjects, which might increase the generalisability of the results.

5.3.3.4 Theoretical guide issues

The theoretical framework of this study was the Theory of Unpleasant Symptoms. To date, this theory appears to be the most comprehensive theory explaining symptom cluster in cancer population. The hypothetical associations between influencing factors and cluster of symptoms were supported in this study. The mechanisms and component part(s) of Qigong (breathing method, meditation, and gentle exercise) responsible for these factors were clearly delineated from the current study’s research design. It demonstrated that the theory is valid to explain symptom clustering in lung cancer patients.

5.3.3.5 Cost-effectiveness issues

Cost-effectiveness is another important outcome to address in future trials. The present study suggests an add-on value of this Qigong. Costs in the current study mainly concerned additional personnel used to deliver the intervention. Theoretically, this cost could

be offset by the cost of poor symptom management (such as frequency of hospitalisation, length of hospital stays, and pharmacological treatments). Future studies may need to explicitly address the issue of resource utilisation and cost-effectiveness in of adopting Qigong to control symptoms.

5.4 Methodological issues

5.4.1 Subject recruitment issue

Successful recruitment of patients is known to be one of the most challenging aspects in the conduct of randomised controlled trials. Inadequate patient retention during the conduct of trial affects conclusive results (McDonald et al., 2006).

There was great challenge related to successful recruitment context in this study that was high dropped out because the most lung cancer patients were diagnosed at the advanced stages. Normally, patients in the advanced stage were suffering from more discomfort and physical weakness that deters them from participating in the study (Nguyen, Tran, & Le, 2009). Many patients came to the hospital for treatments when a tumour had grown and spread widely. Anh and Duc (2002) reported that most lung cancer patients in Vietnam are diagnosed in the hospital at advanced stages (65-80%). The reason for this is the poor knowledge and awareness of the public and general practitioners at the community levels of the Vietnamese healthcare system (Long, Thanasilp, & Thato, 2016). Moreover, some patients leave the intervention group due to patient or doctors' choices, treatment complications such as their doctors changed treatment plan due to results from laboratory blood test, or their doctor had an urgent duty. Some patients could not eat or too tired when received chemotherapy or radiotherapy, and some patients had to transfer to other hospital or laboratory for gene test. Therefore, patients refused to continue participating in the trial.

In response to the recruitment challenge, the research student interacted with staff at hospitals regarding clinical trial recruitment by explaining to the staff the criteria and

procedures for recruitment. To ensure the healthcare professionals and patients to understand the purpose of the study is very important to gain their participation and even retain them in the study, rather than them dropping out. Considering the cultural belief and nature of disease when choosing the type of intervention, Qigong is suitable for Vietnamese cancer patients, where most cancer patients stay at home due to the overloading of oncology hospitals. Regarding the problem of doctors scheduling appointments for subjects that might clash with the intervention sessions, the research student assessed the computer system to check the appointment date and compared with the time for intervention sessions. If the time point clashed, the research student discussed with the doctors and found an appropriate time for both purposes.

The literature has shown that very often there are not sufficient patients to join the study or researchers had to wait for a long time because there are no patients to recruit (Heard, O'Toole, Naimpally, & Bressler, 2017). Patients did not want to join the trial because they believed that they would die soon, did not understand about the trial, and had advanced cancer. However, in this study, we recruited from two hospitals; therefore, the number of lung cancer patients was good enough for the recruitment process. The research student conducted a survey about the number of patients and the routine of lung cancer treatment in Vietnamese context before making the research plan. Even that the recruitment rate was slow during the first 3 months.

The results show that even though patients were advised of the voluntary nature of the study and that they could choose not to participate, the high rates of study participation (low refusal), and then the high rate of drop out (low commitment) likely reflects sociocultural responses. This can be explained by the findings of Lakes et al., (2012) whereby Asian patients are more likely to agree to participate in research than patients in Western countries are but also easy to withdraw (easy to join but also easy to withdraw). Remarkably,

there were 11 patients who refused to participate, as they were poor, and the hospital was a long distance from their home. The dropout rate in the Qigong group and control group were 60.2% and 39.8%, respectively. The dropout rate was possibly lower in the control group because they hope and wait to learn Qigong.

The research student learnt that successful recruitment of subjects is critically dependent on factors such as volume/turnover of patients, realistic study protocols and stability of the patient population. The sample size needed to reach an adequate power in a study is inversely proportional to the intervention effect squared. To increase the recruitment rate, a researcher should concern and manage the cultural aspect, patients' characteristics, and the local hospitals' authority perspective.

5.4.2 The study questionnaires issue

The data collection forms included 12 pages of seven questionnaires scales, to assess and measure included criteria, primary and secondary outcomes, which is quite long. The contents of each questionnaire are medical terms that were difficult for patients to understand and patients need explanation in simple term because most of them had secondary school level. In addition, patients were tired and need to go back home as soon as soon after medical follow-up/consultation. Moreover, distance between hospitals and patients' home is on average 150 km (range from 10 km to 1200 km) and spending about 3 to 4 hours by bus that was the most challenging of the recruitment process and follow-up of the RCT in this population.

To manage the above issue, appropriate training of the research assistants (who responsible for data collection) on research and recruitment methods was performed. Pre-discussion on the data collection process with patients and caregivers was conducted to help patients become familiar with the questionnaires. In addition, the disease progression of lung cancer, and treatments effects were explained in detail. Moreover, sometimes research

assistant provided free soft drink or milk to encourage patients that help patients to manage their feelings and increase their endurance during data collection.

In the beginning, some patients had difficulty understanding the questionnaires. Research assistants had to explain in appropriate ways to help them understand questions accurately. Then research student and assistants sat together to discuss which items were difficult for patients to understand and unified the same ways to explain the question to patients. Research assistants took time to explain terms to patients and asked for help from family members when explaining the questionnaires in an accurate, easy to understand way. The data collection at baseline took longer time than that at the end of intervention and follow-up points. Data collection was arranged when they were waiting for a medical consultation.

The research student had some difficulty in coordinating data collection in two hospitals that are geographically separate. Therefore, the research student and research assistants used video calls to discuss the related issues when implementing the research process.

After adopting these strategies, data collection forms included all crucial items to evaluate baseline characteristics and outcomes. To easily collect, to avoid interferences and to limit related cost in data collection, these forms were consistent and organised in a logical order, according to the timing of the procedures amongst RCTs. Data collection forms were easy to complete properly, and unnecessary secondary variables were avoided, as well as possible nonresponse and write-in responses. Baseline data collection included items needed to confirm eligibility, to permit randomisation and to collect predictors for possible stratification. Follow-up data collection encompasses information on primary and secondary outcomes. In addition, another crucial element was prepared the questionnaire and other related documents in advance. Timeline document reported all the crucial steps of the starting

RCT, with realistic and achievable time frame. The data collection was conducted in appropriate ways and most of patients can go home as they expected. Patients were able to complete the questionnaires after the strategies were adopted. In cases, patients went home before completing the questionnaire, the research assistant contacted them and gave them a telephone call to complete it. If there were incomplete items, they were treated as missing data.

The research student learnt that data collection form should be easy for subjects to read, to avoid interferences and to limit related cost in data collection. These forms should be consistent and organised in a logical order, according to the timing of procedures amongst RCTs. Baseline data collection included items needed to confirm eligibility, to permit randomisation and to collect predictors for possible stratification. Follow-up data collection encompasses information on primary and secondary outcomes.

In the future, the researcher should consider measures to facilitate the patients to complete the questionnaires, such as avoiding medical terms that are difficult to understand, beginning data collection when they are waiting before consultation, arranging a more comfortable place, or calling patients by the telephone to complete unfinished questionnaires. In addition, researchers can help to establish trust and rapport with study patients, providing adequate explanations to facilitate data collection.

5.4.3 Randomisation and blinding issues

A key aspect of RCTs is the method of randomisation. Conducting the study with correct randomisation are key elements that help us to ensure the strong validity of the study. Random allocation of patients in the study or in the control group assures that all subjects' known, and unknown characteristics are similar and balanced between groups at the beginning of RCTs. Therefore, the study group will differ for treatment-type assigned only, avoiding the selection bias. Consequently, it is mandatory to report all the aspects of the

randomisation process: the randomisation method, personnel involved (physician, nurse, and technician), randomisation timing, existence of a randomisations register (Heard et al., 2017). In the current study, patients in both groups were recruited from the same hospitals. They may have met each other and shared Qigong practice during their stay at the hospital. Despite indicating their understanding of this part of the research process prior to study commencement, some of the subjects allocated to the control group attended the Qigong group training sessions despite being allocated to the control group. Even though their allocation to the other group was explained again, they were reluctant to leave the group even when informed that they could join it at a later stage (waitlist).

Blinding is the method to prevent the possible bias derivate from the knowledge of group allocation of a patient. Allocation concealment is a method that can be used when blinding is not possible and, as Schulz and Grimes (2002) reported, conveys a strong message of bias prevention (Heard et al., 2017). In this study, blinding subjects was not possible in this study, subjects were required to learn and practice Qigong five days a week if they were allocated to the intervention group and therefore it was not possible to blind subjects to the intervention, but it was possible to conceal the intervention during random allocation.

In response to randomisation and blinding issue, blinding subjects was not possible but the researcher who collected data from subjects was blinded to the group allocation of subjects to minimise bias. In the current study, subjects were randomly allocated to the control or intervention group. The process of random allocation was explained to subjects prior to entering the study. Random allocation occurred after an explanation to subjects and via the use of block randomisation that was performed by the computer. The block of six was used to allocate the participant to one of the groups, enabling the subjects' variables to all have an equal opportunity to be randomly allocated and controlling for potential confounding bias.

The block randomisation was used by administering the intervention group of the trial at some times and administering the control group at other times (Keogh, Bachmann, Shepstone, Hewitt, Howe, Ramsay, Song, Miles, Torgerson, & Miles, 2007); it was less likely that the two groups will meet and discuss the intervention or share intervention materials, thus decreasing the likelihood of contamination. The block randomisation method was designed to randomize subjects into groups that result in equal sample sizes. This method was used to ensure a balance in sample size across groups over time. Block six are small and balanced with predetermined group assignments, which keeps the numbers of subjects in each group similar at all times (Suresh, 2011). The block size is determined by the researcher and should be a multiple of the number of groups (i.e., with two treatment groups, block size of either 4, 6, or 8). Blocks are best used in smaller increments as researchers can more easily control balance (Lachin, Matts, & Wei, 1988).

The block randomisation method was utilized, and the online application Research Randomizer was employed to produce the randomisation number table. The randomisation table was prepared and kept by a person (a lecturer from Nam Dinh university of Nursing) who did not know the design of the clinical trial and was not involved in any procedures of the implementation of this study. The research student and other study team members did not participate in the preparation of the randomisation. Meanwhile, the research student and the two RAs were also not allowed to participate in the process of identifying the participants' eligibility for study participation. Two oncology nurses (one at each hospital) who were not involved in any other procedures of the pilot RCT took responsibility for screening the lung cancer patients and identifying their eligibility for study participation. When a potential participant was identified as eligible for participating in this study and the related informed consent was completed, the research student called the person who was responsible for randomisation to receive the corresponding random number to determine the group

assignment for the enrolled participant. In addition, the strategies to prevent the patients in the two groups to communicate, such as recruiting subjects on a certain day of the week to be assigned to one group so that patients would not meet the other group who will follow up on another day of the week.

Performance bias indicates "systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest" (Higgins & Green, 2008) (p. 195). A blinding design for the study participants, the researchers, and the outcome assessment and a standard intervention/treatment protocol can help to minimise potential performance bias that can occur during a study's implementation (Higgins & Green, 2008). Blinding is an important methodological feature of RCTs to minimise bias and maximise the validity of the results. Researchers should strive to blind participants, healthcare practitioners, data collectors, outcome adjudicators, data analysts and any other individuals involved in the trial. However, this statement is not always possible, especially in a non-pharmacology trial. A single blind RCT is when the investigator but not the study participants know which treatment has been allocated.

According to the Consolidated Standards of Reporting Trials (CONSORT) statement, participants should be blinded to group assignment to control for the psychological effects associated with knowing group assignment. Participant knowledge of group assignment may bias the study in terms of altered attitudes, compliance, cooperation, and attendance (Schulz et al., 2010). Blinding of health care providers (Qigong master) is especially important when knowledge of group assignment may affect normal care treatment decisions, cause a provider to monitor changes more closely, or result in increased excitement or enthusiasm (Page & Persch, 2013). In the current study, blinding was not feasible with the researcher, statistician, Qigong Master, or participants. Thus, it was limited by an increased likelihood of bias,

participant dissatisfaction with no treatment status, dropouts, and preconceived notions about treatment.

Although balance in sample size may be achieved with this method, groups may be generated that are rarely comparable in terms of certain covariates. For example, one group may have more participants with secondary diseases (e.g., diabetes, hypertension, etc.) which could confound the data and may negatively influence the results of the clinical trial. Pocock and Simon (1975) stressed the importance of controlling for these covariates because of serious consequences to the interpretation of the results. Such an imbalance could introduce bias in the statistical analysis and reduce the power of the study. Hence, sample size and covariates must be balanced in clinical research.

To support subject in the control group who went to the intervention session and practiced at home, research students had already explained the need to remain in the assigned group and reminded them that the intervention would be given to the control group later with full reassurance and explanation. To reduce the chance of meeting and sharing Qigong practice, and also because the study groups differ for treatment type assigned only, avoiding selection bias and the process of random allocation was explained to subjects prior to entering the study.

The research student learnt that the future research should choose and report the methods of randomisation correctly. Balance the study group using stratification technique if possible. At least, outcomes evaluation should be blinded. This is factual knowledge about the strength of random allocation. That research student had learned to do perfect/better randomisation.

5.4.4 Adherence and attrition issues

Adherence in this trial is defined as the extent to which the clinical trial participant's behaviour coincides with the trial protocol in terms of keeping appointments, taking Qigong

intervention, and following the practicing at home (Robiner, 2005). Attrition is defined as when individuals drop out of the control or treatment group over the course of the evaluation (Hollen, Gralla, Cox, Eberly, & Kris, 1997). Researchers have been focused on adherence and attrition to the intervention regimens in clinical trials because of the profound effect that reduced adherence has on the trial sample size (Robiner, 2005).

A sufficient sample size is fundamental to detect a reliable statistical difference among the study groups. The sample size needed to reach an adequate power in a study is inversely proportional to the intervention effect squared. Consequently, considering that frequently the effect of the studied intervention is relatively small, the number of patients needed is relatively large. Research evidence suggests that the age of patients is a common predictor of attrition, although the direction of the effect of age is less consistent. Overall, lack of awareness, transportation issues, family or job commitment and concerns related to the requirement and cost of the trial were the major factors inhibiting lung cancer patients and sustaining a clinical trial (Brown, 2000).

The data on those who refuse to participate or drop out are seldom available due to human subject research guidelines, and/or a lack of published reports about barriers to recruitment and adherence in trials. Although these issues are more widely recognised in developed countries since they are crucial to the success of RCTs (Fayter, McDaid, & Eastwood, 2007; Ross, Grant, Counsell, Gillespie, Russell, & Prescott, 1999), this issue is often not highlighted in developing countries such as Vietnam.

Due to heavy disease burden of lung cancer patients, which sometimes affects exercising significantly, such as breathlessness and fatigue, because patients were at difference stages of disease that may affect Qigong practicing, and as patients were from different provinces, urban areas and rural areas, the environment for practice may be different.

Adherence to the protocol was determined by self-reports on the logbooks but patients did not complete them. Approximately 53% of participants (n = 41/78) self-reported practice of ≥ 3 h per week at two weeks, which corresponds to 30 minutes per day. Unfortunately, completion of logbooks was so poor at 6 weeks that these data could not be used. Since research student reminded them every week, it was possible that they did not want to fill it out. It may be too being demanding to fill out, too boring, too time consuming, or sometime patients were too sick. All subjects were advised not to seek any other regular exercise during the trial period and reminded them at all phone calls or face to face meetings at hospitals. This is desirable. In fact, sometimes patients complied with the request to do no other exercise because they used to not do exercise, or maybe they are too sick to do exercise.

Subjects dropped out were older than those not dropping out (57.94 and 55.74 years, p = 0.04). Of the 78 patients in the Qigong group, 548 (61.5%) completed the 6-week intervention program, and 66 (84.6%) completed at least half of the 6-week intervention. The practice adherence rate was 61.5%. The participants did not complete the intervention because of voluntary withdrawal (n = 12), perceived discomforts of breathing during practicing Qigong (n = 7), a lack of motivation (n = 9), and lost contact (n = 2). Some of the challenges that were noted as portrayed by the participant emerged from their values, beliefs, and experiences with illness and hospital system. Some of the notable challenges mentioned by the participants/patients were; (1) when going to the hospital, the doctor prescribed a lot of medicine and we will be happy, (2) it is better to work with a doctor rather than work with a nurse, and (3) anyway after all I will die so do not want to practice Qigong.

In an ideal scenario, every subject enrolled in an RCT would follow instructions and complete their allocated treatment as described in the protocol, thus contributing data which were complete in all respects (Lewis & Machin, 1993). Nevertheless, unfortunately, a practical problem that investigators usually come across in RCT is that subjects do not always

follow instructions. Moreover, in this study, the dropping out of subjects is a problem (Feinman, 2009; Frangakis & Rubin, 1999).

The attrition rate in this study did differ significantly between the intervention and control groups. Therefore, it is reasonable to argue that the reasons for withdrawal were directly related to the nature of the intervention, but is contextually relevant to the nature of the lung disease itself (Yorke et al., 2015). It was observed that patients who withdrew were significantly more likely to report greater symptom cluster (fatigue and anxiety), and older age (57.94 and 55.74 years, $p = 0.04$) at baseline, compared with those who did not. This was consistent with the main reason for attrition being deteriorating status among patients with lung malignancies. Attrition rates in this study are higher compared with most reports of attrition rates in previous studies of lung cancer (Chan, 2011; Chen, Tsai, Wu, Lin, & Lin, 2015). This finding is understandable, given the poorer prognosis and the potential for rapid deterioration associated with lung cancers (Chan, Chan, Yates, & Molassiotis, 2017). The impact of missing outcomes on the study results was evaluated through sensitivity analysis, indicating consistent results with available data analysis, thereby providing further confidence in the study findings.

The attrition of ill patients is a common problem in clinical longitudinal studies in oncology (Velikova, Coens, Efficace, Greimel, Grønvold, Johnson, Singer, Van, Young, & Bottomley, 2012). The attrition rate in the current study (50%) was lower than in Qigong study with hepatocellular carcinoma cancer (53.5%). However, this was higher than other Qigong studies with other types of cancer such as breast cancer, gastric cancer, and prostate cancer (Vu et al., 2017) which suggests that repeated symptoms and QOL assessment are feasible even in patients with poor health status.

To manage the above issues, all patients in the Qigong group were asked to complete logbooks of their Qigong practice at home to allow for the calculation of overall practice

adherence. In addition, engaging the support of family members so that these patients can ‘be released’ temporarily to focus on their own health and wellbeing, without feeling guilty. There is a cultural belief among patients that they are responsible for their family and should not spare time to take care of themselves. They tried to do the best things for their family and not really care about themselves during short survivor time based the on their lung cancer treatment situation (Evans, 2007). Moreover, they follow the eightfold path of Buddhism that encompasses understanding of life, right motives, right speech, perfect conduct, right livelihood, self-discipline, right-mindedness and perfect meditation. Therefore, peace and quiet for meditation is appreciated. Patients also believe in reincarnation, and that actions in this life will affect the quality of life in a future reincarnation.

Remarkably, the researcher assessed the subjects’ compliance with the home program by asking, testing, reminding them to practice Qigong, and filling out the logbook every week through phone calls to encourage participants to practice and ensure that the training dose is adequate by recording in a diary logbook. The research student also received many telephone calls to ask about related Qigong practice and reporting of some minor problems by patients and patients' family members during the whole study; for example, the location for Qigong practice, using other music, practicing more than one time per day, and sometime patients prefer to practice exercises that are familiar to them for a long time. To facilitate communication with subjects, at the beginning, research student registered a phone number only use for the research project.

In fact, most of the patients stayed at the hospital during the time of two-week Qigong training and not many patients were required to come all the way to the hospital and attend the two-week Qigong workshop. Some subjects did not attend the workshops due to a number of reasons, such as being too tired, meeting with a family member or relative, and under treatment process. To solve these issues, the research student had made an alternative time to

help those patients following the training sections such as extending training time or additional training sessions. Therefore, research student stayed at hospitals almost 24 hours to support the subjects throughout the research process.

It may be too demanding for the patients to write about their exercise in the logbook. Considering the disease or symptom burden on lung cancer patients, it may be a burden to fill out a logbook. Nevertheless, the purpose of having a logbook is to manage intervention adherence. Therefore, research students advised patients asking patients' family to fill out for them, also simplify the recording method, space out the time interval of filling out the logbook. In addition, research students verbally asked patients when they come back for follow-up during the intervention period. Despite all these efforts majority of the subjects did not complete the log record. Thus, the data of log record was not included in the analysis in this study.

The results obtained from the work on this study should prompt researchers to consider carefully the challenges of conducting research on lung cancer patients with high dropout rate. Because of high symptom burden, the debilitating nature of the symptom such as breathless, fatigue and anxiety, and since patients with a Buddhist perspective much emphasis are put on the importance of having a clear mind (Morgan, 1986), they may be reluctant to take medications that are mind altering and will need side effects explained to them thoroughly. They may prefer the use of home remedies – for example, rice porridge (one-part rice to two parts water) may be considered beneficial for convalescence. Therefore, in the future, researchers should include cultural belief as another aspect of adherence.

5.4.5 The Qigong intervention

Qigong could be highly beneficial for lung cancer patients in the Vietnamese population. Following the plan of intervention, subjects were required to receive a 90 minutes' Qigong training and meeting twice a week for the first 2 weeks. Then they practiced

at home for at least 30 min a day, 5 days per week, over 4 weeks and kept a log of the frequency, minutes of practice, and level of skills. This may somehow be a burden for some lung cancer patients.

In response to the intervention that was the complex issue, educating subjects on clinical trial by research student during routine both in and outpatient department visits. Focusing on knowledge-based information such as Qigong theory, Qigong regulation, and Qigong practicing regulation were conveyed to the patient to increase their interest to participate in a physical activity and Qigong based clinical trials. Creating positive understanding about clinical trials among staffs and patients through meeting and discussion. Training session was designed and implemented based on Qigong theory, Qigong regulation, Qigong practicing regulation, and timetable of patients' treatment (Appendix 8b).

During the Qigong training sessions, some subjects had difficulties learning Qigong at hospitals and many were tired. Sometimes they coughed or reported dizziness. Some patients found it too difficult to follow the many steps of Qigong practice. Therefore, the Qigong Master and research students had to spend more time helping patients learn in appropriate ways. During the two-week Qigong training at the hospital, research students arranged the stereo system to play Qigong music to encourage patients to practice Qigong. Moreover, they guided to patients how to open the Qigong DVD with a DVD player or laptop or helped patients to download it onto a smartphone so that it was more convenient for subjects to watch the video. Telephone follow-up was also available through the study to explain and support patients' practicing for two weeks at both hospitals and at home.

The research student learnt that conducting interventions like the Qigong trial is often challenging, particularly in trials of complex interventions which involve multiple time of practices, require behavioural changes (Oh et al., 2010), and require the engagement of multilingual, multicultural groups with varying educational levels (Ford et al., 2008).

Therefore, the researcher should encourage and facilitate the subjects to take up the intervention program.

5.4.6 Intervention fidelity issue

Intervention fidelity is the ongoing assessment and monitoring in a study that helps to enhance reliability and internal validity. The process helps to ensure that an intervention or treatment has been implemented as intended and that the interventions have been accurately tested. Intervention fidelity plays a critical role in research, as it affects the internal and external validity of study findings, as well as the effect size of a tested intervention and statistical power (Chang, Chao, Jang, & Lu, 2018; Hasson, Blomberg, & Dunér, 2012). Intervention fidelity also helps to increase confidence that the changes in the outcome of interest have resulted from manipulation of the independent variables rather than effects of potential confounds. An intervention fidelity was shown in five areas: intervention design, training providers, intervention delivery, receipt, and enactment (Chang et al., 2018).

In the current study, the issues include inadequate information on a lack of reported training for interventionists who deliver Qigong interventions (training providers); lack of sufficient instruction and supervision to ensure success and compliance in Qigong practice (intervention delivery and receipt); and a lack of monitoring of practicing Qigong at home (enactment). The researcher was using a logbook; the correct doses of Qigong practice at home cannot be recorded and incorporated into the interpretation of research outcomes, which may result in bias in a study's findings. Therefore, monitoring and assessing intervention fidelity in efficacy trials plays an important role in interpreting the validity of relationships between the interventions and study outcomes and ruling out alternative explanations that could influence the study outcomes.

The research student suggests that to preserve the validity of findings in future Qigong studies, researchers should provide clear descriptions in relation to the components of

treatment fidelity, including intervention design, training of instructors, intervention delivery and receipt, and enactment. Such as 1) when Qigong Masters are employed, their previous training should be included based on a training protocol; 2) direct class observation and active comparison groups should be used to minimise and assess potential non-specific treatment effects that may influence participants' behaviour or expectations of study outcomes; 3) Subjects should be required to complete daily exercise logs to track the frequency of home practice; and 4) a weekly phone call combined with auto SMS to remind patients every day what is being conducted to understand their home practice.

5.4.7 Statistical considerations

The two statistical approaches (the intention to treat analysis using the LOCF method and per-protocol analysis) were not adopted in the current study, as the per-protocol analysis faces sample bias, as the final subjects may not represent those that are randomised, and the intention to treat analysis using the LOCF method to impute missing values faces estimation bias. However, because of its ease of implementation and low computational complexity, these approaches are considered the commonest methods in most clinical research (Gueorguieva & Krystal, 2004). Mixed-effects models have advantages over these conventional methods by using the most available information across different time-points of measurement and adjusting for missing data (as long as they are missing at random). In fact, implementing both the conventional as well as the mixed-effect models in data analysis has become an emerging trend (Ng, 2009). However, the current study adhered to the conventional method of analysing the data. The total attrition rates for the two groups are 60% and 40%, respectively, and although comparable, they are high. In addition, the rate of treatment discontinuation among the Qigong training group of 38% is almost double compared with the initial planning. Control measures to minimise both the attrition rates and treatment discontinuation rates are definitely indicated.

Multiple comparisons increase the risk of random significances (type 1 error). We sought to limit this risk by reducing the number of variables analysed in the current study and selecting core QOL dimensions and symptoms that matched the defined conversation content categories, i.e. global quality of life, functioning, and symptom score. Nevertheless, a large number of comparisons were made within the current study and some positive findings may be due to random effects (Puetz & Herring, 2012). To avoid the overestimation of associations, the interpretation of the results focused on patterns rather than on single outcomes. In addition, GEE handles missing data uses the "all available pairs" method, in which all non-missing pairs of data are used in the estimating the working correlation parameters. Because the long form of the data was being used, we only lose the observations that the subject is missing, not all measurements.

5.5 Experience of conducting RCT in Vietnam

Randomised controlled trials (RCT) which have superior status amongst experimental design studies, are widely regarded as the gold standard for evaluation of health care programs (Schneider & Whitehead, 2013; Thompson, 2004), and are considered the most appropriate way to evaluate the impact of such an intervention in clinical practice (Lijmer & Bossuyt, 2002). The reputation of rigorously conducted RCTs enables the identification of a well-developed and applied study to be considered high-level evidence on which future practice in healthcare is based (Seers & Critelton, 2001; Walker, 2005). The current RCT with the above advantage, therefore, the research student faced challenge when conducting but adopted strategic to ensure the study protocol was uphold and that was maintained within limitations.

5.5.1 Patients and hospital staff in Vietnam are not familiar with RCT study

With regard to the number of RCTs, there are many that have been conducted and are considered high-level evidence for research outcome in developed countries. However,

Vietnam is a developing country. There are many limitations in the healthcare system in term of research and assessment of health outcomes, there are few of RCT that were conducted. Remarkably, there is a lack of understanding about clinical trials, such as recruitment criteria, randomisation, and blinding among the patients, nurses, and hospitals' manager. They often have doubts and worries about non-pharmacological trials. Because of these problems, during the data collection, patients and staff members asked many questions when the research student introduced the study to them.

The recruitment rate was low during the first 3 months. In addition, there are some social and cultural issues related to trial participation and patients' cultural beliefs. Patients prefer to work with a doctor rather than work a nurse because Vietnamese people believe that nurses are specialists in the care of patients in the hospital, under the direction of the doctor (Vietnamese Dictionary, 2004). Since the subjects in this study were lung cancer patients at stage III and stage IV, some patients had the perspective that anyway, "after all, I will die so do not want to practice Qigong".

In response to patients and hospitals in Vietnam not being familiar with research study issues, the research student adopted the following strategies: Knowledge-based information such as overview of the study, kind of Qigong intervention, and benefits were conveyed to the patients to increase their interest in participating in a physical activity based on clinical trials. Educating subjects on clinical trials was performed by research students both at in-patient wards and outpatient department visits in the hospitals. Subjects were educated about the objective of the study, the design, the intervention, the outcome measurements, the implication of the study, and the right of the patients. Moreover, creating a positive understanding about clinical trials among hospitals' manager, staffs, and patients through meeting and discussion. Research student explained to doctors and nurses that the RCT can provide data and evidence about supportive and palliative care for lung cancer patients. In

addition, based on outcomes of the RCT, the department's manager may re-structure the patient's room, or change the usual care routine to support patients more.

Providing an adequate, clear, and concise explanation about trial procedures to study patients during the informed consent process is important. Training was focused on addressing common misconceptions about RCTs, particularly equipoise and informed consent. Time was allowed for patients to talk to the researcher about their concerns of participating in the trial. In addition, the research student also spent time exploring the concerns of patients and their family members. Therefore, patients and clinical staff understood more about clinical trials. However, some patients still preferred to work with a doctor rather than a nurse.

With regard to the patients' perspective that anyway, "after all, I will die so do not want to practice Qigong", the research student talked about cancer patients in Thailand and Vietnam who practiced Qigong and believed in Buddhism; they focused on their health. The story somehow helped patients feel better and encouraged them practice Qigong.

The research student learnt that this issue of the study provides important insights into contextual and cultural issues that need to be considered in the development of cancer interventions in the Vietnamese context. Therefore, the future study should prepare in advance a detailed study protocol including cultural issues such as the belief of the patients with serious illness and the concern of health care provider with non-pharmacological intervention in palliative care for cancer patients. A procedure manual with a timetable for education and discussion times may be necessary according to the complexity of the RCT and the demanded tasks to enhance the understanding of hospital staff.

5.5.2 Negotiation of access and data collection issues

With regard to this issue, before, during, and after implementation of the trial, the research student had to contact with hospitals authority to get permission for ethical

consideration, facilities, and staff cooperation. Hospital administration staff were too busy and did not have time to cooperate; also, a lack of support, the fact that the research student tried to make an appointment with them but waited for a week or even a month before meeting, and the fact that the student had to take time to negotiate access and data collection issues and get permission from two research hospitals as managers are too busy is important. Hospitals lacked a comfortable place for patients during data collection and Qigong training due to the overloading situation at hospitals.

In response to negotiation of access and data collection issues, building a relationship with manager and committee based on Vietnamese culture such as communicating with them about the details of the study. Moreover, considering a different approach to communicate with the manager. Then, they understand the significance of the study and the problem of not having a suitable room to meet patients could be explained. Taking and sharing to get help from staffs and managers, such as talk to doctors who responsibility for patients' treatment, staff nurses who responsibility for caring for patients in the departments. To do this approach, the research student attended all briefings of the department on the morning of each day to know and take noted all key persons and related issue.

After adopting the above strategies, the research student obtained full permission and support. In addition, we found a comfortable room to talk with patients and a suitable room in which to teach Qigong. With regard to the ethical issue, the research management department in two hospitals and the Nam Dinh University of Nursing worked together to coordinate research issues and consider the ethical application process for the research student to conduct the research in appropriate ways.

The research student learnt that the researcher needs to be conscientious, have professional integrity, plan meticulously, and develop good interpersonal skills with the hospital staff.

5.5.3 Dual identity of the research assistant as a nurse and nurse-researcher

The research assistant faced the dilemma of dual responsibility as a nurse and as a research nurse. Nurses were supposed to provide direct care to the cancer patients as usual, but at the same time, they were supposed to help in the Qigong research. Therefore, the cooperation between the research assistant was interrupted by other staffs in the usual care process. In addition, they sometimes need to do research duties but at the same time are charged with caring for other patients.

In response to the dual identity of the research assistant as a nurse and nurse-researcher, one professional coach, who had been engaged in teaching Qigong to clients at the UNESCO Centre for Supporting Community's Heath for at 12 years, was employed to guide the subjects' training. To reduce the workload of the research assistant, the research student had been engaged in guiding and supporting patients follow the Qigong lesson. He also supervised the training of patients to guarantee the quality of their learning.

Nurses who help in this trial were advised to make a detailed plan and timetable during the time of the trial. This involved delivering care to patients in the morning and then focusing on research in the afternoon. In addition, research student talked and negotiated with manager at the department to reduce duties and provide support for research assistants to help them during the data collection at hospitals.

The research student learnt that the dilemma for nurse researchers: Research assistant faced a dilemma of dual responsibility as a nurse and as a research nurse. They were supposed to provide direct care to the cancer patients as usual. At the same time, they were supposed to help in the Qigong research. It was difficult at times to separate the two, hence posing a challenge. Therefore, in the future research, the researcher should consider getting help from research assistants who are not nurses of the hospitals to relieve their current duty, such as the workload or the routine in the hospital. In addition, hospital culture such as day and night

shift setting, work assignments, equipment management, emulation and reward should be considered to make the research plan and implementation reasonable.

5.6 The uniqueness and value of this study

5.6.1 Qigong and the lung cancer population

Regarding lung cancer patients, previously, people thought that lung cancer had short lifetimes and was too tired to practice Qigong. Therefore, another strength of the current study is the high recruitment rate identified in the RCT, which may have been due to the high level of lung cancer among the Vietnamese population, the safety, and convenience of the Qigong approach used in this study and the favourable effects of Qigong on managing symptoms. The high recruitment rate also reflects a promising acceptability and generalisability of the Qigong intervention among lung cancer populations. This information provides important implications that more well-designed studies are necessary for future research to explore the value of Qigong in cancer symptom management, not only because of its beneficial effects on targeted health conditions but also because of its features of safety and convenience, which have shown excellent acceptability and clinical utility among cancer patients.

5.6.2 Qigong and managing symptom cluster

The strengths of the current study include the research design and implementation. Different from other Qigong trials published in the current literature, the design of the current study is RCT and follows the Theory of Unpleasant Symptoms (Lenz & Pugh, 2008). In the theory, physiological, psychological and situational factors are antecedents that influence the symptom experience. The symptom experience includes the distress, duration, intensity and quality of each symptom. Specific outcomes include function, cognition, and physical performance. Qigong is a system of self-practicing physical exercise which includes breathing regulation (modulation of autonomic nervous system and improving ventilatory

function & oxygenation), mind regulation (possibly Synchronizing neural activities stabilizing mood), and postural regulation (movement exercises). These components can apply to TUS flowing physiological factors, psychological factors, and situational factors. This is the first study to adopt Qigong to manage this symptom cluster of Vietnamese lung cancer patients. Therefore, it would be the unique contribution to the literature in this field.

5.6.3 Measuring instruments

Among several research papers that studied different forms of Qigong, only a few focused on cluster symptoms, and used both cluster symptoms and QOL outcome measures, as they were worried about the burden on patients (Chan, Lee, Suen, & Tam, 2011; Vu et al., 2017). Nevertheless, among them, none were performed in Vietnamese contexts. Our follow-up assessments of both psychological and physiological aspects further revealed whether Qigong could still exert effects on the subjects over a longer period after the formal intervention are finished which enabled us to investigate the effects of Qigong in a more comprehensive manner than previous studies.

5.6.4 Promotion value

One of our aims was to introduce a no pharmacological modality, which can reduce symptoms and anxiety and improve QOL among cancer patients. It is advocated that the traditional and old-fashioned presentation of Qigong needs to be re-packaged with modernized elements if we want to promote it to other population that include other cancer patients than the elderly and those with poor health. Our study is a rather innovative trial in terms of sharing a suitable and comprehensive Qigong protocol that is easy to work out, and can be practiced anytime, anywhere with comfortable clothes (Thanasilp, 2013). We hope that it can meet the current palliative care trend and workout structure. In fact, doctors in the two hospitals have advised patients to practice Qigong and share it with other patients. More specifically, hospital leaders have arranged a private room for patients to use for studying

and practicing Qigong. As well as screening videos on television, screens in hospitals to encourage patients to find workout routines appropriate to each person's illness. These are things that were not previously considered in hospitals.

5.7. Limitations of the current study

There are several notable features to this study, including the recruitment of adequate numbers, the inclusion of two cohorts (immediate, delayed training groups) which allows for assessment of reproducibility between groups, the use of standardized measures to determine outcomes, and attention to adherence to protocol with the amount of practice. In addition, there is also a consideration of those who attain outcomes that are considered to represent clinically meaningful changes. Although our results are promising, several limitations of the current study should be noted.

5.7.1 The subjects and generalisability

The subjects were mainly recruited from the two hospitals from the Northern part of Vietnam, only patients with lung cancer and presenting cluster of three symptoms fatigue, dyspnoea and anxiety were recruited, which may limit the generalisability of our results. The male subjects outnumbered the female subjects in our study. The demographic characteristics (e.g., age) of the drop group were quite different from the active group. It might be better if we could identify more subjects and then allocate them to either group. All of these limitations might affect the generalisability of the present findings.

The literature shows that individual patients given the same treatment for the same condition appear to respond differently from one another. This observation, combined with our understanding of the complex mechanisms of diseases and therapies and the potential importance of myriad patient-specific factors (e.g., age, sex, illness severity, comorbidities, co-treatment and molecular differences influencing pharmacokinetics and dynamics), has led to a widely held assumption that the observed variation in treatment response seen between individuals is not merely random, but stable and potentially predictable. Nevertheless,

statistical analyses aimed at discovering the heterogeneity of treatment effects among groups of individuals (subgroup analyses of parallel arm randomised trials) typically fail to find compelling and reliable evidence for the presence of such heterogeneity. For example, statistically significant differences in Qigong effects between men and women are reported, but a systematic review indicates that the frequency of these interactions across studies suggests that the vast majority occur by chance (Wallach et al., 2016).

5.7.2 Adherence and attrition

The rate of drop out was high at the sixth week of intervention and the 12th week follow-up (38%, 60.2% in the Qigong group and 15%, 40% in the waitlist control group). The main reason was that many subjects voluntarily withdrew from the study process. In addition, there was no fixed time to "enter static" and practice. There were also some patients who reported that their perspective was "letting go", so they were not able to achieve the complete Qigong achievement. This may explain why the differences between the two groups were more significant at six weeks than at 12 weeks.

Low compliance with protocols, lack of motivation to continue participating influence intervention impact, and can be other potential sources of bias and an indicator that the intervention is inappropriate for the recruited subjects (Vu et al., 2017). Oh et al. (2010) reported similar low adherence rate for their 10-week Qigong trial held at Sydney, which documented a dropout rate of 33%; reasons for the dropout were not identified but with multi-ethnic population, there may be added issues of varying language, culture, social norms and group acceptance. To the best of our knowledge, this trial is the first study to explore the effects of a Qigong trial among lung cancer patients in the Vietnamese context. Thus, the information gathered here would be useful to provide insight into the possible barriers in recruitment and adherence of an intervention based clinical trial.

5.7.3 Experimental design

Blinding the subjects to their treatment allocation was not possible due to the nature of the intervention. The inclusion of a control group was nonetheless important to compare changes between those who did and did not receive Qigong intervention and to control for changes in self-reported symptoms and QOL that may occur over time without an intervention. We acknowledge that some of the benefits reported from the Qigong intervention may be due to experimental bias and confounding factors (e.g., extra care vs. non-extra care), participants' expectancy (placebo effects), and social interactions due to be a member of a group. To control for this in a future study, a third group, nontherapeutic but with the same amount of contact time could be offered, although this would present logistical issues. It would also be interesting to investigate any relationship between the Qigong dosage level (including home practice) and efficacy. We attempted to do this in the current study with the participants' home diary, but unfortunately, at the end of 12 weeks, <50% of participants returned the diary.

Research evidence suggests that age of patients is a common predictor of attrition, although the direction of the effect of age is less consistent. Some studies reported older patients whilst others reported younger patients to be at a greater risk of leaving (Honas, Early, Frederickson, & O'brien, 2003). This study showed that dropout patients were older than non-dropout patients. As Asian countries have stronger family bonds and expected social roles, it is not uncommon for these patients to commit energy and time for the family and to put preference to family events (Loh, Lee, Quek, & Murray, 2012) over their individual needs. This finding calls for proactive planning to be in place when recruiting Asian patients especially for trial with long-term commitment (more than two months). There may be a need to engage the support of family members so that these patients can 'be released' temporarily to focus on their own health and wellbeing, without feeling guilty.

5.7.4 The Qigong protocol

Furthermore, although the Qigong protocol was developed by Chulalongkorn University, Thailand that agreed that it was suitable for Vietnamese lung cancer patients to practice, we did not have an objective assessment tool to indicate how much the subjects could master the exercise. Like other mindful exercises (e.g., yoga) and some sports (e.g., Karate), the performance of the athlete is commonly assessed by the experience of the master or coach cross time. It is not common to use tools to evaluate this. "Mind regulation," "breathe regulation" and "body regulation" are three key elements of qigong. Whether the participant can do well in these three aspects might have an effect on the outcome of body-mind well-being. The effects of qigong might be discounted if some subjects could not follow the protocol. To tackle this problem, we provided the patients with DVD and hand-outs for home practice. From our observations, in the beginning, some Qigong trainees had difficulty in doing certain postures, but we did not report the numbers. After two weeks, they were more accustomed to the protocol and showed much improvement. Nevertheless, some subjects occasionally reported difficulties in managing the techniques. It might be due to the disease burdens of the subjects during they joined this program. Therefore, even though we accurately followed DVD training, the level of difficulty should be further considered if this Qigong protocol is to be used in future investigations. Moreover, a cross-sectional design comparing the veterans (e.g., practiced over one year) and the novices might allow us to better ascertain whether the length of practice time is related to the effectiveness of Qigong.

5.7.5 Experimenter effect

Although we tried to deal with the problem of non-specific effect by introducing the block randomisation, we still faced the possibility of the experimenter-expectancy effect. Since the investigators have a dual role (i.e., researcher and nurse) in this study, their unconscious bias might discount the internal validity of the study results. In addition, this

was a mid-term result, which cannot explain the long-term effects of Qigong. Investigating whether the reported benefits are sustainable in the long term with continued practice warrants investigation. We tried to telephone the subjects 6 months after the program. Among those who could still be contacted, only one of them continued to practice our protocol. They stated that as the class no longer met, their motivation to practice gradually decreased. It was very difficult to be self-disciplined to keep regular practice. Therefore, we suggest future studies to extend the training for a longer period and to include more follow-up measurements (3-months and 6-months afterward). It might maintain the interest of the participants and provide more information about the possible ongoing effects.

Conducting clinical trials in any setting is challenging. However, the lung cancer population can be particularly daunting. Implementing a Qigong-intervention adds to the investigators' anxieties. Unexpected challenges occur, regardless of the care with which the research plans and executes the study. In sharing and discussing, researcher can contribute to science by allowing others to learn from his/her experience. There is no one faith for the Vietnamese lung cancer patients, but rich and varied religious traditions. Most of them have Buddhist perspective. The patients should be asked about their faith or needs whilst in the hospital to ensure that they are being met. Recommending the patients following regulation of Qigong practice, however, can flexible time and duration to practice base on their real situation during the trial.

5.7.6 The measurement tools

Qigong learning process was lacked checklist for two weeks training at hospitals, missed follow-up assessment and qualitative information about perfective of subjects to Qigong practicing. Moreover, this study measured objective indicators and lack of psychological data. The presence of repeats time measurement, other patients, and family member, as well as "the letting go perspective" from lung cancer patients, which compromised the internal validity of the study, might have affected objective indicators.

Since to date, no previous reference on the subjective assessment of qi feelings was available, therefore we lacked an instrument to measure between those who could feel qi and those who could not and between those who practice more and those who practiced less. It is hoped that, in future designs, a more systematic and a representative tool can be formulated to capture the feelings of qi, which might be beneficial to the scientific study of Qigong and to uncover the mysterious mask of the invisible qi. If more funding is available, we suggest future studies to include objects measurements to detect the brain activities of the qi state.

5.7.7 Statistical analysis

Moreover, when investigating characteristics between the active subjects and the dropout subjects, due to a significant difference in age and gender, baseline values of fatigue, etc., we could not apply the LOCK and per-protocol approach to deal with missing data forms. For comparisons between the qigong group and waitlist group subjects, computation variables were also used in some outcome variables such as cluster symptom, functional scales, symptom scales, and LC 13 total scores. Conducting multiple tests probably increased the probability of Type I error. Therefore, caution should be used when interpreting the findings.

Improving the quality of symptom management delivered to lung cancer patients is an urgent health-care need. This dissertation describes a clinical trial designed to improve cluster of three symptoms (fatigue, dyspnoea, and anxiety) and management cough, QOL in Vietnamese lung cancer population. We describe several challenges as well as to address the logistical challenges we encountered. In addition, we discuss several problems that arose during the study and the ways in which we approached these challenges. It is our hope that the insights and strategies gained from this study will assist others in designing future studies and addressing anticipated challenges.

5.8 Conclusions

The current study was designed to examine the effects of Qigong on dyspnoea, fatigue, and anxiety in lung cancer patients as a symptom cluster. The hypotheses of this study were that patients with lung cancer who received Qigong training intervention showed greater improvement in symptom cluster (dyspnoea, fatigue, and anxiety), QOL and cough than those who received usual care, as assessed immediately after completion of the Qigong intervention, and at 6-weeks follow-up. One hundred and fifty-six patients from two hospitals in Vietnam participated in the study. The results of the current study suggest that Qigong was not a promising treatment for relieving this symptom cluster assessed symptoms at week 6 after the intervention. The long-term effect of Qigong on the symptom cluster at week 12 was inconclusive. However, Qigong was effective on the single symptom of dyspnoea and cough as well as improving patients' QOL. In addition, Qigong needed more than 6 weeks to improve dyspnoea and the intervention was more effective at managing respiratory symptoms in males more than in females in this population. The conclusion is that the symptom cluster had a trend only in improvement, and as those found to be significantly improved (i.e. cough) were secondary outcomes, the effect of Qigong on managing respiratory symptoms needs to be further investigated before concrete conclusions are drawn.

The study not provides evidence for the assessment and management of fatigue, dyspnoea, and anxiety as a symptom cluster, but the findings are encouraging and add to the theoretical body of knowledge on cancer symptom management. Researchers are encouraged to advance the theory, measurement, and management of respiratory symptom, especially in relation to clarifying the mechanisms of the interrelationship among symptoms within a cluster, and to investigate treatment interventions. Clinically, it is prudent for clinicians to view some symptoms as a cluster where they influence and will be influenced by each other. Managing symptoms in a cluster should be regarded as a contemporary approach in the provision of effective and efficient cancer and palliative care.

REFERENCES

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., & de Haes, J. C. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, *85*(5), 365-376.

Alacacıoğlu, A., Öztop, İ., & Yılmaz, U. (2012). The Effect of anxiety and depression on quality of life in Turkish non small lung cancer patients. *Turkish Thoracic Journal, 13*(2), 50-55.

American Psychiatric Association. (2005). *Diagnostic and Statistical Manual of Mental Disorders* (4 ed.). Washington, DC: American Psychiatric Association.

American Thoracic Society. (1999). Dyspnea. Mechanisms, assessment, and management: a consensus statement. American Thoracic Society. *American Journal of Respiratory and Critical Care Medicine, 159*(1), 321-340.

Anant, M., Guleria, R., Pathak, A. K., Bhutani, M., Pal, H., Charu, M., & Kochupillai, V. (2005). Quality of life measures in lung cancer. *Indian Journal of Cancer, 42*(3), 125-132.

Anh, P. T., & Duc, N. B. (2002). The Situation with cancer control in Vietnam. *Japanese Journal of Clinical Oncology, 32*, 92-97. doi:10.1093/jjco/hye127

Armstrong, T. (2003). Symptoms experience: A Concept Analysis. *Oncology Nursing Forum, 30*(4), 601-606.

Barsevick, A. M., Dudley, W. N., & Beck, S. L. (2006). Cancer-related fatigue, depressive symptoms, and functional status: a mediation model. *Nursing Research, 55*(5), 366-373.

Barsevick, K. W., Lillian Nail, Susan Beck, William Dudley. (2006). Symptom cluster research: conceptual, design, measurement, and analysis Issues. *Journal of Pain and Symptom Management, 31*(1), 85-95.

Bergman, B., Aaronson, N., Ahmedzai, S., Kaasa, S., & Sullivan, M. (1994). The EORTC QLQ-LC13: a modular supplement to the EORTC core quality of life questionnaire (QLQ-C30) for use in lung cancer clinical trials. *European Journal of Cancer, 30*(5), 635-642.

Bjordal, K., Graeff, A., Fayers, P., Hammerlid, E., Pottelsberghe, C., Curran, D., Ahlner-Elmqvist, M., Maher, E., Meyza, J., & Bredart, A. (2000). A 12 country field study of the EORTC QLQ-C30 (version 3.0) and the head and neck cancer specific module (EORTC QLQ-H&N35) in head and neck patients. *European Journal of Cancer, 36*(14), 1796-1807.

Borneman, T., Ferrell, B., Koczywas, M., & Cristea, M. (2008). Symptom Concerns and Use of Supportive Services in Patients with Lung Cancer. *Clinical Lung Cancer, 9*(5), 288-295.

Borneman, T., Ferrell, B., Sun, V., Piper, B. F., & Koczywas, M. (2008). Reducing barriers to pain and fatigue management. *Oncology Nursing Forum, 35*(3), 509-510.

Borneman, T., Koczywas, M., Cristea, M., Reckamp, K., Sun, V., & Ferrell, B. (2008). An interdisciplinary care approach for integration of palliative care in lung cancer. *Clinical Lung Cancer, 9*(6), 352-360.

Boyes, A. W., Girgis, A., D'Este, C., & Zucca, A. C. (2012). Prevalence and correlates of cancer survivors' supportive care needs 6 months after diagnosis: a population-based cross-sectional study. *BMC Cancer, 12*, 150-150.

Bozcuk, H., Dalmis, B., Samur, M., Ozdogan, M., Artac, M., & Savas, B. (2006). Quality of life in patients with advanced non-small cell lung cancer. *Cancer Nursing, 29*(2), 104-110.

Brant, J. M., Beck, S., & Miaskowski, C. (2010). Building dynamic models and theories to advance the science of symptom management research. *Journal of Advanced Nursing, 66*(1), 228-240.

Brown, J. K., Cooley, M. E., Chernecky, C., & Sarna, L. (2011). A Symptom cluster and sentinel symptom experienced by women with lung cancer. *Oncology Nursing Forum, 38*(6), 425-435.

Brown, L. F., & Kroenke, K. (2009). Cancer-Related fatigue and its associations with depression and anxiety: A Systematic review. *Psychosomatics, 50*(5), 440-447.

Bui, C. V., Le, V. C., & Nguyen, C. H. (2010). Prognostic factors in non-small cell lung cancer (in Vietnamese). *Ho Chi Minh City Journal of Medicine, 14*(4), 397 - 407.

Cahalin, L. P., Braga, M., Matsuo, Y., & Hernandez, E. D. (2002). Efficacy of diaphragmatic breathing in persons with chronic obstructive pulmonary disease: a review of the literature. *Journal of Cardiopulmonary Rehabilitation and Prevention, 22*(1), 7-21.

Cairns, L. (2012). Managing breathlessness in patients with lung cancer. *Nursing Standard, 27*(13), 44-49.

Campo, R. A., Agarwal, N., LaStayo, P. C., O'Connor, K., Pappas, L., Boucher, K. M., Gardner, J., Smith, S. L., Kathleen, C., & Kinney, A. Y. (2014). Levels of fatigue and distress in senior prostate cancer survivors enrolled in a 12-week randomized controlled trial of Qigong. *Journal of Cancer Survivorship, 8*(1), 60-69.

Cella, D., Eton, D., Hensing, T. A., Masters, G. A., & Parasuraman, B. (2008). Relationship between symptom change, objective tumor measurements, and performance status during chemotherapy for advanced lung cancer. *Clinical Lung Cancer, 9*(1), 51-58.

Cella, D. F., & Tulsky, D. S. (2009). Quality of life in cancer: definition, purpose, and method of measurement. *Cancer Investigation 11(3), 327-336*.

Cella, D. F., Tulsky, D. S., Gray, G., Sarafian, B., Linn, E., Bonomi, A., Silberman, M., Yellen, S. B., Winicour, P., & Brannon, J. (1993). The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *Journal of Clinical Oncology, 11*(3), 570-579.

Chan, A.W., Tetzlaff, J. M., Altman, D. G., Laupacis, A., Gøtzsche, P. C., Krleža, K., Hróbjartsson, A., Mann, H., Dickersin, K., & Berlin, J. A. (2013). SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Annals of Internal Medicine, 158*(3), 200-207.

Chan, A. W., Lee, A., Suen, L. K., & Tam, W. W. (2011). Tai chi Qigong improves lung functions and activity tolerance in COPD clients: a single blind, randomized controlled trial. *Complementary Therapies in Medicine, 19*(1), 3-11.

Chan, C. W., Richardson, A., & Richardson, J. (2005). A study to assess the existence of the symptom cluster of breathlessness, fatigue and anxiety in patients with advanced lung cancer. *European Journal of Oncology Nursing, 9*(4), 325-333.

Chan, C. W. H., Chang, A. M., Leung, S. F., & Mak, S. S. S. (2007). Reducing breathlessness, fatigue, and anxiety in Chinese patients undergoing lung cancer radiotherapy in Hong Kong. *Hong Kong Medical Journal, 13*(2), 4-7.

Chan, C. W. H., Richardson, A., Richardson, J. (2011). Managing Symptoms in Patients with Advanced Lung Cancer During Radiotherapy: Results of a Psychoeducational Randomized Controlled Trial. *Journal of Pain and Symptom Management, 41*(2), 347-357.

Chan, D. N.S. (2012). Supportive care needs and health-related quality of life among Chinese lung cancer survivors. *Advances in Lung Cancer, 01*(02), 5-12.

Chan, R. J., Chan, A., Yates, P., & Molassiotis, A. (2017). A step forward in addressing cancer survivorship in the Asia-Pacific region. *BMC Medicine, 15*(1), 17-26.

Chang, P.S., Chao, A. M., Jang, M., & Lu, Y. Y. (2019). Intervention fidelity in Qigong randomized controlled trials: A method review. *Geriatric Nursing, 40*(1), 84-90 .

Chansungnoen, J. (2007). *Effects of the symptom management combined with qigong practice program on fatigue among caregivers of head injury patients.* (Master), Chulalongkorn, Bangkok, Thailand. (560092)

Chen, E., Nguyen, J., Cramarossa, G., Khan, L., Leung, A., Lutz, S., & Chow, E. (2011). Symptom clusters in patients with lung cancer: a literature review. *Expert Review of Pharmacoeconomics & Outcomes Research, 11*(4), 433-439.

Chen, H., Tsai, C., Wu, Y., Lin, K., & Lin, C. (2015). Randomized controlled trial on the effectiveness of home-based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *British Journal of Cancer, 112*(3), 438-445.

Chen, K., Liu, T., & Liu, T. (2010). *Chinese Medical Qigong*: Singing Dragon.

Chen, K., Yeung, R. (2002). A review of qigong therapy for cancer treatment. *Journal of International Society of Life Information Science*, *20*(2), 532-540.

Chen, L., Antras, L., Duh, M. S., Neary, M., & O'Brien, M. E. (2008). Symptom assessment in relapsed small cell lung cancer: cross-validation of the patient symptom assessment in lung cancer instrument. *Journal of Thoracic Oncology, 3*(10), 1137-1145.

Chen, Z., Meng, Z., Milbury, K., Bei, W., Zhang, Y., Thornton, B., Liao, Z., Wei, Q., Chen, J., & Guo, X. (2013). Qigong improves quality of life in women undergoing radiotherapy for breast cancer. *Cancer, 119*(9), 1690-1698.

Chernecky, C., Sarna, L., Waller, J. L., & Brecht, M. (2004). Assessing coughing and wheezing in lung cancer: a pilot study. *Oncology Nursing Forum, 31*(6), 1095-1101.

Cheville, A. L., Novotny, P. J., Sloan, J. A., Basford, J. R., Wampfler, J. A., Garces, Y. I., Jatoi, A., & Yang, P. (2011). Fatigue, dyspnea, and cough comprise a persistent symptom cluster up to five years after diagnosis with lung cancer. *Journal of Pain and Symptom Management, 42*(2), 202-212.

Chung, K. F. (2006). Measurement of cough. *Respiratory Physiology & Neurobiology, 152*(3), 329-339.

Cooley, M. E. (2000). Symptoms in adults with lung cancer: A systematic research review. *Journal of Pain and Symptom Management, 19*(2), 137-153.

Cotes, J. E., Chinn, D. J., & Miller, M. R. (2006). *Lung function: physiology, measurement and application in medicine* (6th ed.). Massachusetts: Blackwell.

Craig, A. D., & Craig, A. (2009). How do you feel-now? The anterior insula and human awareness. *Nature Reviews Neuroscience, 10*(1), 59-70.

Crampton, B. (1995). Evaluation research on Chinese qigong based on qigong master Yan Xin's ten observable attributes of qigong. June 17th - 19th, 1995, first Yang Xin, Qigong Science Symposium, New Haven, Connecticut, USA.

Cu, X. T., To, K. D., & Nguyen, V. C. (2000). Clinical manifestations of lung cancer in late adult and elderly (Vietnamese). *Journal of Practical Medicine, 6*, 7-8.

Dales, R. E., Bélanger, R., Shamji, F. M., Leech, J., Crépeau, A., & Sachs, H. J. (1994). Quality of life following thoracotomy for lung cancer. *Journal of Clinical Epidemiology, 47*(12), 1443-1449.

Daubenmier, J., Sze, J., Kerr, C. E., Kemeny, M. E., & Mehling, W. (2013). Follow your breath: respiratory interoceptive accuracy in experienced meditators. *Psychophysiology, 50*(8), 777-789.

Dean, G. E., Finnell, D. S., Scribner, M., Wang, Y.J., Steinbrenner, L. M., & Gooneratne, N. S. (2010). Sleep in lung cancer: the role of anxiety, alcohol and tobacco. *Journal of Addictions Nursing, 21*(2-3), 130-138.

Degner, L. F., & Sloan, J. A. (1995). Symptom distress in newly diagnosed ambulatory cancer patients and as a predictor of survival in lung cancer. *Journal of Pain and Symptom Management, 10*(6), 423-431.

DiSalvo, W., Joyce, M., Tyson, L., Culkin, A., & Mackay, K. (2008). Putting evidence into practice: Evidence-based interventions for cancer-related dyspnea. *Clinical Journal of Oncology Nursing, 12*(2), 341-352.

Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E. S., Humphreys, J., Lee, K., Miaskowski, C., Puntillo, K., Rankin, S., & Taylor, D. (2001). Advancing the science of symptom management. *Journal of Advanced Nursing, 33*(5), 668-676.

Dodd, M., Miaskowski, C., & Paul, S. M. (2001). Symptom clusters and their effect on the functional status of patients with cancer. *Oncology Nursing Forum, 28*(3), 466-470.

Doyle, S., Lloyd, A., & Walker, M. (2008). Health state utility scores in advanced non-small cell lung cancer. *Lung Cancer, 62*(3), 374-380.

Du, J., Wood, P. A., Burch, J. B., Grutsch, J. F., Gupta, D., Tyer, K., Lis, C. G., Levin, R. D., Quiton, D. F., Reynolds, J. L., & Hrushesky, W. J. (2010). Actigraphic assessment of daily sleep-activity pattern abnormalities reflects self-assessed depression and anxiety in outpatients with advanced non-small cell lung cancer. *Psycho-Oncology, 19*(2), 180-189.

El, A. H., Lau, C. T., Wu, C. C., Drake, R. L., Abbott, G. F., & Rice, T. W. (2014). International association for the study of lung cancer (IASLC) lymph node map: radiologic review with CT illustration. *Radiographics, 34*(6), 1680-1691.

Ernst, E. (2002). Research ethics questioned in Qigong study. *Alternative Therapies in Health and Medicine, 8*(4), 18-25.

Esper, P. (2010). Symptom cluster in individuals living with advanced cancer. *Seminars in Oncology Nursing, 26*(3), 168-174.

Evans, H. M. (2007). Do patients have duties? *Journal of medical ethics, 33*(12), 689-694.

Fayers, P., Aaronson, N., Bjordal, K., Groenvold, M., Curran, D., & Bottomley, A. (2012). The EORTC QLQ-C30 Scoring Manual. 2001. *Published by: European Organisation for Research and Treatment of Cancer, Brussels*.

Fayter, D., McDaid, C., & Eastwood, A. (2007). A systematic review highlights threats to validity in studies of barriers to cancer trial participation. *Journal of Clinical Epidemiology, 60*(10), 991-990.

Feinman, R. D. (2009). Intention-to-treat. What is the question? *Nutrition & metabolism, 6*(1), 1-7.

Feinstein, M. B., Krebs, P., Coups, E. J., Park, B. J., Steingart, R. M., Burkhalter, J., Logue, A., & Ostroff, J. S. (2010). Current dyspnea among long-term survivors of early-stage non-small cell lung cancer. *Journal of Thoracic Oncology, 5*(8), 1221-1226.

Ferlay, J., Shin, H.R., Bray, F., Forman, D., Mathers, C., & Parkin, D. M. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer, 127*, 2893-2917.

Fernandez, C., Rosell, R., Abad-Esteve, A., Monras, P., Moreno, I., Serichol, M., & Roviralta, M. (1989). Quality of life during chemotherapy in non-small cell lung cancer patients. *Acta Oncologica, 28*(1), 29-33.

Finnegan, J., Molassiotis, A., Richardson, A., & Ream, E. (2013). A systematic review of complementary and alternative medicine interventions for the management of cancer-related fatigue. *Integrative Cancer Therapies, 12*(4), 276-290.

Fong, S. S., Ng, S. S., Luk, W., Chung, L. M., Wong, J. Y., & Chung, J. W. (2014). Effects of qigong training on health-related quality of life, functioning, and cancer-related symptoms in survivors of nasopharyngeal cancer: a pilot study. *Evidence-Based Complementary and Alternative Medicine, doi: http://dx.doi.org/10.1155/2014/495274*.

Fong, S. S. M., et al.. (2015). The effects of a 6-month Tai Chi Qigong training program on temporomandibular, cervical, and shoulder joint mobility and sleep problems in nasopharyngeal cancer survivors. *Integrative Cancer Therapies, 14*(1), 16-25.

Fontana, G. A., & Widdicombe, J. (2007). What is cough and what should be measured? *Pulmonary Pharmacology and Therapeutics*, *20*(4), 307-312.

Frangakis, C. E., & Rubin, D. B. (1999). Addressing complications of intention-to-treat analysis in the combined presence of all-or-none treatment-noncompliance and subsequent missing outcomes. *Biometrika, 86*(2), 365-379.

Froelicher, E. S., Gortner, S. R., Halliburton, P., Janson, S., Miaskowski, C., Savedra, M. C., Stotts, N. A., Taylor, D., & Underwood, P. R. (1994). A model for symptom management, *Journal of Nursing Scholarship*, 26(4), 272-276.

Fu, J., & Wang, S. (1995). Qigong plus herbal medicine in treating late-stage stomach cancer in the elderly. *Understanding of true qi cultivation and sublimation. Beijing, China: Chinese Publisher of Constructive Materials*.

Fu, J., & Zou, Z. (1995). Qigong combined with chemotherapy in the treatment of gastric cancer. *Understanding of true qi cultivation and sublimation. Beijing, China: Chinese Publisher of Constructive Materials*.

Furley, D. J., & Wilkie, J. S. (2014). *Galen: On respiration and the arteries*. New Jersey: Princeton University Press.

Genç, F., & Tan, M. (2011). Symptoms of patients with lung cancer undergoing chemotherapy and coping strategies. *Cancer Nursing, 34*(6), 503-509.

Gift, A., Jablonski, A., Stommel, M., & Given, C. W. (2004). Symptom clusters in elderly patients with lung cancer. *Oncology Nursing Forum, 31*(2), 203-210.

Gift, A., Stommel, M., Jablonski, A., & Given, W. (2003). A cluster of symptoms over time in patients with lung cancer. *Nursing Research, 52*(6), 393-400.

Gift, A. G., Moore, T., & Soeken, K. (1992). Relaxation to reduce dyspnea and anxiety in COPD patients. *Nursing Research, 41*(4), 242-246.

Gosselink, R. (2004). Breathing techniques in patients with chronic obstructive pulmonary disease (COPD). *Chronic Respiratory Disease, 1*(3), 163-172.

Greenhalgh, J., Long, A. F., & Flynn, R. (2005). The use of patient reported outcome measures in routine clinical practice: lack of impact or lack of theory? *Social Science & Medicine, 60*(4), 833-843.

Gueorguieva, R., & Krystal, J. H. (2004). Move over anova: progress in analyzing repeated-measures data andits reflection in papers published in the archives of general psychiatry. *Archives of General Psychiatry, 61*(3), 310-317.

Haak, T., & Scott, B. (2008). The effect of Qigong on fibromyalgia (FMS): a controlled randomized study. *Disability and Rehabilitation, 30*(8), 625-633.

Harle, A. S., Blackhall, F. H., Smith, J. A., & Molassiotis, A. (2012). Understanding cough and its management in lung cancer. *Current Opinion in Supportive and Palliative Care, 6*(2), 153-162.

Hasson, H., Blomberg, S., & Dunér, A. (2012). Fidelity and moderating factors in complex interventions: a case study of a continuum of care program for frail elderly people in health and social care. *Implementation science, 7*(1), 23-30.

Heard, K., O'Toole, E., Naimpally, R., & Bressler, L. (2017). *Real-world challenges to randomization and their solutions*. JPAL North America Retrieved from povertyactionlab.org/na.

Henly, S. J., Kallas, K. D., Klatt, C. M., & Swenson, K. K. (2003). The notion of time in symptom experiences. *Nursing Research, 52*(6), 410-417.

Henoch, I., Bergman, B., & Danielson, E. (2008). Dyspnea experience and management strategies in patients with lung cancer. *Psychooncology, 17*(7), 709-715.

Henoch, I., Bergman, B., & Gaston, F. (2006). Validation of a Swedish version of the Cancer Dyspnea Scale. *Journal of Pain and Symptom Management, 31*(4), 353-361.

Henoch, I., Bergman, B., Gustafsson, M., Gaston, F., & Danielson, E. (2007). The impact of symptoms, coping capacity, and social support on quality of life experience over time in patients with lung cancer. *Journal of Pain and Symptom Management, 34*(4), 370-379.

Henoch, I., Bergman, B., Gustafsson, M., Gaston, F., & Danielson, E. (2008). Dyspnea experience in patients with lung cancer in palliative care. *European Journal of Oncology Nursing, 12*(2), 86-96.

Henry, J. D., & Crawford, J. R. (2005). The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. *British Journal of Clinical Psychology, 44*(2), 227-239.

Higgins, J. P., & Green, S. (Eds). (2008). *Cochrane handbook for systematic reviews of interventions*. West Sussex: John Wiley & Sons.

Hollen, P. J., & Gralla, R. J. (1996). *Comparison of instruments for measuring quality of life in patients with lung cancer.* Paper presented at the Seminars in Oncology.

Hollen, P. J., Gralla, R. J., Cox, C., Eberly, S. W., & Kris, M. G. (1997). A dilemma in analysis: issues in the serial measurement of quality of life in patients with advanced lung cancer. *Lung Cancer, 18*(2), 119-136.

Hollen, P. J., Gralla, R. J., Kris, M. G., Cox, C., Belani, C. P., Grunberg, S. M., Crawford, J., & Neidhart, J. A. (1994). Measurement of quality of life in patients with lung cancer in multicenter trials of new therapies. Psychometric assessment of the Lung Cancer Symptom Scale. *Cancer, 73*(8), 2087-2098.

Honas, J. J., Early, J. L., Frederickson, D. D., & O'brien, M. S. (2003). Predictors of attrition in a large clinic-based weight-loss program. *Obesity, 11*(7), 888-894.

Hong, E. (2003). The effect of Yudongkong exercise in fatigue, difficulty of daily activities and symptoms of side effect in advanced gastric cancer patients receiving chemotherapy. *PhD dissertion. Seoul, Korea: Yonsei University*.

Hopwood, P., & Stephens, R. J. (2000). Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. *Journal of Clinical Oncology, 18*(4), 893-903.

Huang, S.M., Tseng, L.M., Chien, L.Y., Tai, C.J., Chen, P.H., Hung, C. T., & Hsiung, Y. (2016). Effects of non-sporting and sporting qigong on frailty and quality of life among breast cancer patients receiving chemotherapy. *European Journal of Oncology Nursing, 21*, 257-265.

Hudson, A. L., Gandevia, S. C., & Butler, J. E. (2011). Control of human inspiratory motoneurones during voluntary and involuntary contractions. *Respiratory Physiology & Neurobiology, 179*(1), 23-33.

Huebner, J., Rosé, C., Geissler, J., Gleiter, C., Prott, F., Muenstedt, K., Micke, O., Muecke, R., Buentzel, J., & Bottomley, A. (2014). Integrating cancer patients' perspectives

into treatment decisions and treatment evaluation using patient-reported outcomes–a concept paper. *European Journal of Cancer Care, 23*(2), 173-179.

Huhmann, M., & Camporeale, J. (2012). Supportive care in lung cancer: Clinical Update. *Seminars in Oncology Nursing, 28*(2), 1-10.

Hung, N. C., Minh, L. H., Dung, P. X., & Thinh, D. H. Q. (2008). Action plan for cancer control in Ho Chi Minh city. *Ho Chi Minh City Medical Journal, 12*(4), 1-7.

Hung, R., Krebs, P., Coups, E. J., Feinstein, M. B., Park, B. J., Burkhalter, J., & Ostroff, J. S. (2011). Fatigue and functional impairment in early-stage non-small cell lung cancer survivors. *Journal of Pain and Symptom Management, 41*(2), 426-435.

Hutchinson, S. A., & Wilson, H. S. (1997). The theory of unpleasant symptoms and Alzheimer's disease. *Scholarly Inquiry for Nursing Practice, 12*(2), 143-158.

Ishikawa, N. M., Thuler, L. C., Giglio, A. G., Baldotto, C. S., de Andrade, C. J., & Derchain, S. F. (2010). Validation of the Portuguese version of functional assessment of cancer therapy-fatigue (FACT-F) in Brazilian cancer patients. *Supportive Care in Cancer, 18*(4), 481-490.

Iyer, S., Roughley, A., Rider, A., & Taylor, G. (2013). The symptom burden of non-small cell lung cancer in the USA: a real-world cross-sectional study. *Supportive Care in Cancer 22* (1), 181-187.

Iyer, S., Taylor, G., & Roughley, A. (2013). Symptom burden and quality of life in advanced non-small cell lung cancer patients in France and Germany. *Lung Cancer, 81*(2), 288-293.

Jacobsen, P. B., Donovan, K. A., Vadaparampil, S. T., & Small, B. J. (2007). Systematic review and meta-analysis of psychological and activity-based interventions for cancer-related fatigue. *Health Psychology, 26*(6), 660-667.

Jahnke, R., Larkey, L., Rogers, C., Etnier, J., and Lin, F. (2010). A comprehensive reviewof health benefits of Qigong and Tai Chi. *American Journal of Health Promotion, 24*(6), 1-25.

Joyce, M., Schwartz, S., & Huhmann, M. (2008). Supportive Care in Lung Cancer. *Seminars in Oncology Nursing, 24*(1), 57-67.

Kaasa, S., & Mastekaasa, A. (1988). Psychosocial well-being of patients with inoperable non-small cell lung cancer: the importance of treatment-and disease-related factors. *Acta Oncologica, 27*(6), 829-835.

Karlberg, J. P. E., & Speers, M. A. (Eds.) (2010). *Reviewing clinical trials: a guide for the ethics committee*. Retrieved from https://bioethicsresearchreview.tghn.org/site_media/media/articles/Reviewing_Clinical_Trials_-_English.pdf

Kathiresan, G., Clement, & Sankaranarayanan. (2010). Dyspnea in lung cancer patients: a systematic review. *Lung Cancer: Targets and Therapy, 10*, 141-150.

Keegan, L. (1998). Getting comfortable with alternative & complementary therapies. *Nursing, 28*(4), 50-57.

Keogh, M., Bachmann, M., Shepstone, L., Hewitt, C., Howe, A., Ramsay, C. R., Song, F., Miles, J., Torgerson, D., & Miles, S. (2007). Contamination in trials of educational interventions, *Health Technology Assessment*, *11*(43), 1–128.

Khue, L. N., & Minh, H. V. (2011). Prevalence and intensity of smoking in Vietnamese, *Ho Chi Minh City Medical Journal*, *15*(2), 94-100.

Kim, H. J., McGuire, D. B., Tulman, L., & Barsevick, A. M. (2005). Symptom clusters: Concept analysis and clinical implications for cancer nursing. *Cancer Nursing, 28*(4), 270-282.

Kim, J., & Shin, W. (2014). How to do random allocation (randomization). *Clinics in Orthopedic Surgery, 6*(1), 103-109.

Kimman, M., Norman, R., Jan, S., Kingston, D., & Woodward, M. (2013). The burden of cancer in member countries of the Association of Southeast Asian Nations (ASEAN). *Asian Pacific Journal of Cancer Prevention, 13*, 411-420.

King, M. T., Bell, M. L., Costa, D., Butow, P., & Oh, B. (2014). The Quality of Life Questionnaire Core 30 (QLQ-C30) and Functional Assessment of Cancer-General (FACT-G) differ in responsiveness, relative efficiency, and therefore required sample size. *Journal of Clinical Epidemiology, 67*(1), 100-107.

Kirkova, J., Aktas, A., Walsh, D., Rybicki, L., & Davis, M. P. (2010). Consistency of symptom clusters in advanced cancer. *American Journal of Hospice & Palliative Medicine, 27*(5), 342-346.

Koczywas, M., Williams, A. C., Cristea, M., Reckamp, K., Grannis, F. W., Jr., Tiep, B. L., Uman, G., & Ferrell, B. (2013). Longitudinal changes in function, symptom burden, and quality of life in patients with early-stage lung cancer. *Annals of Surgical Oncology, 20*(6), 1788-1797.

Krakauer, E. L., Ngoc, N. T. M., Green, K., Van Kham, L., & Khue, L. N. (2007). Vietnam: Integrating palliative care into HIV/AIDS and cancer care. *Journal of Pain and Symptom Management, 33*(5), 578-583.

Krishnasamy, M., Wilkie, E., & Haviland, J. (2001). Lung cancer health care needs assessment: patients' and informal carers' responses to a national mail questionnaire survey. *Palliative Medicine, 15*(3), 213-227.

Kuo, T.T., & Ma, F.C. (2002). Symptom distresses and coping strategies in patients with Non-small Cell Lung Cancer. *Cancer Nursing, 25*(4), 309-317.

Kvale, P. A. (2006). Chronic cough due to lung tumors: ACCP evidence-based clinical practice guidelines. *Chest, 129*(1), 147-153.

Lacasse, C., & Beck, S. L. (2007). Clincal assessment of symptom clusters. *Seminars in Oncology Nursing, 23*(2), 106-112.

Lachin, J. M., Matts, J. P., & Wei, L. (1988). Randomization in clinical trials: conclusions and recommendations. *Controlled Clinical Trials, 9*(4), 365-374.

Lai, Y. L., Chan, C. W. H., & Lopez, V. (2007). Perceptions of dyspnea and helpful interventions during the advanced stage of lung cancer: Chinese patients' perspectives. *Cancer Nursing, 30*(2), 2-8.

Lam, W.Y. (2004). A randomized, controlled trial of Guolin qigong in patients receiving transcatheter arterial chemoembolisation for unresectablehepatocellular carcinoma. *HKU Theses Online (HKUTO).*

Lane, M. A. (2011). Spinal respiratory motoneurons and interneurons. *Respiratory Physiology & Neurobiology, 179*(1), 3-13.

Larkey, L. K., Roe, D. J., Weihs, K. L., Jahnke, R., Lopez, A. M., Rogers, C. E., Oh, B., & Guillen, J. (2015). Randomized controlled trial of Qigong/Tai Chi easy on cancer-related fatigue in breast cancer survivors. *Annals of Behavioral Medicine, 49*(2), 165-176.

Larsson, M., Ljung, L., & Johansson, B. B. K. (2012). Health-related quality of life in advanced non-small cell lung cancer: correlates and comparisons to normative data. *European Journal of Cancer Care, 21*(5), 642-649.

Lee, E. H. (2005). Relationships of mood disturbance, symptom experience, and attentional function in women with breast cancer based upon the theory of unpleasant symptoms. *Taehan Kanho Hakhoe Chi, 35*(4), 728-736.

Lee, M. S., et al.. (2007). Qigong for cancer treatment: a systematic review of controlled clinical trials. *Acta Oncologica, 46*(6), 717-722.

Lee, M. S., Oh, B., & Ernst, E. (2011). Qigong for healthcare: an overview of systematic reviews. *JRSM short reports, 2*(2), 1-5.

Lee, Chen, H.H., & Yeh, M.L. (2006). Effects of chan-chuang qigong on improving symptom and psychological distress in chemotherapy patients. *The American journal of Chinese medicine, 34*(01), 37-46.

Lenz, E. R., & Pugh, L. C. (2008). Theory of Unpleasant Symptoms. In Smith & Liehr (Eds.), *Middle range theory for nursing* (2nd ed.). New York: Springer Publishing Company.

Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: an update. *Advances in Nursing Science, 19*(3), 14-27.

Leppert, W., Turska, A., Majkowicz, M., Dziegielewska, S., Pankiewicz, P., & Mess, E. (2012). Quality of life in patients with advanced lung cancer treated at home and at a palliative care unit. *American Journal of Hospice and Palliative Medicine, 29*(5), 379-387.

Lewis, J., & Machin, D. (1993). Intention to treat who should use ITT? *British Journal of Cancer, 68*(4), 647-650.

Liao, Y. C., Liao, W. Y., Shun, S. C., Yu, C. J., Yang, P. C., & Lai, Y. H. (2011). Symptoms, psychological distress, and supportive care needs in lung cancer patients. *Supportive Care in Cancer, 19*(11), 1743-1751.

Lidstone, V., Butters, E., Seed, P. T., Sinnott, C., Beynon, T., & Richards, M. (2003). Symptoms and concerns amongst cancer outpatients: identifying the need for specialist palliative care. *Palliative Medicine, 17*(7), 588-595.

Lijmer, J. G., & Bossuyt, P. M. (2002). Diagnostic testing and prognosis: the randomized controlled trial in diagnostic research. *The Evidence Base of Clinical Diagnosis, 61*, 11-17.

Loh, S., & Lee, S. (2015). The Qigong and quality of life trial: Implications for women in cancer survivorship phase. *Journal of Womens Health, 4*(3), 181-187.

Loh, S. Y., Lee, S. Y., & Murray, L. (2014). The Kuala Lumpur Qigong trial for women in the cancer survivorship phase-efficacy of a three-arm RCT to improve quality of life. *Asian Pacific Journal of Cancer Prevention, 15*(19), 81-87.

Loh, S. Y., Lee, S. Y., Quek, K. F., & Murray, L. (2012). Barriers to participation in a randomized controlled trial of Qigong exercises amongst cancer survivors: lessons learnt. *Asian Pacific Journal of Cancer Prevention, 13*(12), 6337-6342.

Long, N. H., Thanasilp, S., & Thato, R. (2016). A causal model for fatigue in lung cancer patients receiving chemotherapy. *European Journal of Oncology Nursing, 21*, 242-247.

Lou, Y., Yates, P., McCarthy, A., & Wang, H. (2013). Fatigue self-management: a survey of Chinese cancer patients undergoing chemotherapy. *Journal of Clinical Nursing, 22*(7-8), 1053-1065.

Lovibond, P. F., & Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335-343.

Lutz, S., Norrell, R., Bertucio, C., Kachnic, L., Johnson, C., Arthur, D., Schwarz, M., & Palardy, G. (2001). Symptom frequency and severity in patients with metastatic or locally recurrent lung cancer: a prospective study using the Lung Cancer Symptom Scale in a community hospital. *Journal of Palliative Medicine, 4*(2), 157-165.

Maguire, R., Stoddart, K., Flowers, P., McPhelim, J., & Kearney, N. (2014). An Interpretative Phenomenological Analysis of the lived experience of multiple concurrent symptoms in patients with lung cancer: A contribution to the study of symptom clusters. *European Journal of Oncology Nursing, 18*(3), 310-315.

Maringwa, J., Quinten, C., King, M., Ringash, J., Osoba, D., Coens, C., Martinelli, F., Reeve, B. B., Gotay, C., Greimel, E., Flechtner, H., Cleeland, C. S., Schmucker-Von Koch, J., Weis, J., Van Den Bent, M. J., Stupp, R., Taphoorn, M. J., Bottomley, A., Project, E. P., & Group, B. C. (2011). Minimal clinically meaningful differences for the EORTC QLQ-C30 and EORTC QLQ-BN20 scales in brain cancer patients. *Annals of Oncology, 22* (9), 2107-2112.

Markaki, M., Tsamardinos, I., Langhammer, A., Lagani, V., Hveem, K., & Røe, O. D. (2018). A validated clinical risk prediction model for lung cancer in smokers of all ages and exposure types: A HUNT Study. *EBioMedicine, 31, 36-46*.

McCabe, C., Begley, C., Collier, S., & McCann, S. (2008). Methodological issues related to assessing and measuring quality of life in patients with cancer: implications for patient care. *European Journal of Cancer Care, 17*(1), 56-64.

McGarvey, L. P., & Morice, A. H. (2006). Clinical cough and its mechanisms. *Respiratory Physiology & Neurobiology, 152*(3), 363-371.

Ministry of Health (2008). *National project on prevention and control of cancer from 2008 to 2010*. Retrieved from http://benhvienk.com/pcut/du-an-quoc-gia-ve-pcut/268-du-an-quoc-gia-ve-pcut-giai-doan-2008-2010-phan-1.

Ministry of Health (2012). *Guidelines on palliative care for cancer and AIDS patients*. Ha Noi: Medical Publishing Houses.

Minton, O., & Stone, P. (2009). A systematic review of the scales used for the measurement of cancer-related fatigue (CRF). *Annals of Oncology, 20*(1), 17-25.

Minton, O., Stone, P., Richardson, A., Sharpe, M., & Hotopf, M. (2008). Drug therapy for the management of cancer related fatigue. *Cochrane Database of Systematic Reviews, 2008*(1). doi:10.1002/14651858

Mitchell, S. A., & Beck, S. L. (2009). Putting Evidence into Practice: Improving Oncology Patient Outcomes. *Clinical Journal of Oncology Nursing*, *11*, 99-113.

Mitchell, S. A., Bethesda, M., & Berger, A. M. (2006). Cancer-related fatigue: The evidence base for assessment and management. *Cancer Journal*, *12*, 374-387.

Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gøtzsche, P. C., Devereaux, P., Elbourne, D., Egger, M., & Altman, D. G. (2010). CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomized trials. *Journal of Clinical Epidemiology, 63*(8), 1-37.

Molassiotis, A., Bryan, G., Caress, A., Bailey, C., & Smith, J. (2010). Pharmacological and non-pharmacological interventions for cough in adults with respiratory and non-respiratory diseases: A systematic review of the literature. *Respiratory Medicine CME, 3*(4), 199-206.

Molassiotis, A., Ellis, J., Wagland, R., Williams, M. L., Bailey, C. D., Booton, R., Blackhall, F., Yorke, J., & Smith, J. A. (2012). The Manchester cough in lung cancer scale: the development and preliminary validation of a new assessment tool. *Journal of Pain and Symptom Management, 45*(2), 179-190.

Molassiotis, A., & Lowe, M. (2010). Symptom experience and symptom clustering over time in patients with lung cancer. *European Journal of Oncology Nursing, 14,* 50-57.

Molassiotis, A., Lowe, M., Blackhall, F., & Lorigan, P. (2011a). A qualitative exploration of a respiratory distress symptom cluster in lung cancer: cough, breathlessness and fatigue. *Lung Cancer, 71*(1), 94-102.

Molassiotis, A., Lowe, M., Ellis, J., Wagland, R., Bailey, C., Lloyd, M., Tishelman, C., & Smith, J. (2011b). The experience of cough in patients diagnosed with lung cancer. *Supportive Care in Cancer, 19*(12), 1997-2004.

Molassiotis, A., Wengstrom, Y., & Kearney, N. (2010). Symptom cluster patterns during the first year after diagnosis with cancer. *Journal of Pain and Symptom Management, 39*(5), 847-858.

Montazeri, A., Gillis, C. R., & McEwen, J. (1998). Quality of life in patients with lung cancer: a review of literature from 1970 to 1995. *Chest, 113*(2), 467-481.

Moore, S., Corner, J., Haviland, J., Wells, M., Salmon, E., Normand, C., Brada, M., & Smith, I. (2002). Nurse led follow up and conventional medical follow up in management of patients with lung cancer: randomized trial. *BMJ, 325*(7373), 1-7.

Morgan, K. W. (1986). The path of the Buddha: Buddhism interpreted by Buddhists. *Journal of the American Oriental Society, 77* (1), 61-69.

Morrow, G., Lindke, J., & Black, P. (1992). Measurement of quality of life in patients: psychometric analyses of the Functional Living Index-Cancer (FLIC). *Quality of Life Research, 1*(5), 287-296.

Murphy, G. P., Lawrence, W., & Lenhard, R. (1995). *American Cancer Society textbook of clinical oncology* (1st ed). American Cancer Society Publications.

Mustian, K. M., Katula, J. A., Gill, D. L., Roscoe, J. A., Lang, D., & Murphy, K. (2004). Tai Chi Chuan, health-related quality of life and self-esteem: a randomized trial with breast cancer survivors. *Supportive Care in Cancer, 12*(12), 871-876.

Ng, H.p. B. (2009). *Effect of Qigong on physical and psychosocial status of Chinese COPD patients: a randomized controlled trial.* (Thesis) The Hong Kong Polytechnic University.

Ngo, Q. C. (2003). Primary lung cancer treated in respiratory department, *Bach Mai Hospital Journal, 2,* 5-10.

Ngoan L., T. (2006). Cancer mortality in a Hanoi population, Viet Nam, 1996-2005. *Asian Pacific Journal of Cancer Prevention, 7*(1), 127-130.

Ngoan, L. T., Fukumitsu, S., Kaneko, S., & Yoshimura, T. (2001). Differences in Cancer Risks in the South and North of Viet Nam. *Asian Pacific Journal of Cancer Prevention, 2*(3), 193-198.

Nguyen, B. Đ., Tran, V. T., & Le, T. D. (2009). Clinical manifestation, diagnosis, staging, and survival. In Bui & Hoang (Eds.), *Lung Cancer* (pp. 134-177). Ha Noi: Medical Press.

Nguyen, L. T., Alexander, K., & Yates, P. (2018). Psychoeducational intervention for symptom management of fatigue, pain and sleep disturbance cluster among cancer patients: A Pilot Quasi-experimental Study. *Journal of Pain and Symptom Management, 55(*6*),1459-1472*.

Nguyen, T. M. P., & Tran, Q. H. (2010). Study clinical characteristics and valued diagnoses for primary lung cancer ò percutaneous fine-core biospy by CT-guided. *Ho Chi Minh City Medical Journal, 14*(4), 342 - 347.

Nguyen, T. T. N., Tran, K. L., Bui, N. L., Vos, T., Ngo, Đ. A., & Nguyen, T. H. (2011). The burden of diseases and injuries in Vietnam in 2008 (in Vietnamese). Ha Noi: Medical Press.

Nicklasson, M. (2013). *Quality of life assessment in patients with lung cancer: Clinical implications*. Ineko AB, Gothenburg, Sweden.

Norton, P. J. (2007). Depression Anxiety and Stress Scales (DASS-21): Psychometric analysis across four racial groups. *Anxiety, Stress, and Coping, 20*(3), 253-265.

Oh, B., P., Mullan, B., Clarke, S., Beale, P., Pavlakis, N., et al. (2010). Impact of medical qigong on quality of life, fatigue, mood and inflammation in cancer patients: a randomized controlled trial. *Ann Oncology, 21*, 608-614.

Oh, B., Butow, P., Boyle, F., Beale, P., Costa, D., Pavlakis, N., Bell, D., Davis, E., Choi, S., & Lee, M. (2014). Effects of Qigong on quality of life, fatigue, stress, neuropathy, and sexual function in women with metastatic breast cancer: A feasibility study. *International Journal of Physical Medicine & Rehabilitation, 2014*. doi: 10.4172/2329-9096.1000217

Oh, B., Butow, P., Mullan, B., Clarke, S., Beale, P., Pavlakis, N., Kothe, E., Lam, L., & Rosenthal, D. (2010). Impact of medical Qigong on quality of life, fatigue, mood and inflammation in cancer patients: a randomized controlled trial. *Annals of Oncology, 21*(3), 608-614.

Oh, B., Butow, P., Mullan, B., Hale, A., Lee, M. S., Guo, X., & Clarke, S. (2011). A critical review of the effects of medical Qigong on quality of life, immune function, and survival in cancer patients. *Integrative Cancer Therapies*, *1*(2), 101-110.

Oh, B. (2012). Effect of medical qigong on cognitive function, quality of life, and a biomarker of inflammation in cancer patients: a randomized controlled trial. *Supportive Care in Cancer, 20,* 1235-1242.

Oh, B. (2014). Effects of Qigong on quality of life, fatigue, stress, neuropathy, and sexual function in women with metastatic breast cancer: A feasibility study. *American Journal of Physical Medicine & Rehabilitation, 2* (4), 217-223.

Oh, B. G., Kim, C. J., Lee, W. H., & Kim, S. S. (2004). Correlates of fatigue in Koreans with chronic lung disease. *Heart Lung, 33*(1), 13-20.

Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., Mcfadden, E. T., & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology, 5*(6), 649-656.

Okuyama, T., Tanaka, K., Akechi, T., Kugaya, A., Okamura, H., Nishiwaki, Y., Hosaka, T., & Uchitomi, Y. (2001). Fatigue in ambulatory patients with advanced lung cancer: prevalence, correlated factors, and screening. *Journal of Pain and Symptom Management, 22*(1), 554-564.

Olson, K., & Morse, J. M. (2005). Delineating the concept of fatigue using a pragmatic utility approach. In Cutcliffe & McKenna (Eds.), *The essential concepts of nursing* (pp. 141 - 159). London: Elsevier Churchill Livingstone.

Osoba, D., Aaronson, N., Zee, B., Sprangers, M., & Te Velde, A. (1997). Modification of the EORTC QLQ-C30 (version 2.0) based on content validity and reliability testing in large samples of patients with cancer. *Quality of Life Research, 6*(2), 103-107.

Osoba, D., Bezjak, A., Brundage, M., Zee, B., Tu, D., & Pater, J. (2005). Analysis and interpretation of health-related quality-of-life data from clinical trials: basic approach of The National Cancer Institute of Canada Clinical Trials Group. *European Journal of Cancer, 41*(2), 280-287.

Osoba, D., Rodrigues, G., Myles, J., Zee, B., & Pater, J. (1998). Interpreting the significance of changes in health-related quality-of-life scores. *Journal of Clinical Oncology, 16*(1), 139-144.

Ostroff, J. S., Krebs, P., Coups, E. J., Burkhalter, J. E., Feinstein, M. B., Steingart, R. M., Logue, A. E., & Park, B. J. (2011). Health-related quality of life among early-stage, non-small cell, lung cancer survivors. *Lung Cancer, 71*(1), 103-108.

Page, S. J., & Persch, A. C. (2013). Recruitment, retention, and blinding in clinical trials. *American Journal of Occupational Therapy, 67*(2), 154-161.

Pallant, J. (2013). SPSS Survival Manual: A step by step guide to data analysis using IBM SPSS. *Aotearoa New Zealand Social Work, 26*(4), 92-93.

Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. (2005). Global cancer statistics, 2002. *CA: A Cancer Journal for Clinicians, 55*(2), 74-108.

Pavord, I. D., & Chung, K. F. (2008). Management of chronic cough. *The Lancet, 371*(9621), 1375-1384.

Pbert, L., Madison, J. M., Druker, S., Olendzki, N., Magner, R., Reed, G., Allison, J., & Carmody, J. (2012). Effect of mindfulness training on asthma quality of life and lung function: a randomized controlled trial. *Thorax, 67*(9), 769-776.

Peddle, C. J., Bell, G., Fenton, D., McCargar, L., & Courneya, K. S. (2012). Feasibility and preliminary efficacy of progressive resistance exercise training in lung cancer survivors. *Lung Cancer, 75*(1), 126-132.

Penson, D. F., & Wei, J. T. (Eds.). (2006). *Clinical research methods for surgeons.* Retrieved from https://link.springer.com/content/pdf/10.1007%2F978-1-59745-230-4.pdf

Peuckmann, V., Elsner, F., Krumm, N., Trottenberg, P., & Radbruch, L. (2010). Pharmacological treatments for fatigue associated with palliative care. *Cochrane Database of Systematic Reviews*, doi: https://doi.org/10.1002/14651858.CD006788.pub2.

Phạm, V. L. (2010). The application of Gama knife in operation for lung cancer patients in Hue University of Medicince and Pharmacy's hospital. *Hue University Journal of Science, 63*, 107-120.

Phoophiw, S. (2011). *The Effect of integrative management and Thai qigong meditation exercise program on fatigue among persons with heart failure.* (Master), Chulalongkorn University, Bangkok, Thailand. (4508)

Phuong, N. T. T. (2013). *Lung cancer in Vietnam*. Paper presented at the National strategies for cancer control, Hanoi, Vietnam.

Phuong, N. T. T. (2014). *Quality of life of stage IV cancer patients before and after admission to palliative care unit in Ha Noi Oncology Hospital 2013.* Paper presented at the National Nursing Research, Nam Dinh, Vietnam.

Pirl, W. F., Temel, J. S., Billings, A., Dahlin, C., Jackson, V., Prigerson, H. G., Greer, J., & Lynch, T. J. (2008). Depression after diagnosis of advanced non-small cell lung cancer and survival: A pilot study. *Psychosomatics, 49*(3), 218-224.

Pocock, S. J., & Simon, R. (1975). Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. *Biometrics*, 103-115.

Podnos, Y. D., Borneman, T. R., Koczywas, M., Uman, G., & Ferrell, B. R. (2007). Symptom concerns and resource utilization in patients with lung cancer. *Journal of Palliative Medicine, 10*(4), 899-903.

Polanski, J., Jankowska-Polanska, B., Rosinczuk, J., Chabowski, M., & Szymanska, A. (2016). Quality of life of patients with lung cancer. *OncoTargets and Therapy, 9*, 10-23.

Portney, L. G., & Watkins, M. P. (2009). *Foundations of clinical reasearch: Applications to practice* (3 ed.). New Jersey: Pearson Education.

Porzsolt, F., & Tannock, I. (1993). Goals of palliative cancer therapy. *Journal of Clinical Oncology, 11*(2), 378-381.

Prechawong, S. (2011). *The effect of Qigong practice and health reaching on dysnea in patients with chronic obstructive pulmonary disease.* (Master), Chulalongkorn University, Bangkok (Thailand).

Pudtong, N., Aungsuroch, Y., & Jitpanya, C. (2014). Symptom clusters in Thai patients with advanced lung cancer. *Lung Cancer, 28*(3), 183-189.

Puetz, T. W., & Herring, M. P. (2012). Differential effects of exercise on cancer-related fatigue during and following treatment: A Meta-Analysis. *American Journal of Preventive Medicine, 43*(2), 1-24.

Quast, E., & Williams, M. T. (2009). Distress with breathing in people with lung cancer: A systematic review. *The Internet Journal of Allied Health Sciences and Practice, 7*(4), 1-11.

Radbruch, L., Strasser, F., Elsner, F., Gonçalves, J. F., Løge, J., Kaasa, S., Nauck, F., Stone, P., & Care, P. (2008). Fatigue in palliative care patients - An EAPC approach. *Palliative Medicine, 22*(1), 13-32.

Ranson, M., Davidson, N., Nicolson, M., Falk, S., Carmichael, J., Lopez, P., Anderson, H., Gustafson, N., Jeynes, A., & Gallant, G. (2000). Randomized trial of paclitaxel plus supportive care versus supportive care for patients with advanced non-small-cell lung cancer. *Journal of the National Cancer Institute, 92*(13), 1074-1080.

Reamrhom, C. (2008). *Effects of symptom management program conbind with Qigong on anxiety and fatigue in breast cancer patients receiving chemotherapy.* (Master), Chulalongkorn University, Bangkok, Thailand. (4083)

Redeker, N. S., Lev, E. L., & Ruggiero, J. (2000). Insomnia, fatigue, anxiety, depression, and quality of life of cancer patients undergoing chemotherapy. *Scholarly Inquiry for Nursing Practice, 14*(4), 275-290.

Reishtein, J. L. (2005). Relationship between symptoms and functional performance in COPD. *Research in Nursing & Health, 28*(1), 39-47.

Reyes, C. C., Anderson, K. O., Shete, S., Bruera, E., & Yennurajalingam, S. (2012). Early referral to supportive care specialists for symptom burden in lung cancer patients: a comparison of non-Hispanic whites, Hispanics, and non-Hispanic blacks. *Cancer, 118*(3), 856-863.

Ries, A. L., Bauldoff, G. S., Carlin, B. W., Casaburi, R., Emery, C. F., Mahler, D. A., Make, B., Rochester, C. L., ZuWallack, R., & Herrerias, C. (2007). Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. *CHEST Journal, 131*(5), 4-42.

Robiner, W. N. (2005). Enhancing adherence in clinical research. *Contemporary Clinical Trials, 26*(1), 59-77.

Ross, S., Grant, A., Counsell, C., Gillespie, W., Russell, I., & Prescott, R. (1999). Barriers to participation in randomized controlled trials: a systematic review. *Journal of Clinical Epidemiology, 52*(12), 1143-1156.

Rubleak, U. (2006). *The effect of symptom management combined with qigong practice program on fatigue of cerebrovascular caregivers.* (Master), Chulalongkorn, Bangkok, Thailand. (3754)

Sancier, K., & Hole, L. (2001). Qigong and neurologic illness. *Alternative and Complementary Treatment in Neurologic Illness. Pennsylvania: Churchill Livingstone*, 197-220.

Schipper, H., Clinch, J., & Olweny, C. L. (1996). Quality of life studies: definitions and conceptual issues. *Quality of life and Pharmacoeconomics in Clinical Trials, 2*, 11-23.

Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *BMC Medicine, 8*(1), 1-7.

Scott, H. R., McMillan, D. C., Forrest, L. M., Brown, D. J., McArdle, C. S., & Milroy, R. (2002). The systemic inflammatory response, weight loss, performance status and survival in patients with inoperable non-small cell lung cancer. *British Journal of Cancer, 87*(3), 264-267.

Scott, J. A., Lasch, K. E., Barsevick, A. M., & Piault, E. (2011). Patients' experiences with cancer-related fatigue: A review and synthesis of qualitative research. *Oncology Nursing Forum, 38*(3), 191-203.

Seers, K., & Critelton, N. (2001). Quantitative research: designs relevant to nursing and healthcare. *NT Research, 6*(1), 487-500.

Seyidova, D., Davis, M. P., & Walsh, D. (2011). Review Article: A Systematic review of cancer-related fatigue measurement questionnaires. *American Journal of Hospice and Palliative Medicine, 28*(2), 119-129.

Sharp, L., Carsin, A. E., & Timmons, A. (2013). Associations between cancer-related financial stress and strain and psychological well-being among individuals living with cancer. *Psycho-Oncology, 22*(4), 745-755.

Shneerson, C., Taskila, T., Gale, N., Greenfield, S., Chen, Y.F. (2013). The effect of complementary and alternative medicine on the quality of life of cancer survivors: A systematic review and meta-analyses. *Complementary Therapies in Medicine, 21*, 417-429.

Siangphairoj, K. (2006). *The effect of dyspnea management focusing on qigong practice program on quality of life among patients with chronic obstructive pulmonary disease.* (Master), Chulalongkorn, Bangkok, Thailand. (3766)

Simpson, C. B., & Amin, M. R. (2006). Chronic cough: State-of-the-art review. *Otolaryngology - Head and Neck Surgery, 134*(4), 693-700.

Smith, E. (1992). Dyspnea and quality of life. *Quality of Life: A Nursing Challenge, 1*, 31-38.

Smith, E. L., Hann, D. M., Ahles, T. A., Furstenberg, C. T., Mitchell, T. A., Meyer, L., Maurer, L. H., Rigas, J., & Hammond, S. (2001). Dyspnea, anxiety, body

consciousness, and quality of life in patients with lung cancer. *Journal of Pain and Symptom Management, 21*(4), 323-329.

Sprangers, M., & Schwartz, C. (1999). The challenge of response shift for quality of life based clinical oncology research. *Annals of Oncology, 10*(7), 747–749.

Sprangers, M. A. G., Cull, A., Groenvold, M., Bjordal, K., Blazeby, J., & Aaronson, N. K. (1998). The European Organization for Research and Treatment of Cancer Approach to Developing Questionnaire Modules: An Update and Overview. *Quality of Life Research, 7*(4), 291-300.

Steele, R., & Fitch, M. I. (2008). Why patients with lung cancer do not want help with some needs. *Supportive Care in Cancer, 16*(3), 251-259.

Stone, P., Richards, M., A'Hern, R., & Hardy, J. (2000). A study to investigate the prevalence, severity and correlates of fatigue among patients with cancer in comparison with a control group of volunteers without cancer. *Annals of Oncology, 11*(5), 561-567.

Sun, Q., & Zhao, L. (1988). *Clinical observation of qigong as a therapeutic aid for advanced cancer patients.* Paper presented at the First World Conference for Academic Exchange of Medical Qigong.

Suresh, K. (2011). An overview of randomization techniques: an unbiased assessment of outcome in clinical research. *Journal of Human Reproductive Sciences, 4*(1), 8-15.

Swanson, S., Dolce, A., Marsh, K., Summers, J., & Sheldon, L. K. (2008). Interventions to prevent and treat anxiety: a review of the evidence and implications for practice. *Oncology Nursing Forum, 35*(3), 525-525.

Szabó, M. (2010). The short version of the Depression Anxiety Stress Scales (DASS-21): Factor structure in a young adolescent sample. *Journal of Adolescence, 33*(1), 1-8.

Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2000). Development and validation of the Cancer Dyspnea Scale: a multidimensional, brief, self-rating scale. *British Journal of Cancer, 82*(4), 800-805.

Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2002). Impact of Dyspnea, Pain, and Fatigue on Daily Life Activities in Ambulatory Patients with Advanced Lung Cancer. *Journal of Pain and Symptom Management, 23*(5), 417-423.

Thanasilp, S. (2013). *Thai Qigong guide book step by step*. In Thanasilp (Ed.), (pp. 32). Retrieved from http://digitalmedia.co.th/demo/CU-2013/1/

Thang, T. B., & Chuong, N. V. (2012). Clinical features and staging of non-small cell lung cancer (Vietnamese). *Journal of Practical Medicine, 804*(1), 110-113.

Thompson, E., Sola, I., & Subirana, M. (2005). Non-invasive interventions for improving well-being and quality of life in patients with lung cancer: A systematic review of the evidence. *Lung Cancer, 50*(2), 163-176.

Thongteratham, N., Pongthavornkamol, K., Olson, K., Ratanawichitrasin, A., Nityasuddhi, D., & Wattanakitkrilert, D. (2015). Effectiveness of Tai Chi Qi Qong Program for Thai Women with Breast Cancer: A Randomized Control Trial. *Pacific Rim International Journal of Nursing Research*, *19*(4), 280-294.

Tishelman, C., Petersson, L.-M., Degner, L. F., & Sprangers, M. A. G. (2007). Symptom Prevalence, Intensity, and Distress in Patients With Inoperable Lung Cancer in Relation to Time of Death. *Journal of Clinical Oncology, 25*(34), 5381-5389.

Townsend, M. C. (2009). *Psychiatric mental health nursing: concepts of care in evidence-based practice*. Philadelphia: F. A. Davis Company.

Tran, T. D., Tran, T., & Fisher, J. (2013). Validation of the depression anxiety stress scales (DASS) 21 as a screening instrument for depression and anxiety in a rural

community-based cohort of northern Vietnamese women. *BMC psychiatry, 13*(1), 1-7.

Tsai, J.S., Wu, C.H., Chiu, T.Y., & Chen, C.Y. (2010). Significance of symptom clustering in palliative care of advanced cancer patients. *Journal of Pain and Symptom Management, 39*(4), 655-662.

Tsang, H. W., Cheung, L., & Lak, D. C. (2002). Qigong as a psychosocial intervention for depressed elderly with chronic physical illnesses. *International Journal of Geriatric Psychiatry, 17*(12), 1146-1154.

Tsang, H. W., Mok, C. K., Au Yeung, Y. T., & Chan, S. Y. (2003). The effect of Qigong on general and psychosocial health of elderly with chronic physical illnesses: a randomized clinical trial. *International Journal of Geriatric Psychiatry, 18*(5), 441-449.

Tung, N. D. (2010). Cancer control program in Thua Thien Hue, Vietnam, 2008 - 2009. *Journal of Science, Hue University, 61*, 511-517.

Uronis, H. E., Shelby, R. A., Currow, D. C., Ahmedzai, S. H., Bosworth, H. B., Coan, A., & Abernethy, A. P. (2012). Assessment of the psychometric properties of an English version of the cancer dyspnea scale in people with advanced lung cancer. *Journal of Pain and Symptom Management, 44*(5), 741-749.

Varcarolis, E. M. (2014). *Essentials of Psychiatric Mental Health Nursing-Revised Reprint*: Elsevier Health Sciences.

Velikova, G., Coens, C., Efficace, F., Greimel, E., Grønvold, M., Johnson, C., Singer, S., Van, L., Young, T., & Bottomley, A. (2012). Health-related quality of life in EORTC clinical trials - 30 years of progress from methodological developments to making a real impact on oncology practice. *European Journal of Cancer Supplements, 10*(1), 141-149.

Vietnamese Dictionary. (Ed.) (2004) Open Dictionary Online: GNU General Public.

Vos, M. S., Putter, H., Houwelingen, H. C., & Haes, H. C. (2011). Denial and social and emotional outcomes in lung cancer patients: the protective effect of denial. *Lung Cancer, 72*(1), 119-124.

Vu, D. V., Molassiotis, A., Ching, S. S. Y., & Le, T. T. (2017). Effects of Qigong on symptom management in cancer patients: A systematic review. *Complementary Therapies in Clinical Practice, 29*, 111-121.

Vu, V. V., Hanh, V. T. X., Giang, P. T. T., & Hoang, T. T. H. (2010). Studying the situation of pain and quality of life in advanced cancer patient patients at HCMC oncology hospital. *Ho Chi Minh City Medical Journal, 14*(4), 811 - 822.

Vuong, D. A., Velasco, M., Lai, T. D., & Busse, R. (2009). Temporal Trends of Cancer Incidence in Vietnam, 1993-2007. *Asian Pacific Journal of Cancer Prevention, 10*, 1-6.

Walker, W. (2005). The strengths and weaknesses of research designs involving quantitative measures. *Journal of Research in Nursing, 10*(5), 571-582.

Wallach, J. D., Sullivan, P. G., Trepanowski, J. F., Steyerberg, E. W., & Ioannidis, J. P. (2016). Sex based subgroup differences in randomized controlled trials: empirical evidence from Cochrane meta-analyses. BMJ 2016. doi: https://doi.org/10.1136/bmj.i5826.

Walsh, D., Donnelly, S., & Rybicki, L. (2000). The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. *Supportive Care in Cancer, 8*(3), 175-179.

Wang, C. W., Chan, C. L. W., Ho, R. T., Tsang, H. W., Chan, C. H. Y., & Ng, S.M. (2013). The effect of qigong on depressive and anxiety symptoms: a systematic review and

meta-analysis of randomized controlled trials. *Evidence-Based Complementary and Alternative Medicine, 2013.* doi: http://dx.doi.org/10.1155/2013/716094.

Wang, M. (2014). Generalized Estimating Equations in Longitudinal Data Analysis: A Review and Recent Developments. *Advances in Statistics, 2014*. doi:http://dx.doi.org/10.1155/2014/303728

Wang, R., Zhu, W., Yuan, Z., Lu, H., Gao, Y., Fan, L., Wang, J., Rowland, K. M., Courneya, K. S., & Schneider, C. (2009). Effects of long-term Guo Lin Qigong practice on cancer survivors' quality of life and aerobic capacity: A preliminary report. *Medicine & Science in Sports & Exercise*, *41*(5), 111-117.

Wang, S. Y., Tsai, C. M., Chen, B. C., Lin, C. H., & Lin, C. C. (2008). Symptom clusters and relationships to symptom interference with daily life in Taiwanese lung cancer patients. *Journal of Pain and Symptom Management, 35*(3), 258-266.

Wang, Y.Y., Li, X.X., Liu, J.P., Luo, H., Ma, L.X., & Alraek, T. (2014). Traditional Chinese medicine for chronic fatigue syndrome: a systematic review of randomized clinical trials. *Complementary Therapies in Medicine, 22*(4), 826-833.

Wang, Y., & Ye, M. (2002). Analysis of psychological error factors in assessment of therapeutic effect of qigong rehabilitation in cancer patients. *Acta Universitatis Traditionis Medicalis Sinensis Pharmacologiaeque Shanghai, 16*(3), 20-22.

Wang, Y. G., & Carey, V. (2003). Working correlation structure misspecification, estimation and covariate design: implications for generalised estimating equations performance. *Biometrika, 90*(1), 29-41.

Wayne, P. M., Lee, M., Novakowski, J., Osypiuk, K., Ligibel, J., Carlson, L., & Song, R. (2017). Tai Chi and Qigong for cancer-related symptoms and quality of life: a systematic review and meta-analysis. *Journal of Cancer Survivorship, 12*(2), 256-267.

Weinfurt, K. P. (1995). Multivariate analysis of variance. In Grimm & Yarnold (Eds.), *Reading and understanding multivariate statistics* (pp. 245-276). Washington, DC, US: American Psychological Association.

Whitley, G. G. (1992). Concept analysis of anxiety. *Nursing Diagnosis, 3*(3), 107-116.

WHO. (2010). World health statistics 2010. Retrieved from https://www.who.int/whosis/whostat/EN_WHS10_Full.pdf?ua=1

Williams, A. C., Grant, M., Tiep, B., Kim, J. Y., & Hayter, J. (2012). Dyspnea Management in Early-Stage Lung Cancer. *Journal of Hospice & Palliative Nursing, 14*(5), 332-340.

Winningham, M. (1995). Fatigue: The missing link to quality of life. *Quality of Life-A Nursing Challenge, 4*, 2-7.

Xará, S., Amaral, T. F., & Parente, B. (2011). Undernutrition and quality of life in non small cell lung cancer patients. *Revista Portuguesa de Pneumologia (English Edition), 17*(4), 153-158.

Xiao, C. (2010). The state of science in the study of cancer symptom clusters. *European Journal of Oncology Nursing, 14*, 417-434.

Yeh, M.L., & Chung, Y.C. (2016). A randomized controlled trial of qigong on fatigue and sleep quality for Non-Hodgkin's lymphoma patients undergoing chemotherapy. *European Journal of Oncology Nursing, 23*, 81-86.

Yellen, S. B., Cella, D. F., Webster, K., Blendowski, C., & Kaplan, E. (1997). Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *Journal of Pain and Symptom Management, 13*(2), 63-74.

Yorke, J., Brettle, A., & Molassiotis, A. (2012). Nonpharmacological interventions for managing respiratory symptoms in lung cancer. *Chronic Respiratory Disease, 9*(2), 117-129.

Yorke, J., Lloyd, M., Smith, J., Blackhall, F., Harle, A., Warden, J., Ellis, J., Pilling, M., Haines, J., Luker, K., & Alex, M. (2015). Management of the respiratory distress symptom cluster in lung cancer: a randomized controlled feasibility trial. *Supportive Care in Cancer, 23*(11), 3373-3384.

Yost, K. J., & Eton, D. T. (2005). Combining distribution-and anchor-based approaches to determine minimally important differences: the FACIT experience. *Evaluation & The Health Professions, 28*(2), 172-191.

Young, E. C., Brammer, C., Owen, E., Brown, N., Lowe, J., Johnson, C., Calam, R., Jones, S., Woodcock, A., & Smith, J. A. (2009). The effect of mindfulness meditation on cough reflex sensitivity. *Thorax, 64*(11), 993-998.

Zeng, Y., et al. (2014). Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses. *Complementary Therapies in Medicine, 22*, 173-186.

Zhang, L.L., Wang, S.Z., Chen, H.L., & Yuan, A.Z. (2016). Tai Chi Exercise for Cancer-Related Fatigue in Patients with Lung Cancer Undergoing Chemotherapy: A Randomized Controlled Trial. *Journal of Pain and Symptom Management, 51*(3), 504-511.

Zhao, I., & Yates, P. (2008). Non-pharmacological interventions for breathlessness management in patients with lung cancer: a systematic review. *Palliative Medicine, 22*(6), 693-701.

Appendices

Appendix 1: Outline and Timelines of the Assessments

Item	Before Randomisation	Intervention period (1-6 weeks after randomisation)	Follow-up at
	-2 to -1 week (T0)	6 weeks (T1)	12 weeks (T2)
Eligible assessment			
Performance status	X		
Inclusion criteria	X		
Exclusion criteria	X		
Baseline measurement	X		
Primary outcomes			
Dypsnea	X	X	X
Fatigue	X	X	X
Anxiety	X	X	X
Secondary outcomes			
Quality of life	X	X	X
Cough	X	X	X

The 'X' indicates at which point of the trial the respective assessments will take place.

Appendix 2: Information Sheet for Participants

INFORMATION SHEET

To: The participants

You are cordially invited to join the research "Effect of Qigong on the symptom cluster of dyspnoea, fatigue, and anxiety in Vietnamese lung cancer patients: A randomised controlled trial". This study is designed to examine the effects of Qigong on dypsnea, fatigue, and anxiety in lung cancer patients as a symptom cluster.

Objective of the study: The primary aim of this study is to assess the effect of Qigong on managing dypsnea, fatigue, and anxiety (as a cluster) in lung cancer patients. The secondary aim of this study is exploring the effect of Qigong on cough another common symptom linked with dyspnoea and fatigue as a cluster, and QOL in lung cancer patients.

Study design: The design of this study is a randomised controlled trial with two parallel groups in a 1:1 allocation ratio with allocation concealment and assessor blinding. Eligible participants will be enrolled from National Lung Hospital and Nam Dinh general hospital will be randomised to the 6-week Qigong intervention or the 6-week wait-list control group, to examine effects of Qigong of a two weeks training followed by home-based health Qigong practice for 6 weeks in the intervention (compared to wait-list control group) on lung cancer patients.

Intervention: The intervention in this study will be based on a protocol that was enacted by Chulalongkorn University, Thailand. Subjects in the intervention group will receive a 60 minutes' Qigong training, meeting twice a week for the first 2 weeks to intensify proper learning of the Qigong intervention. Thereafter, subjects will be asked to practice at home for at least 30 min a day, 5 days per week, over 4 weeks and to keep a log of the

frequency, minutes of practice, and level of skills. The home exercises will be exactly the same as that learned in the training sessions and an instructional DVD and guidebook will also be given to subjects. Wait-list control group will receive usual care that provide by the hospitals or caregivers and will receive Qigong training after follow-up period.

Outcomes measurement: All outcomes will be measured at baseline before randomisation, at 6-week (at the end of intervention), and 12-week (after 6-week follow-up period). Data will be collected using a questionnaire, checklist through interview.

Implication of the study: It is envisaged that the results of this study may have an influence on health policy resources, health care services, education and research. The results may also be impetus for health promotion campaigns to promote new intervention in supportive care.

Right of the patients: You have every right to withdraw from the study before or during the measurement without penalty of any kind. All information related to you will remain confidential and will be identifiable by codes known only to the researcher.

Contacts information: If you have any complaints about the conduct of this research study, please do not hesitate to contact Miss Cherrie Mok, Secretary of the Human Subjects Ethics Sub-Committee of the Hong Kong Polytechnic University in person or in writing (c/o Research Office of the University), stating clearly the person and department responsible for this study. If you would like more information about this study, please contact Mr. Vu Van Dau at telephone number +84.942. or my supervisor Prof. Alex Molasiotis at telephone number (852) 2766-6396 (Office).

Thank you for your interest in participating in this study

Investigator _____

Appendix 3: Consent Form

CONSENT FOR LUNG CANCER PATIENTS PARTICIPATION IN RESEARCH

EFFECT OF QIGONG ON DYSPNOEA, FATIGUE, AND ANXIETY IN VIETNAMESE LUNG CANCER PATIENTS: A RANDOMISED CONTROLLED TRIAL

I _____ hereby consent to participate in the captioned research supervised by _____ and conducted by_____.

I understand that information obtained from this research may be used in future research and published. However, my right to privacy will be retained, i.e., my personal details will not be revealed.

The procedure as set out in the attached information sheet has been fully explained. I understand the benefits and risks involved. My participation in the project is voluntary.

I acknowledge that I have the right to question any part of the procedure and can withdraw at any time without penalty of any kind.

Name of participant _____

Signature of participant _____

Name of researcher _____

Signature of researcher _____

Date _____

Appendix 4: Request for Clearance to Central Lung Hospital' Manager

THE HONG KONG POLYTECHNIC UNIVERSITY
香港理工大學

To: The National Lung Hospital' Manager

From: VU VAN Dau, Hong Kong Polytechnic University, Hong Kong

Date: 01/12/2016

Re: **Request to conduct a study in Central Lung Cancer hospital**

I am a PhD candidate at The Hong Kong Polytechnic University in Hong Kong, pursuing a Doctor of Philosophy Degree (PhD).

I am conducting a study entitled **"EFFECT OF QIGONG ON THE SYMPTOM CLUSTERS OF DYSPNOEA, FATIGUE AND ANXIETY IN VIETNAMESE LUNG CANCER PATIENTS: A RANDOMISED CONTROLLED TRIAL"**

Therefore, I would like to request permission to conduct a study in Central Lung Hospital.

Before I commence the study, the ethical approval letters from The Hong Kong Polytechnic University and Vietnamese Ministry of Health's Sciences Research Committee will be obtained.

The study will be conducted under the supervision of Prof. Alex Molasiotis.

I will be grateful if my request meets your favorable consideration.

Yours faithfully,

Principal Investigator

Appendix 5: ECOG Performance Status (Oken, Creech, Tormey, Horton, Davis, Mcfadden, & Carbone, 1982)

These scales and criteria are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis.

Grade	ECOG
0	Asymptomatic (Fully active, able to carry on all pre-disease activities without restriction)
1	Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature. For example, light housework, office work)
2	Symptomatic, <50% in bed during the day (Ambulatory and capable of all self - care but unable to carry out any work activities. Up and about more than 50% of waking hours)
3	Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours)
4	Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair)
5	Dead

Name of participant _____

Signature of participant _____

Name of researcher _____

Signature of researcher _____

Date _____

Appendix 6: Dyspnoea, Fatigue, and Anxiety Intensity Rating Scale

The questions listed below will ask about how you are feeling at the moment. Please circle the number on the table of the questions that best shows what is happening to you at the present time.

1. How breathless do you feel?

Directions: If zero is NO shortness of breath and 10 is the WORST POSSIBLE shortness of breath, where would you place your shortness of breath right now?

No Shortness Of Breath	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst possible Shortness of Breath

2. How tired do you feel?

Directions: If zero is NO tired and 10 is the EXTREMELY tired, where would you place your shortness of breath right now?

Not at all	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Extremely tired

3. How worried do you feel about what is happening to you?

Directions: If zero is NO worried and 10 is the VERY worried, where would you place your shortness of breath right now?

Not at all	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Very worried

Name of participant _____

Signature of participant _____

Name of researcher _____

Signature of researcher _____

Date _____

Appendix 7: Demographic Characteristics Form

Date:

_____

Code number: _____ **Hospital**: _____

Age: _____ **Time from diagnosis**: ____months

Gender: Male____ Female____

Cancer type: NSLCC _____ SLCC _____

Stage: Stage I Stage II Stage III Stage IV

Treatment

Number of cycle: _____

Tumor removal surgery before: _____

Additional notes on treatments: _____

Others: _____

Education: Primary____ Secondary_____ High school___

Vocational school___ University and higher_____

Religion

Non-religion___ Buddhism_____ Christian_____ Others_____

Employment status

Current worker_____ Non-current worker_____

Marital status:

Current married_____ Divorce _____ Separate _____ Nerve married

_____

Appendix 8a. A Guide to Buddhist Qigong (Thanasilp, 2013)

Before starting, stand quietly in a loose standing posture for a few minutes, allowing your body and mind to relax. Keep your head straight as you practise the form, and your shoulders relaxed. Hand movements should be coordinated with your breathing, and both should be in a continuous, fluidic movement. Breathing is very important in Qigong: In general, breathe in for yin (inward) movements, out for yang (outward), in long, controlled breaths, and allow your breath to naturally follow the movements as they change.

Buddhist	Contents	Graphics
1. Harmonize breathing	Relaxing the mind, stand naturally with your legs shoulder width apart, drop and relax the shoulders. Keep the hips straight, and your gravity in the centre, and slowly raise the arms to shoulder height, when palms facing back then rising slowly breath in slowly. When the hand is raised to chin overturned waist. Then, while lowering	

Buddhist	Contents	Graphics
	the body and bending the knees, bring the arms down, exhaling on the downward, and inhaling on the upward. Repeat 10 times.	

Buddhist	Contents	Graphics
2. Opening the Chest	Stand naturally, with your legs straight, and raise your hands to the front of your chest. Separate your arms to your side as you open your chest and breathe in. Bring the hands back to the body in a circling motion, finishing with the hands in front of the stomach as you bend your legs and breathe out. Repeat 10 times.	

Buddhist	Contents	Graphics
3. Separating Clouds by Wheeling Arms	From a standing position, bend both knees into a horse stance. Simultaneously, place both hands in front of your body, palms towards your stomach. Raise both arms above your head and separate, breath in, as the arms come down bend the legs and straighten as they cross; the palms circle outward and upward over your head, then bring them down and around back to the front of the stomach, like the collection of energy from the sky, breath-out. Repeat 10 times.	

Buddhist	Contents	Graphics
4. Deep breathe	This position will be like the first position. But imagine the difference is keeping your feet on the ground like roots of a tree. Sucking the vitality from the ground. Focus on hand both sides. Repeat 10 times.	

Buddhist	Contents	Graphics
5. Qigong energy production	Keep your hands in front of chest put hands on opposite direction, rotate hands to focus the energy will feel pushed or hot, there is Qigong energy will feel repulsion between two hands. After practicing Qigong would observe hands will be able to feel the glare, energy has been increased. Two hands can capable cure or treatment for other people. Repeat 5 minutes.	

Buddhist	Contents	Graphics
6. Keep qigong energy	Hold the energy above the lower abdominal area in front of the umbilical. Breathing gently while relax a bit. Repeat 5 minutes.	

Buddhist	Contents	Graphics
7. Meditation	5 – 10 minutes	

Appendix 8b. Training Sessions

Session	Theme	Duration	Contents	Responsible
1	Learning the fundamental concepts of Qigong	5’	What is Qigong and briefly history, and beneficial effects	Qigong Master
	Practicing natural breathing and mindfulness	5’	Practicing natural breathing and mindfulness	Qigong Master
2	Practicing movement 1 to 4	5’	Demonstration of movement 1 to 4 by the Qigong master	Qigong Master
		5’	Practicing movement 1	Qigong Master Researcher
		5’	Practicing movement 2	
		5’	Practicing movement 3	
		5’	Practicing movement 4	
		5’	Reviewing movement 1 to 4	
		5’	Break	
3	Practicing movement 5 to 7	5’	Demonstration of movement 5 to 7 by the Qigong master	Qigong Master Researcher
		5’	Practicing movement 5	
		5’	Practicing movement 6	
		5’	Practicing movement 7	
		5’	Reviewing movement 5 to 7	
4	Reviewing movement 1 to 7	10’	Practicing and reviewing movement 1 to 7	Qigong Master
5	Learning the skills and techniques to continuing practice at home	10’	Guiding the skills and techniques to continuing practice at home	Researcher

Appendix 9: Subject's Physical Activity Log

Date _____

Name of participant _____

Day of week	Time of Day	Description of Activity (Type and Intensity Level)	Duration

Signature of participant _____

Appendix 10: The Functional Assessment of Cancer Therapy-Fatigue Subscale (FACT-F)

(Yellen, Cella, Webster, Blendowski, & Kaplan, 1997)

Please circle or mark one number per line to indicate your response as it applies to the **past 7 days**

No	Item	Not at all	A little bit	Some what	Quite a bit	Very much
1	I feel fatigued	0	1	2	3	4
2	I feel weak all over	0	1	2	3	4
3	I feel listless ("washed out")	0	1	2	3	4
4	I feel tired	0	1	2	3	4
5	I have trouble stating things because I am tired	0	1	2	3	4
6	I have trouble finishing things because I am tired	0	1	2	3	4
7	I have energy	0	1	2	3	4
8	I am able to do my usual activities	0	1	2	3	4
9	I need to sleep during the day	0	1	2	3	4
10	I am too tired to eat	0	1	2	3	4
11	I need help doing my usual activities	0	1	2	3	4
12	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
13	I have to limit my social activity because I am tired	0	1	2	3	4

Appendix 10: The Functional Assessment of Cancer Therapy-Fatigue Subscale (FACT-F)

(Yellen, Cella, Webster, Blendowski, & Kaplan, 1997) – Vietnamese

Hãy khoanh tròn hoặc đánh dấu một số trên mỗi dòng để chỉ phản ứng của bạn khi nó được áp dụng cho **7 ngày qua**

Số	Nội dung	Không	Một ít	Một Chút	Mệt Vừa	Rất mệt
1	Tôi cảm thấy mệt	0	1	2	3	4
2	Tôi cảm thấy yếu toàn bộ	0	1	2	3	4
3	Tôi cảm thấy bơ phờ	0	1	2	3	4
4	Tôi mệt	0	1	2	3	4
5	Tôi gặp khó khăn khi bắt đầu điều bởi vì tôi đã mệt mỏi	0	1	2	3	4
6	Tôi gặp khó khăn khi kết thúc mọi thứ bởi vì tôi đã mệt mỏi	0	1	2	3	4
7	Tôi có năng lượng	0	1	2	3	4
8	Tôi có thể làm các sinh hoạt bình thường của tôi	0	1	2	3	4
9	Tôi cần phải ngủ trong ngày	0	1	2	3	4
10	Tôi quá mệt mỏi để ăn	0	1	2	3	4
11	Tôi cần giúp đỡ làm các sinh hoạt bình thường của tôi	0	1	2	3	4
12	Tôi thất vọng bởi quá mệt mỏi để làm những điều tôi muốn làm	0	1	2	3	4
13	Tôi phải hạn chế hoạt động xã hội của tôi bởi vì tôi mệt mỏi	0	1	2	3	4

Appendix 10: FACT-F scoring and interpretation

Item number	Reverse Item		Item response	Item Score
1	4	-		=
2	4	-		=
3	4	-		=
4	4	-		=
5	4	-		=
6	4	-		=
7	0	+		=
8	0	+		=
9	4	-		=
10	4	-		=
11	4	-		=
12	4	-		=
13	4	-		=

Sum individual item score: _____

Multiply by 13: _____

Divide by number of items answered: _____

Appendix 11: The Cancer Dyspnoea Scale

(Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2000)

We would like to ask you about your breathlessness or difficulty in breathing. Please answer each question by circling only the numbers that best describes the breathing difficulty that you felt during the past few days. Base your response on your first impression.

No	Item	Not at all	A little	Some-what	Consid-erably	Very much
		1	2	3	4	5
1	Can you inhale easily?	1	2	3	4	5
2	Can you exhale easily?	1	2	3	4	5
3	Can you breathe slowly?	1	2	3	4	5
4	Do you feel short of breath?	1	2	3	4	5
5	Do you feel breathing difficulty accompanied by palpitations and sweating?	1	2	3	4	5
6	Do you feel as if you are panting?	1	2	3	4	5
7	Do you feel such breathing difficulty that you don't know what to do about it?	1	2	3	4	5
8	Do you feel your breath is shallow?	1	2	3	4	5
9	Do you feel your breathing may stop?	1	2	3	4	5
10	Do you feel your airway has become narrower?	1	2	3	4	5
11	Do you feel as if you are drowning?	1	2	3	4	5
12	Do you feel as if something is stuck in your airway?	1	2	3	4	5

Appendix 11: The Cancer Dyspnoea Scale - Vietnamese

(Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2000)

Chúng tôi muốn hỏi bạn về khó thở hoặc khó khăn của bạn trong khi thở. Hãy trả lời từng câu hỏi bằng cách khoanh tròn những con số mô tả tốt nhất cách khó thở mà bạn cảm thấy trong vài ngày qua. Căn cứ trả lời của bạn về ấn tượng đầu tiên của bạn.

No	Item	Khôn khó thở	Hơi khó thở	Khỏ thở nhẹ	Khó thở nặng	Rát khó thở
1	Bạn có thể hít vào một cách dễ dàng?	1	2	3	4	5
2	Bạn có thể thở ra một cách dễ dàng?	1	2	3	4	5
3	Bạn có thể hít thở chậm?	1	2	3	4	5
4	Bạn có cảm thấy khó thở?	1	2	3	4	5
5	Bạn có cảm thấy khó thở kèm theo đánh trống ngực và đổ mồ hôi?	1	2	3	4	5
6	Bạn có cảm thấy như thể bạn đang thở hổn hển?	1	2	3	4	5
7	Bạn có cảm thấy khó thở như vậy mà bạn không biết phải làm gì về nó?	1	2	3	4	5
8	Bạn có cảm thấy hơi thở của bạn là nông cạn?	1	2	3	4	5
9	Bạn có cảm thấy hơi thở của bạn có thể dừng lại?	1	2	3	4	5
10	Bạn có cảm thấy đường thở của bạn đã trở nên hẹp?	1	2	3	4	5
11	Bạn có cảm thấy như thể bạn đang chết đuối?	1	2	3	4	5
12	Bạn có cảm thấy như thể một cái gì đó là bị mắc kẹt trong đường thở của bạn?	1	2	3	4	5

Appendix 12: DASS21 (Anxiety)

Please read each statement and circle a number 0, 1, 2 or 3 that indicates how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

No	**During the past week**	Not at all	A Little	Quite a Bit	Very much
		0	1	2	3
1	I was aware of dryness of my mouth	0	1	2	3
2	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
3	I experienced trembling (eg, in the hands)	0	1	2	3
4	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
5	I felt I was close to panic	0	1	2	3
6	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
7	I felt scared without any good reason	0	1	2	3

Appendix 12: DASS21 - Vietnamese

Vui lòng đọc mỗi câu và khoanh tròn một con số 0, 1, 2 hoặc 3 cho biết có bao nhiêu lựa chọn áp dụng cho bạn trong tuần qua. Không có câu trả lời đúng hay sai. Đừng dành quá nhiều thời gian vào bất kỳ nội dung nào.

Số	**During the past week**	Không	Một ít	Vừa phải	Rất nhiều
		0	1	2	3
1	Tôi đã cảm thấy khô miệng	0	1	2	3
2	Tôi có thấy khó thở (ví dụ, thở nhanh quá mức, khó thở, trong trường hợp không gắng sức)	0	1	2	3
3	Tôi thấy có run rẩy (chân, trong tay)	0	1	2	3
4	Tôi đã lo lắng về những tình huống mà trong đó tôi có thể hoảng sợ và cư sử như một thằng ngốc	0	1	2	3
5	Tôi cảm thấy tôi đã gần hoảng sợ	0	1	2	3
6	Tôi đã cảm nhận được hoạt động của trái tim tôi trong trường hợp không gắng sức (ví dụ, ý nghĩa của việc tăng nhịp tim, tim mất một nhịp)	0	1	2	3
7	Tôi cảm thấy sợ hãi mà không cần bất kỳ lý do cụ thể	0	1	2	3

Appendix 13: Manchester Cough in Lung Cancer Scale (Molassiotis et al., 2012)

This questionnaire asks you to describe your experience of cough in the past week.

Please answer question one and then read the instructions before completing the rest of the questionnaire

	Never	Some of the time	Often	Most of the time	All of the time
1. In the past week how often have you coughed?	1	2	3	4	5

If you answered "Never" to question 1, please stop completing the questionnaire and return it to us.

If you indicated that you have experienced cough in the past week, then please complete the rest of the questionnaire.

For each question, please circle one option that best describes your experience <u>over the past week</u>.

	Never	Some of the time	Often	Most of the time	All of the time
2. Do you have difficulty breathing when you cough?	1	2	3	4	5
3. Do you have difficulty bringing up sputum (phlegm) when you cough?	1	2	3	4	5
4. Does your cough disturb your sleep?	1	2	3	4	5
5. Does your cough distress you?	1	2	3	4	5
6. Does coughing make you frustrated?	1	2	3	4	5
7. Do you worry that your cough means that your condition is getting worse?	1	2	3	4	5
8. Do you feel in control of your cough?	1	2	3	4	5
9. Does coughing interrupt your conversations or telephone calls?	1	2	3	4	5
In question 10, you should indicate how severe your cough has been in the past week.					
	Very Mild	Mild	Moderate	Severe	Very Severe
10. Please rate how severe you think your cough is.	1	2	3	4	5

Appendix 13: Manchester Cough in Lung Cancer Scale - Vietnamese

Bảng câu hỏi này yêu cầu bạn mô tả kinh nghiệm của bạn ho trong tuần qua.

Hãy trả lời một câu hỏi và sau đó đọc các hướng dẫn trước khi hoàn tất phần còn lại của câu hỏi

	Chưa bao giờ	Thỉnh thoảng	Thường xuyên	Đa số thời gian	Tất cả
1. Trong tuần qua bạn thường có ho như thế nào?	1	2	3	4	5

Nếu bạn trả lời "Không bao giờ" cho câu hỏi 1, hãy dừng lại hoàn thành bảng câu hỏi và gửi lại cho chúng tôi.

Nếu bạn cho rằng bạn đã có kinh nghiệm ho trong tuần qua, sau đó xin vui lòng hoàn thành phần còn lại của câu hỏi.

Đối với mỗi câu hỏi, hãy khoanh tròn một lựa chọn phù hợp nhất với kinh nghiệm của bạn trong tuần qua.

	Chưa bao giờ	Thỉnh thoảng	Thường xuyên	Đa số thời gian	Tất cả
2. Bạn có khó thở khi ho?	1	2	3	4	5
3. Bạn có gặp khó khăn trong việc đưa đờm ra (dịch nhờn) khi ho?	1	2	3	4	5
4. Ho có ảnh hưởng đến giấc ngủ của bạn?	1	2	3	4	5
5. Liệu ho có làm bạn khó chịu?	1	2	3	4	5
6. Ho có làm bạn thất vọng?	1	2	3	4	5
7. Bạn lo lắng rằng bạn ho có nghĩa là tình trạng bệnh của bạn đang tồi tệ hơn?	1	2	3	4	5
8. Bạn có cảm thấy bạn có thể kiểm soát ho của bạn?	1	2	3	4	5
9. Ho có ngắt cuộc nói chuyện của bạn hoặc khi bạn gọi điện thoại?	1	2	3	4	5
Trong câu hỏi 10, bạn nên chỉ ra mức độ nghiêm trọng ho của bạn đã được trong tuần qua.					
	rất nhẹ	Nhẹ	Trung bình	Nặng	Rất nặng
10. Vui lòng đánh giá mức độ nghiêm trọng của ho mà bạn nghĩ là	1	2	3	4	5

Appendix 14: EORTC QLQ-C30

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

No	**During the past week**	**Not at all**	**A Little**	**Quite a Bit**	**Very much**
		1	2	3	4
1	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2	Do you have any trouble taking a long walk?	1	2	3	4
3	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4	Do you need to stay in bed or a chair during the day?	1	2	3	4
5	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
	During the past week:	**Not at all**	**A Little**	**Quite a Bit**	**Very much**
6	Were you limited in doing either your work or other daily activities?	1	2	3	4
7	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8	Were you short of breath?	1	2	3	4
9	Have you had pain?	1	2	3	4
10	Did you need to rest?	1	2	3	4
11	Have you had trouble sleeping?	1	2	3	4
12	Have you felt weak?	1	2	3	4
13	Have you lacked appetite?	1	2	3	4
14	Have you felt nauseated?	1	2	3	4
15	Have you vomited?	1	2	3	4

No	During the past week	Not at all	A Little	Quite a Bit	Very much
16	Have you been constipated?	1	2	3	4
17	Have you had diarrhea?	1	2	3	4
18	Were you tired?	1	2	3	4
19	Did pain interfere with your daily activities?	1	2	3	4
20	Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21	Did you feel tense?	1	2	3	4
22	Did you worry?	1	2	3	4
23	Did you feel irritable?	1	2	3	4
24	Did you feel depressed?	1	2	3	4
25	Have you had difficulty remembering things?	1	2	3	4
26	Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27	Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28	Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4
	For the following questions please circle the number between 1 and 7 that best applies to you				
29	How would you rate your overall health during the past week? 1 2 3 4 5 6 7 Very poor ... Excellent				
30	How would you rate your overall quality of life during the past week? 1 2 3 4 5 6 7 Very poor ... Excellent				

Appendix 14: EORTC QLQ-C30 – Vietnamese

Chúng tôi đang quan tâm đến một số thông tin về bạn và sức khỏe của bạn. Xin vui lòng trả lời các câu hỏi bởi chính bạn bằng cách khoanh tròn các con số thích hợp nhất đối với trường hợp của bạn. Không có câu trả lời "đúng" hay "sai". Thông tin mà bạn cung cấp sẽ được giữ kín hoàn toàn.

No	**Nội dung**	**Không có**	**Ít**	**Nhiều**	**Rất Nhiều**
		1	2	3	4
1	Bạn có thấy khó khăn khi thực hiện những công việc gắng sức, ví dụ như xách một túi đồ nặng hay một vali?	1	2	3	4
2	Bạn có thấy khó khăn khi đi bộ một khoảng dài?	1	2	3	4
3	Bạn có thấy khó khăn khi đi bộ một khoảng ngắn bên ngoài nhà mình?	1	2	3	4
4	Bạn có cần nằm nghỉ trên giường hay trên ghế suốt ngày?	1	2	3	4
5	Bạn có cần giúp đỡ khi ăn, mặc, tắm rửa hay đi vệ sinh?	1	2	3	4
	Trong tuần vừa qua:	**Không có**	**Ít**	**Nhiều**	**Rất Nhiều**
6	Bạn dã có bị hạn chế thực hiện trong việc làm của bạn hoặc trong các công việc hàng ngày khác?	1	2	3	4
7	Bạn đã có bị hạn chế trong theo đuổi các sở thích của bạn hay trong các hoạt động giải trí khác?	1	2	3	4
8	Bạn đã có bị thở nhanh không?	1	2	3	4
9	Bạn đã bị đau gì không?	1	2	3	4
10	Bạn đã cần phải nghỉ ngơi không?	1	2	3	4
11	Bạn có bị mất ngủ?	1	2	3	4

12	Bạn có cảm thấy yếu sức?	1	2	3	4
13	Bạn có bị ăn mất ngon?	1	2	3	4
14	Bạn có cảm giác buồn nôn?	1	2	3	4
15	Bạn có bị nôn?	1	2	3	4
16	Bạn có bị bón?	1	2	3	4
17	Bạn có bị tiêu chảy?	1	2	3	4
18	Bạn đã có bị mệt không?	1	2	3	4
19	Cơn đau có cản trở sinh hoạt hàng ngày của bạn?	1	2	3	4
20	Bạn đã có bị khó khăn khi tập trung vào công việc gì, như khi đọc báo hay xem truyền hình?	1	2	3	4
21	Bạn đã có cảm thấy căng thẳng?	1	2	3	4
22	Bạn đã có lo lắng?	1	2	3	4
23	Bạn đã có cảm thấy dễ bực tức?	1	2	3	4
24	Bạn đã có cảm thấy buồn chán?	1	2	3	4
25	Bạn đã gặp khó khăn khi phải nhớ lại một sự việc?	1	2	3	4
26	Tình trạng thể lực của bạn hoặc việc điều trị bệnh gây cản trở cuộc sống gia đình của bạn?	1	2	3	4
27	Tình trạng thể lực của bạn hoặc việc điều trị bệnh gây cản trở cho các hoạt động xã hội của bạn?	1	2	3	4
28	Tình trạng thể lực của bạn hoặc việc điều trị bệnh tạo ra khó khăn tài chánh của bạn?	1	2	3	4
	Đối với những câu hỏi sau, vui lòng khoanh tròn con số trong khoảng từ số 1 đến số 7 mà phù hợp nhất đối với bạn				
29	Bạn tự đánh giá như thế nào về sức khỏe tổng quát của bạn trong tuần qua? 1 2 3 4 5 6 7 Rất kém Tuyệt hảo				
30	Bạn tự đánh giá như thế nào về chất lượng cuộc sống tổng quát của bạn trong tuần qua? 1 2 3 4 5 6 7 Rất kém Tuyệt hảo				

Appendix 14: EORTC QLQ-C30 *Scoring and interpretation:* The QLQ-C30

	Scale	Number of items	Item range*	Item numbers	Function scales
Global health status/QoL	QL	2	6	29,30	
Functional scales					
Physical functioning	PF	5	3	1 to 5	F
Role functioning	RF	2	3	6,7	F
Emotional functioning	EF	4	3	21 to 24	F
Cognitive functioning	CF	2	3	20, 25	F
Social functioning	SF	2	3	26, 27	F
Symptom scales/items					
Fatigue	FA	3	3	10, 12, 18	
Nausea and vomiting	NV	2	3	14, 15	
Pain	PA	2	3	9, 19	
Dyspnoea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite lose	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhoea	DI	1	3	17	
Financial difficulties	FI	1	3	28	

* *Item ranges* is the difference between the maximum and the minimum response to individual items.

For all scales, the *Raw-Score*, RS, is the mean of components items.

$$Raw\text{-}Score = RS = (I_1 + I_2 + \ldots + I_n)/n$$

Then for Functional scales: $Score = [1 - (RS\text{-}1)/\text{range})] \times 100$

and for Symptom scales/items and Global health status/QoL:

$$Score = [(RS - 1)/\text{range}] \times 100$$

Appendix 15: Quality of Life Questionnaire - Lung Module (Bergman et al., 1994)

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

No	**During the past week**	Not at all	A Little	Quite a Bit	Very much
		1	2	3	4
31	How much did you cough?	1	2	3	4
32	Did you cough up blood?	1	2	3	4
33	Were you short of breath when you rested?	1	2	3	4
34	Were you short of breath when you walked?	1	2	3	4
35	Were you short of breath when you climbed stairs?	1	2	3	4
36	Have you had a sore mouth or tongue?	1	2	3	4
37	Have you had trouble swallowing?	1	2	3	4
38	Have you had tingling hands or feet?	1	2	3	4
39	Have you had hair loss?	1	2	3	4
40	Have you had pain in your chest?	1	2	3	4
41	Have you had pain in your arm or shoulder?	1	2	3	4
42	Have you had pain in other parts of your body? If yes, where _____	1	2	3	4
43	Did you take any medicine for pain? 1 No 2 Yes				
	If yes, how much did it help?	1	2	3	4

Appendix 15: Quality of Life Questionnaire - Lung Module - Vietnamese

Đôi khi bệnh nhân trình báo là họ có các triệu chứng hoặc vấn đề sau đây. Xin cho biết quý vị bị các triệu chứng hoặc vấn đề này đến mức nào trong tuần vừa qua. Xin trả lời bằng cách khoanh tròn số thích hợp nhất cho quý vị.

Số	**Trong tuần vừa qua**	Không có	Ít	Nhiều	Rất nhiều
		1	2	3	4
31	Quý vị ho nhiều đến mức nào?	1	2	3	4
32	Quý vị có ho ra máu không?	1	2	3	4
33	Quý vị có bị hụt hơi khi nghỉ ngơi không?	1	2	3	4
34	Quý vị có bị hụt hơi khi đi bộ không?	1	2	3	4
35	Quý vị có bị hụt hơi khi leo lên cầu thang không?	1	2	3	4
36	Quý vị có bị đau miệng hay lưỡi không?	1	2	3	4
37	Quý vị nuốt có khó khăn không?	1	2	3	4
38	Bàn tay hay chân của quý vị có lăn tăn như bị kiến bò không?	1	2	3	4
39	Quý vị có bị rụng mất tóc không?	1	2	3	4
40	Quý vị có đau trong ngực không?	1	2	3	4
41	Quý vị có đau ở cánh tay hay vai không?	1	2	3	4
42	Quý vị có đau ở những phần khác trên cơ thể không? Nếu có, ở đâu_____	1	2	3	4
43	Quý vị có dùng bất cứ loại thuốc giảm đau nào không? 1 Không 2 Có				
	Nếu có, thuốc giúp đỡ đau đến mức nào?	1	2	3	4

Appendix 15: Quality of Life Questionnaire - Lung Module Scoring and interpretation

Scale name	Scale	Number of items	Item range*	Item numbers	Function scales
Symptom scales/items					
Dyspnoea	LCDY	3	3	3, 4, 5	
Coughing	LCCO	1	3	1	
Haemoptysis	LCHA	1	3	2	
Sore mouth	LCSM	1	3	6	
Dysphagia	LCDS	1	3	7	
peripheral neuropathy	LCPN	1	3	8	
Alopecia	LCHR	1	3	9	
Pain in chest	LCPC	1	3	10	
Pain in arm or shoulder	LCPA	1	3	11	
Pain in other parts	LCPO	1	3	12	

* *Item ranges* is the difference between the maximum and the minimum response to individual items.

For all scales, the *Raw-Score*, RS, is the mean of components items.

$$Raw\text{-}Score = RS = (I_1 + I_2 + \ldots + I_n)/n$$

Then for Functional scales: $Score = [1 - (RS\text{-}1)/\text{range})] \times 100$

and for Symptom scales/items and Global health status/QoL:

$$Score = [(RS\text{ -}1)/\text{range}] \times 100$$

Appendix 16 – Timetable

- 11/2016: Confirmation of registration

- 12/ 2016: Ethical approval for the project by School of nursing

- 12/2016 – 01/2017: Preparing Instruments and Qigong books and DVD

- 01/ 2017 – 03/2017: IRB approval by two hospitals

- 3/2017: Research assistant training

- 3/2017 – 12/2017: Intervention and data collection

- 1/ 2018 – 8/2018: Data analysis and final report

- 9/2018 – 3/2019: Editing and final defend

- 1/2019 – 3/2019: Public results

- Trial registry: www.clinicaltrials.gov; Identifier: NCT02977845

Appendix 17 - Letter approved by the Research Ethics committee of the Hong Kong Polytechnic University

THE HONG KONG POLYTECHNIC UNIVERSITY
香港理工大學

To	Molasiotis Alexandros (School of Nursing)		
From	CHIEN Wai Tong, Chair, Departmental Research Committee		
Email	hschien@	Date	02-Dec-2016

Application for Ethical Review for Teaching/Research Involving Human Subjects

I write to inform you that approval has been given to your application for human subjects ethics review of the following project for a period from 23-Nov-2016 to 23-Nov-2018:

Project Title:	EFFECT OF QIGONG ON THE SYMPTOM CLUSTERS OF DYSPNEA, FATIGUE AND ANXIETY IN VIETNAMESE LUNG CANCER PATIENTS: A RANDOMIZED CONTROL TRIAL
Department:	School of Nursing
Principal Investigator:	Molasiotis Alexandros
Project Start Date:	23-Nov-2016
Reference Number:	HSEARS20161125002

You will be held responsible for the ethical approval granted for the project and the ethical conduct of the personnel involved in the project. In the case of the Co-PI, if any, has also obtained ethical approval for the project, the Co-PI will also assume the responsibility in respect of the ethical approval (in relation to the areas of expertise of respective Co-PI in accordance with the stipulations given by the approving authority).

You are responsible for informing the Human Subjects Ethics Sub-committee in advance of any changes in the proposal or procedures which may affect the validity of this ethical approval.

CHIEN Wai Tong

Chair

Departmental Research Committee

Appendix 18 - Letter approved by the Research Ethics committee of the two hospitals

BỆNH VIỆN PHỔI TRUNG ƯƠNG
HỘI ĐỒNG KHOA HỌC & ĐẠO ĐỨC

CỘNG HOÀ XÃ HỘI CHỦ NGHĨA VIỆT NAM
Độc lập-Tự do-Hạnh phúc

Hà Nội, ngày 18 tháng 4 năm 2017

BIÊN BẢN XÉT DUYỆT
ĐỀ TÀI NGHIÊN CỨU KHOA HỌC CÔNG NGHỆ CẤP CƠ SỞ

Hội đồng khoa học và Đạo đức trong nghiên cứu y sinh học, Bệnh viện Phổi Trung ương đã họp vào hồi 16 giờ 00 phút, ngày 18 tháng 4 năm 2017 với 14 thành viên trong hội đồng do PGS.TS. Nguyễn Viết Nhung làm chủ tọa cuộc họp để xét duyệt đề tài nghiên cứu khoa học cấp cơ sở.

Tên đề tài: Đánh giá tác dụng của khí công trong quản lý mệt mỏi, khó thở và lo lắng trên bệnh nhân ung thư phổi tại một số bệnh viện ở Việt Nam

Mã số: 473/2017/NCKH

Chủ nhiệm đề tài: NCS. Vũ Văn Đầu

Thành viên nghiên cứu: TS. Phạm Thị Thu Hương, BSCKII Trần Đức Khánh, CN. Hà Thị Mến, CN. Vũ Mai Lan

1. Hội đồng đã nghe. ThS. Vũ Văn Đầu .....báo cáo đề cương nghiên cứu của đề tài.

2. Các thành viên trong Hội đồng đã góp ý, nhận xét và đánh giá đề cương như sau:

* TS. Lương: vấn đề quan trọng của nghiên cứu đề có giải pháp nhẹ khi hỗ trợ tiêu chảy cho bệnh nhân ung thư phổi. Câu đánh giá tuổi thuần nhất trong đánh giá và cam thiệp ở 2 Bệnh viện khác nhau.
* TS. Công: Đặt vấn đề chưa đưa ra nêu rõ về phương pháp tập luyện khí công. Diễn đạt rõ ràng và viết hoa hơn nữa. đối biết là bộ công cụ
* TS. Hoa: Mô tả lý do chọn 2 BV, cách chọn mẫu 1:1 như thế nào.
* TS. Nhung: làm rõ cỡ mẫu trong đề, phần thiết kế nghiên cứu bổ sung nhãn và đề tài

3. Các thành viên trong Hội đồng đã bỏ phiếu đánh giá đề cương như sau:

14/14 thành viên đồng ý và yêu cầu chỉnh sửa

4. Ý kiến kết luận của Chủ tịch Hội đồng:

- Sửa tên đề tài, "kiểm soát" thay cho "quản lý", nêu rõ 2 BV
- Sửa mục tiêu cuối diễn đạt thêm mục tiêu đánh giá tiên nhỏ thì
- Cần cụ thể trong đề cương thang đo cần sử dụng VD. MRC

CHỦ TỊCH HỘI ĐỒNG KHOA HỌC VÀ ĐẠO ĐỨC

Nguyễn Viết Nhung

THƯ KÝ

Nguyễn Tuấn Anh