QUALITY OF LIFE AND ILLNESS EXPERIENCES AMONG METASTATIC BREAST CANCER WOMEN UNDERGOING CHEMOTHERAPY IN BEIJING: A MIXED METHODS STUDY

GUO YIQIANG

UNIVERSITI SAINS MALAYSIA

2017

QUALITY OF LIFE AND ILLNESS EXPERIENCES AMONG METASTATIC BREAST CANCER WOMEN UNDERGOING CHEMOTHERAPY IN BEIJING: A MIXED METHODS STUDY

by

GUO YIQIANG

Thesis submitted in fulfillment of the requirements

for the degree of

Doctor of Philosophy

JANUARY 2017

ACKNOWLEDGEMENTS

The thesis would not have been completed without the guidance, support and love from a great many of lovely and remarkable individuals. Completing this period of study has been a personal challenge. I would like to thank my supervisor, Dr. Soon Lean Keng, for her constant support, guidance and encouragement throughout this Ph.D. research process. When it comes to writing a manuscript, there is truly no greater blessing than a wise, generous and instrumental mentor. Your patience, flexibility, and wonderful advice are much appreciated. I would also like to extend my thanks to my Co-supervisor, Dr. Azlina Yusuf who has also helped me to read my thesis and manuscript as well in a seamless manner; and provide me invaluable advice. I am extremely thankful to my field supervisor, Prof. Ji Jiafu, and Prof. Li Huiping, who guided me and provided the research field.

I would like to acknowledge the Universiti Sains Malaysia (USM) for their support in providing the Graduate Research Assistant Scheme throughout my Ph.D. study. I wish to thank the administrators of USM and Breast Cancer Ward, Beijing Cancer Hospital for granting me permission to conduct my study and access to the participants. Your kind consideration had provided a great study environment.

I am grateful to all the participants in my research project. Thank you for selfless sharing the time to participate in this study. Without their cooperation, this study would not have been completed. Be thankful to say that research participants' fighting spirit and strength give me life inspiration.

Special thanks go to my parents, sister, and husband. Your unconditional love and encouragement have given me the strength to achieve anything.

TABLE OF CONTENTS

Page

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

ASCO	-	American Society of Clinical Oncology
CINV	-	Chemotherapy-induced Nausea and Vomiting
CRF	-	Cancer-related Fatigue
CT	-	Chemotherapy Treatment
EORTC	-	European Organization for Research and Treatment of Cancer
ER	-	Estrogen Receptor
G-CSF	-	Granulocyte-colony Stimulating Factor
HER	-	Human Epidermal Growth Factor Receptor
HIS	-	Hospital Information System
IARC	-	International Agency for Research on Cancer
MBC	-	Metastatic Breast Cancer
NCCN	-	National Comprehensive Cancer Network
PICC	-	Peripherally Inserted Central Catheter
PoCoG	-	Psycho-Oncology Co-operative Research Group
PR	-	Progesterone Receptor
QoL	-	Quality of Life
WHO	-	World Health Organization

KUALITI HIDUP DAN PENGALAMAN KESEJAHTERAAN KESIHATAN DALAM KALANGAN WANITA PENGHIDAP KANSER PAYUDARA METASTATIK YANG SEDANG MENJALANI KIMOTERAPI DI BEIJING: SUATU KAJIAN KAEDAH CAMPURAN

ABSTRAK

Kanser payudara metastatik (MBC) adalah satu keadaan kesihatan yang tidak boleh disembuhkan dan jangkamasa median kelangsungan hidup adalah 2 hingga 4 tahun selepas diagnosis. Penyelidikan setakat ini kurang memberi tumpuan kepada kualiti kehidupan (QoL) dan pengalaman kesejahteraan kesihatan dalam kalangan wanita China dengan MBC. Oleh itu, kajian ini bertujuan untuk meneroka QoL dan pengalaman kesejahteraan penyakit dalam kalangan wanita MBC menjalani kemoterapi di Beijing, China.

Pendekatan kaedah campuran telah digunakan dalam dua fasa, dengan kaji selidik 176 wanita MBC (kuantitatif) diikuti dengan temubual bersemuka secara mendalam dengan 20 wanita MBC (kualitatif) di Hospital Kanser Universiti Beijing. QoL diukur menggunakan *European Organization for Research and Treatment of Cancer Quality of Life Questionnaire* (EORTC QLQ-C30) dan modul spesifik payudara (QLQ-BR23) versi China. DASS-21 (Skala-21 kemurungan, kebimbangan dan tekanan) telah digunakan untuk mengukur tahap kemurungan, kebimbangan dan tekanan. Disamping itu, gaya menangani diukur menggunakan *Brief COPE* versi China. Menggunakan kaedah persampelan bertujuan, 36 temubual separa berstruktur yang melibatkan 20 wanita MBC telah dijalankan bagi meneroka penceritaan QoL berkenaan pengalaman kesejahteraan kesihatan dan strategi menangani. Analisis diskriptif, kolerasi dan regresi linear umum (GLR) untuk data kuantitatif dan analisis tematik (perbandingan konstan) digunakan untuk data kualitatif.

Dapatan kuantitatif menunjukkan bahawa 63.6% daripada wanita MBC mempunyai QoL yang rendah (≤50), 52.3% mengalami kemurungan, 60.2% mempunyai kebimbangan dan 36.9% mengalami tekanan. GLR mendedahkan bahawa penjangka QoL adalah umur (p=0.003), status perkahwinan (p=0.028), pendapatan bulanan (p=0.020), kefungsian fizikal (p=0.0006), kefungsian emosi (p=0.037), sakit (p=0.028), dyspnea (p=0.028) dan kehilangan selera makan (p<0.001). Kesemua lapan penjangka ini menjelaskan 43.7% daripada QoL global. Penjangka untuk kemurungan adalah kualiti perkahwinan yang teruk, pengekspresian perasaan, menyalahkan diri sendiri dan pengunduran tingkahlaku. Disamping itu, reframing positif berkadaran negatif dengan kemurungan. Kesemua varian yang menentukan kemurungan (R^2) adalah 35.6%. Status perkahwinan, menyalahkan diri sendiri dan pengunduran tingkahlaku adalah penjangka kebimbangan dan menjelaskan 25.2% kepada kebimbangan dalam kalangan wanita MBC. Kualiti perkahwinan yang teruk, menyalahkan diri sendiri, penafian dan pengunduran tingkahlaku adalah penjangka tekanan dan semua penjangka tersebut menyumbang kepada 35.4% varian tekanan. Tiga tema muncul daripada data kualitatif: kehidupan dengan ketidakpastian kesejahteraan/kesihatan, pengalaman peralihan kesejahteraan/kesihatan dan strategi menangani kesejahteraan kepada kesihatan.

Dapatan kajian ini menunjukkan bahawa kesejahteraan fizikal dan psikologi memberi kesan kepada QoL, kemurungan, tekanan, kebimbangan dan gaya menangani dalam kalangan wanita China dengan MBC. Oleh itu, terdapat keperluan untuk professional penjagaan kesihatan dan penggubal polisi kesihatan untuk merancang program dan intervensi sokongan yang sesuai bagi mengurangkan symptom dan meningkatkan QoL wanita MBC.

QUALITY OF LIFE AND ILLNESS EXPERIENCES AMONG METASTATIC BREAST CANCER WOMEN UNDERGOING CHEMOTHERAPY IN BEIJING: A MIXED METHODS STUDY

ABSTRACT

Metastatic breast cancer (MBC) is an incurable illness with a median survival time ranging between 2 to 4 years following diagnosis. Research to date has limited focused on Chinese MBC women's quality of life (QoL) and illness experiences. Thus, this study aimed to explore QoL and disease experience among MBC women undergoing chemotherapy in Beijing, China.

A mixed methods approach was employed in two phases, with a survey of 176 MBC women (quantitative) followed by in-depth face-to-face interviews with 20 MBC women (qualitative) at Beijing University Cancer Hospital. QoL was measured using the Chinese version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and its breast-specific module (QLQ-BR23). The DASS-21 (Depression, Anxiety, and Stress Scale-21) was used to measure the degree of depression, anxiety, and stress, whilst the coping styles were measured using the Chinese version of Brief COPE. Using purposive sampling, 36 semi-structured interviews involving 20 MBC women were conducted to explore QoL narration of illness experiences and coping strategies. Descriptive, correlation, and general linear regression (GLR) analyses of quantitative data and thematic analysis (constant comparative) of qualitative data generated the findings.

Quantitative findings indicated that 63.6% of MBC women have low QoL (≤50), 52.3% have depression, 60.2% have anxiety and 36.9% have stress. GLR

revealed that predictors of QoL including age (p=0.003), marital status (p=0.028), monthly income (p=0.020), physical functioning (p=0.006) and emotional functioning (p=0.037), pain (p=0.028), dyspnea (p=0.028) and appetite loss (p<0.001). All these eight predictors explained 43.7% of the global QoL. Predictors of depression include poor marriage quality, venting, self-blame and behavioral disengagement. Also, depression was negatively associated with positive reframing. All the variances determined the depression (R^2) were 35.6%. Marital status, self-blame and behavioral disengagement were the predictors of anxiety and explained 25.2% variance of anxiety in MBC women. Poor marriage quality, self-blame, denial and behavioral disengagement were the predictors of stress; all those predictors accounted for 35.4% variance of stress. Three themes emerged from the qualitative data: “living with illness/wellness uncertainty”, “illness/wellness transition experience” and ‘illness to wellness coping strategies”.

This study suggests that physical and psychological wellbeing have an impact on the QoL, depression, stress, anxiety and coping among Chinese MBC women. Thus, there is a need for healthcare professionals and healthcare policy makers to plan for the appropriate supportive program and interventions to alleviate symptoms and improve QoL for MBC women.

CHAPTER ONE

INTRODUCTION

1.1 Introduction

Metastatic breast cancer (MBC) represents a significant public health burden across the globe. Living with MBC can be frightening as this disease is the most advanced stage of breast cancer (BC). According to International Agency for Research on Cancer (IARC), new cases of diagnosed BC were estimated 1.67 million in 2012 worldwide (Ferlay *et al.*, 2015). Between the year 2008 and 2012, the rate of new BC cases increased while mortality remained relatively stable based on Global Burden of Cancer Study (GLOBOCAN) data from more than 180 countries (Ferlay *et al.*, 2010; Ferlay *et al.*, 2015). Nevertheless, as country-specific trends differ widely and may vary from global trends, it should be acknowledged that there are wide differences in both incidence and mortality rates (DeSantis *et al.*, 2015; Ferlay *et al.*, 2015). Furthermore, as reported by the Global Status of Metastatic Breast Cancer Decade Report 2005 to 2015, there is no cure for MBC (Cardoso *et al.*, 2014). The report highlighted that there would be an increase of 43 percent in BC associated deaths across the globe from the year 2015 to 2030, of which the majority are a consequence of metastatic disease (Breast Cancer Vision, 2016).

China, recognized as one of the biggest less-developed countries, has an immense cancer problem with BC incidence increased by 80% in young women in the past two decades (Zhang *et al.*, 2010) and the primary type of cancer detected in females (Wang *et al.*, 2012b). Besides, the disease accounts for 15% among all kinds

of cancer in female (Chen *et al.*, 2016). In China, 169,000 new cases of BC were diagnosed in 2008. As reported by Zheng *et al*. (2013), BC was higher in an urban area and since 1973, the death rate from BC has unceasingly increased in China (Zheng *et al.*, 2011). According to Linos *et al.* (2008), the upsurge of BC is pervasive throughout China while the trend in BC incidence and the mortality rate is likely to increase. The population at risk for BC was those women aged 40 to 70 (Zhang *et al.*, 2012).

According to Chen *et al.* (2016) review covering women's issues changing women's live on BC in China concluded that detection, diagnosis, and treatment of breast cancer urgently need improvement. Misdiagnosis, long wait times, drastic surgeries, excessive chemotherapy (CT) and, perhaps most significant, catastrophic expense had led many of Chinese women to avoid detection in the first place, often seeing it as little more than a death sentence. Despite the high incidence of BC reported, there is a lack of significance in diagnosis and detection of BC in its early stages. According to Alsop *et al.* (2012), in Western countries, there were many resources made available for patient education, awareness of BC detection and therapeutic options. Contra to Western countries, a big proportion of BC women in China are diagnosed with Stage III/IV disease (Chen *et al.*, 2016). Apart from the stage IV BC as the first diagnosis, more than 30% of BC women who are in early stage of BC will ultimately progress to metastatic disease (Lu *et al.*, 2009; Redig and McAllister, 2013). As reported, the population of MBC survivors is increasing gradually with median survival 2-3 years for MBC women (Cardoso *et al.*, 2014). In terms with Ganz and Stanton (2015), the scope is wider, and cancer patients can survive longer at least partly attributable to the accessibility of effective target therapy, complementary and alternative medicine at an early stage.

This thesis describes and explains the Chinese MBC women's quality of life (QoL) and illness experiences undergoing chemotherapy (CT) at the Beijing Cancer Hospital, China. This present study reports a gap in knowledge about what QoL and its relationship with illness experiences for Chinese MBC women undergoing CT in China. Presently, no crucial evidence is made available in this particular study. Despite developments in the medical and clinical management of MBC, there is a dearth of knowledge and information about the QoL and illness experiences among MBC women in China. Furthermore, MBC women who underwent CT treatment were known to have confronted element in QoL and illness experiences which contribute to the psychological distress, anxiety, stress, and coping (Saniah and Zainal, 2010; Reed *et al.*, 2012). According to the researchers, women diagnosed with MBC and suffering from this illness trajectory has potential implications for health service provision and care (Saniah and Zainal, 2010; Reed *et al.*, 2012). Measuring QoL in MBC women has been the focus of the importance of which, is critical for health care practice and research study in assessing treatment outcomes. Thus, it was important to explore deeply MBC women's QoL and how the development of MBC influence their illness experiences over time.

1.2 Background of the Study

China, one of the biggest less-developed countries, has an immense cancer problem with BC incidence increased by 80% in young women in the past two decades (Zhang *et al.*, 2010) and BC account for 14.2% among all types of cancer. According to the report in the Global Cancer Statistics 2008, the most commonly diagnosed malignancy among women across the globe with incidence reaching nearly 1.38 million per year and 4.6 million mortality was BC (Ferlay *et al.*, 2010).

MBC and its treatment carry pivotal life-changing events which prompt women to adapt to it. Along with the advancements in the treatment of MBC such as target therapy, more rational and personal CT regimen, many patients were able to survive longer on an effective medicine regimen. However, some were found living with the disease trajectory along with the treatment and an inadequate response to the drug regimen. MBC women suffer from physical and psychosocial issues, which associated with the illness itself and the treatment and the uncertainty of the living in the shadow of death (Bell and Ristovski-Slijepcevic, 2011; Mosher *et al.*, 2013b). Health professionals usually focus on the physical manifestation of the illness and side effects of the treatment; however, little attention was paid on the psychological, social, and spiritual wellbeing (Kamal *et al.*, 2014).

In China, approximately 169,000 new BC cases diagnosed in 2008, and the number of mortality has increased dramatically in urban areas than in the countryside (Zheng *et al.*, 2011). Ziegler *et al.* (2008) reported that the incidence of BC in China will be 87.8 per 100,000 women by the year 2021. Their findings support the Chinese National Family Planning and Reproductive Health Survey (NFPRHS) which also found similar prevalence about the BC incidence rate in China. Coincides with NFPRHS's analysis, new cases of BC incidence will increase dramatically in urban and rural areas across China (Linos *et al.*, 2008).

According to Zhang *et al.* (2012), BC was the second cause of incidence rates among all the cancers in China, with both increasing incidences of morbidity and mortality in next two decades. They note that Chinese population at risk for BC were those women aged 40 to 70 years (Zhang *et al.*, 2012). The International Agency for Research on Cancer (IARC) indicates that the incidence of BC had been sharply

increased from 1985 to 2005 in China, and BC is the commonest among women in Beijing as shown in Figure 1.1 (International Agency for Research on Cancer, 2014).

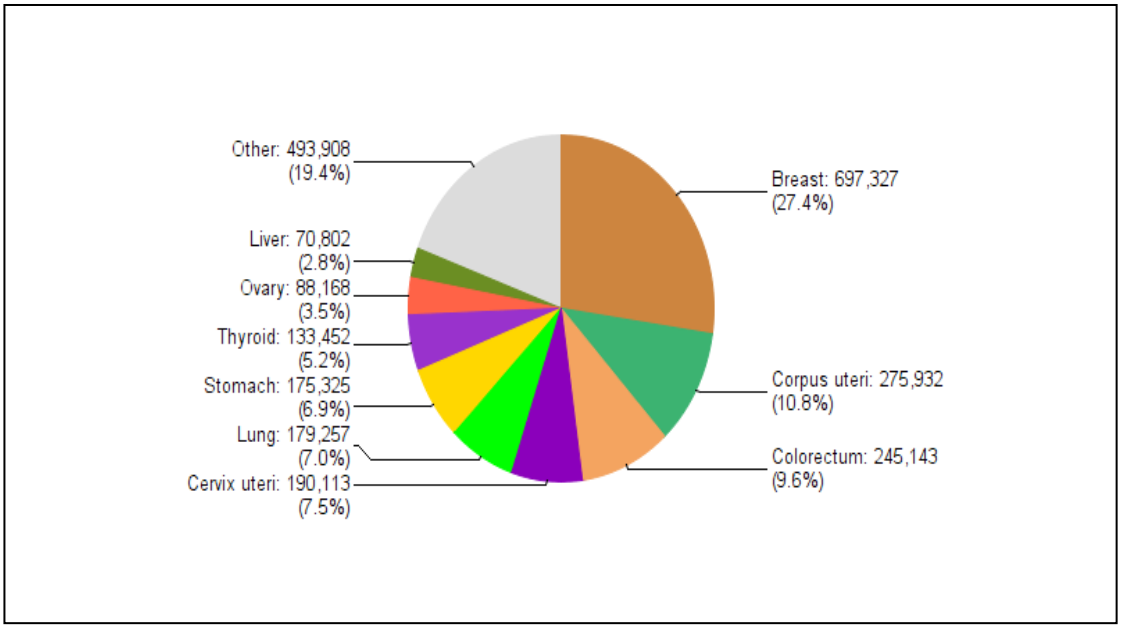

Figure 1.1 Estimated 5-year prevalence cancer cases among women in Beijing, China

[**Source**: International Agency for Research on Cancer (2014)]

There are two cancer specialized hospitals in Beijing: Beijing Cancer Hospital (also known as Peking University Cancer Hospital) and Cancer Hospital Chinese Academy of Medical Sciences. Beijing Cancer Hospital is a teaching and specialist hospital located in Beijing, China (see Figure 1.2). The hospital is affiliated with the Peking University. The hospital is a teaching and research-based hospital, and has earned a reputation as one of China's leading cancer hospitals. The hospital offered an extensive range of services for oncology patients, supported by highly qualified health care specialists. At the Beijing Cancer Hospital, research into the underlying oncologic process and clinical investigation on specific cancer disease go hand in hand, and the hospital is at the forefront of biomedical research, driving the

discoveries that lead to new ways to prevent and treat cancer (Record Statistic Beijing Cancer Hospital, 2012 – 2013, China). Beijing Cancer Hospital was selected as the choice of study setting in this study because of the hospital recognition as a major referral hospital with 790 beds and an annual admission of approximately 1,400 BC patients for medical and surgical management; including palliative care. In addition, the hospital is a renowned cancer center in China devoted exclusively to cancer care, cancer education, and cancer research and cancer prevention.

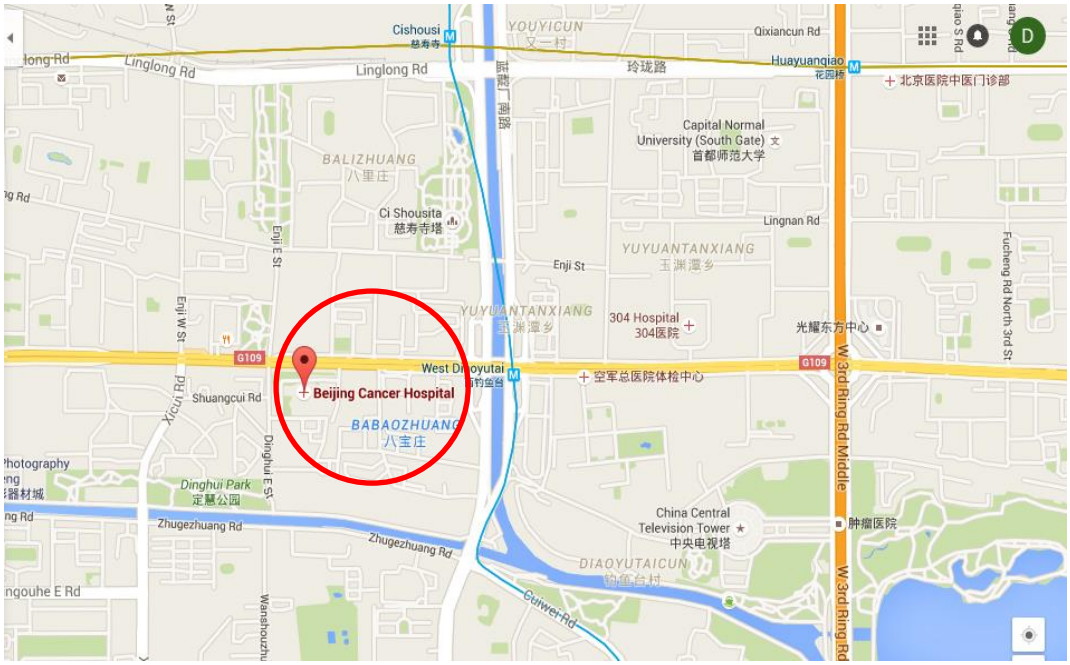

Figure 1.2 Beijing Cancer Hospital, China

(Source: Google map)

Living with MBC can be devastating. The adverse psychological impact of BC is often associated with poor QoL (Montazeri, 2008; Al-Azri *et al.*, 2009; Hopwood *et al.*, 2010; Gaston-Johansson *et al.*, 2013). With the increasing number of BC patients, the survivors are growing. Younger BC women undergoing CT were significantly associated with poorer QoL (Ganz *et al.*, 2003). It was also indicated

that BC women under CT experiences increased psychological disease and little QoL (Schreier and Willians, 2004; So *et al.*, 2010; Liu *et al.*, 2013).

The Psycho-Oncology Co-operative Research Group (PoCoG) in Australia reported that CT can affect patient's QoL in a range of ways such as lessening symptoms, halting or reversing deteriorations in functioning through treatment (PoCoG, 2015). BC patients appear to experience problems in multiple QoL domains following the CT treatment.

Assessment of a patient's QoL is now conceptually viewed as necessary, evidence had shown that CT can be offered to sustain survivorship and QoL. In a review of QoL studies among BC survivors, researchers indicated a need to explore BC patients' QoL associated with treatment modalities. However, only a few studies have examined the association between socio-demographic, the effects of psychosocial factors on QoL and MBC women survivors undergoing CT in China despite routine QoL assessments is recommended in clinical practice (Valderas *et al.*, 2008; Engelen *et al.*, 2012). Furthermore, there is a dearth of studies using the mixed method approach to explore the QoL and illness experiences of Chinese MBC women undergoing chemotherapy in Beijing, China.

1.3 Rationale for the Study

The experience of living with MBC exposes patients to a wide variety of physical, psychological, social and spiritual issues. MBC patients are facing numerous challenges, including QoL concerns derive from the disease and treatment-related side effects. Many of them are experiencing an enhanced awareness of life's brevity; and many of them are prone to have emotional distress, such as symptoms of stress, anxiety, depression and fear of death (Mosher *et al.*, 2013b).

Studies show that younger age, a dearth of social support for example poor financial situation, is associated with greater anxiety level and depression; including poor QoL in cancer patients (Shen *et al.*, 2012; Panjari *et al.*, 2014). The adverse effects of treatment-related symptoms and CT treatment have been linked with QoL (Safaee *et al.*, 2008; Takahashi *et al.*, 2008). Measuring QoL in MBC patients is essential to explore CT treatment outcomes. MBC women who are maladaptive of the diagnosis, treatments, and prognosis may suffer from psychological distress, which predicts poor QoL. It is important to understand how MBC women view their illness and lives, their QoL, illness experiences, and coping strategies. However, many researchers have tried to know MBC patients' emotional response, coping strategies and their QoL predominantly in Western countries. In spite of human are equal; in every culture, a particular set of virtues prized above all others; and this is the case when one compares the East and the West. Cultural differences between Chinese and Western culture are evident. The people of China may have a different emotional response and coping strategies in facing MBC and its treatment. Social, cultural influences on BC and health care practices were one of the bases that shape Chinese women's behavior (Shang *et al.*, 2015). Therefore it is important to conduct this research study to untapped the issue of the knowledge gap within eastern cultural context.

1.4 Problem Statement

MBC itself and the CT treatment are known to affect the QoL of cancer patients. Measuring QoL in MBC women has been the focus of research lately to assess treatment modalities outcomes due to the growing number of MBC patients in China. Also, MBC affects women's depressing, anxiety and coping and therefore studying QoL in women who either lose their lives or undergoing CT is critical. The

situation assumed that women play a major role in the family, as a mother, and or a wife. Examining QoL outcome has become an important topic in MBC care especially those that stresses on exploring MBC women's voice in their illness experiences undergoing CT treatment. The time of diagnosis and disease progression are transition periods of poor adjustment and decreased QoL in MBC patients. Knowledge about QoL and following metastasis undergoing CT may be beneficial for improving clinical care. The present study, therefore, aims to explore this by employing a mixed method research approach to investigate the MBC patients' QoL and illness experiences undergoing CT. Consequently, this led to the researcher to develop the research questions of this study.

1.5 Research Questions

Quantitative research questions:

a) What is the QoL in women diagnosed with MBC undergoing chemotherapy in Beijing Cancer Hospital, China?
b) What is the psychological distress (Depression, Anxiety, and Stress) among MBC women?
c) How do they cope with their MBC diagnosis and treatment?
d) What are the associations between socio-demographic/medical characteristics and the QoL among MBC women undergoing chemotherapy?
e) What are the associations between socio-demographic/medical characteristics and coping styles and psychological distress (depression, anxiety, and stress) of MBC women undergoing chemotherapy?

Qualitative Research Question:

a) What is the MBC women's perception of their QoL after undergoing chemotherapy?
b) How are their experiences after diagnosed with MBC and undergoing chemotherapy?
c) What coping strategies do they adopt during their illness trajectory?
d) What kind of support do they need?

1.6 Aims of the Study

This study aimed to explore QoL and illness experiences among metastatic breast cancer women undergoing chemotherapy in Beijing, China.

1.6.1 Specific Quantitative Objectives

a) To determine the quality of life (QoL), depression, anxiety, stress and coping among MBC women undergoing chemotherapy in Beijing;

b) To explore the correlation between QoL and depression, anxiety and stress;

c) To explore the correlation between coping strategies with depression, anxiety, and stress;

d) To determine the association of socio-demographic characteristics (age, marital status, level of education, working status, household income and self-evaluation of marriage quality) and medical characteristics (time since MBC

diagnosis, bone metastasis, lung metastasis, liver metastasis, brain metastasis, treatment lines, single or combine regimen and metastasis sites) with QoL;

e) To determine the association of socio-demographic characteristics, medical characteristics and coping styles with psychological distress (depression, anxiety, and stress).

1.6.2 Specific Qualitative Objectives

a) To explore the MBC Chinese women's QoL undergoing chemotherapy;

b) To explore the MBC Chinese women's illness experiences undergoing chemotherapy;

c) To explore the MBC Chinese women's support needs;

d) To explore the MBC Chinese women's coping strategies.

1.7 Research Hypotheses

H_A1: There is a significant association between socio-demographic characteristics (age, marital status, level of education, working status, household income and self-evaluation of marriage quality) and medical characteristics (duration of MBC diagnosis, bone metastasis, lung metastasis, liver metastasis, brain metastasis, treatment lines, single or combine regimen and number of metastasis sites) with QoL.

H_A2: There is a significant association between socio-demographic characteristics, medical characteristics and coping styles with depression.

H_A3: There is a significant association between socio-demographic characteristics, medical characteristics and coping styles with anxiety.

H_A4: There is a significant association between socio-demographic characteristics, medical characteristics and coping styles with stress.

1.8 Significance of Quality of Life Research in Metastatic Breast Cancer Trajectory

Studying the oncological literature review indicates that researchers have focused particular attention to QoL in the last twenty years. The majority of the researchers contemplate that QoL is an important topic of interest to study when delivering care to breast cancer patients. Considering many studies on QoL conducted with BC patients, publications in which QoL among MBC women has not rigorously measured in China. Furthermore, in Beijing, approximately 35.5 per 100,000 women suffer from BC. Also, surviving time for women with MBC has prolonged due to new and aggressive treatment modalities. The overall survival time has extended due to the medical development. The purposes of treatments for MBC women has lengthened their survival time and improve their QoL, therefore the general QoL especially more attention should pay on the psychosocial wellbeing. With aggressive therapy which may result in a longer lifespan survivorship, MBC women may experience devastating effects of CT and suffer from sequelae that affect their QoL (Khan *et al.*, 2012). Previous studies have shown that exploring QoL

provides more information about symptoms than measuring adverse events alone (Huschka *et al.*, 2007; Lemieux *et al.*, 2011).

Review of studies noted that QoL is a multifaceted and multidimensional concept, both is unique and personal (Huschka *et al.*, 2007; Lemieux *et al.*, 2011). Hence, data of QoL and illness experiences of MBC women undergoing treatment, especially for chemotherapy recipients, may provide evidence for clinical care to afford patient-centered solutions for an evidence-based selection of optimal treatment and psychosocial intervention.

1.9 Definition of Operational Terms

Following are the terms used in this study:

QoL - According to WHOQOL Group (1998), the term Qol refers to a person's perception of their status in life in the cultural context and value systems in which they live and about their goals expectations, standards, and concerns. In this study, QoL is a broad-ranging concept affected in a complex way by an individual MBC woman's independence, social relationships and their relationship to salient features of their environment.

Illness experiences - The term illness experiences refer to the ways in which people define and adjust to perceived interruptions to their health (Ritzer, 2007). In this study, illness experiences refer to the MBC Chinese women's physical well-being, psychological reaction and the way of coping.

Anxiety	-	In this study, anxiety refers to the MBC Chinese women feeling of restlessness, accompanied by dysphoria and somatic signs and symptoms of tension, focused on the apprehension of possible failure, misfortune, or danger (Colman, 2015)
Major depression	-	In this study, it refers to syndrome experience that plague MBC patients such as depressed mood and/or anhedonia accompanied by alterations in appetite, sleep, activity levels and cognitive function (Miller *et al.*, 2008).
Stress		In this study, stress is measuring a state of persistent arousal and tension with a low threshold for becoming upset or frustrated (Lovibond and Lovibond, 1995a).
Coping strategies	-	Coping strategies refer to psychological and behavioral efforts used to manage the specific external or internal demands that tax a person's resources (Lazarus, 1991). In this study, it refers to the explicit efforts, both behavioral and psychological that MBC women used to control, abide, decrease or minimize /overcome psychological distress/stressful happenings.

Body image - Body image is a person's perception of the aesthetics or sexual attractiveness of their own body. In this study, it refers to an MBC woman's perceptions, thoughts, and feelings about his or her body (Grogan, 2007).

Uncertainty - In this study, it refers to a cognitive, perceptual state that arrays from the feeling of just less than security to indistinctness; and it changes over time and accompanies by intimidating and/or positive feelings/emotions (Hilton, 1994).

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter provides the literature review about the study: Quality of life (QoL) and illness experiences among metastatic breast cancer (MBC) women undergoing chemotherapy (CT), and more specifically among Chinese MBC women at Beijing Cancer Hospital. Reviewing the literature is to gain a thorough understanding of the research topic, identify impending areas for research and knowledge gaps that demand further investigation. By undertaking a literature review, it can help the researcher to unravel scientific evidence and information to a similar study done within the area and compare previous findings, to critique existing results and suggest further studies (Aveyard, 2014). This chapter also provides a summary of the quantitative and qualitative studies to inform, enhance, extend and supplement this study. The final section of this chapter discusses the conceptual framework guiding the data extraction process.

2.2 Breast Cancer in China

Globally, BC is a major public health issue and the incidence varies between less developed and developed regions. To date, BC represents one in four of all cancers. The GLOBOCAN 2012 database revealed a sharp rise in BC cases worldwide. The GLOBOCAN declared that approximately 1.7 million women were diagnosed with BC in 2012 while 6.3 million women were diagnosed with BC in the previous five years (Ferlay *et al.*, 2015).

As published by IARC, the patterns in BC incidence highlighted an increased by 20%, while mortality were 14%. From 184 countries, women were diagnosed with BC in 140 countries across the world. The latest statistics as reported by the World Health Organization (2012) shows a global BC burden escalations to 14.1 million new cases in 2012. Contra to WHO (2012) which shows an increased in BC, Wu *et al.* (2012) study identified a lower BC incidence rates compare to Western countries. Nevertheless, their research indicates that BC incidence among women has increased dramatically in the past 20 years in China.

In China, BC was the primary type of cancer detected in females (Chen *et al.*, 2015) and expected account for approximately 15% of all types of newly diagnosed cancer among Chinese female (Chen *et al.*, 2016). According to Chen *et al.* (2016), the incidence of BC in Chinese female was 268,600 and is the fifth cause of death among Chinese female with the mortality was 69,500 in 2015.

In urbanized city China, BC is the most common cancer, and the disease is identified as the third leading cause of cancer-related mortality among women (Chen *et al.*, 2016). According to (Fan *et al.*, 2014), the burden from BC was reported to increase. About more than 1.6 million Chinese women are expected to develop BC. Along with the population, 1.2 million of Chinese BC women will have disease spread and die from MBC per year. As argued by Fan et al., a total of 12.2% were newly diagnosed BC. China's relative contribution to global rates is indicated to increase fast mainly due to the present population's rising socioeconomic status and unique reproductive patterns. Their review includes disparities between China and high-income countries. The report also includes younger age at onset of BC; the individual one-child policy; lower rates of provision and uptake for screening for

BC; delays in diagnosis that result in more advanced stage of disease at presentation; inadequate resources; and a lack of awareness about BC in the Chinese population.

2.2.1 Risk Factors for Breast Cancer

There is no exact cause of BC. However, there are many risk factors known to increase the probability of a woman developing to BC. Therefore, it is important to distinguish the risk factors of BC to provide individualized care for BC patients for example age, genetics, hormonal factors, radiation exposure, and other factors. Most women diagnosed with BC in 40 or over 40 years old, but the majority of cases occur in women over 50 years old. In China, women aged 45-59 years old are at a higher risk of BC diagnosis (Chen *et al.*, 2016). A female who has a mutation in BRCA1 or BRCA2 tumor expression genes and personal or family history of cancer are at high risk to the development of BC. An increased lifetime exposure to estrogen and progesterone as in those with early menarche or late menopause are prone to have a high risk of developing BC. Also, risk factors include nulliparity or first full-term pregnancy after 30 years old places a woman at increased risk, and oral contraceptives or hormone replacement therapy users and radiation exposure. Other factors were benign breast disease, obesity, dietary fat, alcohol consumption, and socioeconomic status are also the risk factors of BC, ethnicity is associated with BC risk (Martha *et al.*, 2007).

2.2.2 Staging of Breast Cancer

According to American Joint Committee on Cancer (AJCC), BC stage is classified based on the tumor, nodes, metastasis (TNM) as follows (Egner, 2010) (see Table 2.1):

Table 2.1 Breast cancer staging

Stage 0	Tis	N0	M0
Stage IA	T1*	N0	M0
Stage IB	T0	N1mi	M0
	T1*	N1mi	M0
Stage IIA	T0	N1**	M0
	T1*	N1**	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Notes: * T1 includes T1mi; **T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB; M0 includes M0(i+).

Sources:[https://cancerstaging.org/references pools/quickreferences/Cancer%20Staging%20poster%20Picture%20Library/BreastPoster1.jpg]

2.3 Metastatic Breast Cancer

Metastatic breast cancer (MBC) is a treatable but incurable disease, the prognosis can be highly variable and heterogeneous to an individual, and the median survival age is 2 to 3 years (Cardoso *et al.*, 2014). Apart from the stage IV breast cancer as the first diagnosis, more than 30% of BC women with an early stage of BC will ultimately develop metastatic disease (Lu *et al.*, 2009; Redig and McAllister, 2013). The treatments modalities for MBC women and their outlook varies, with some women living for years on stable medical regimens, while some live with a changing target of this deadly disease with aggressive treatments modalities and uneven response to treatment. The BC cells typically spread to bone, lung, liver and

brain. Multiple metastases are more common than the single metastasis site (Saha *et al.*, 2013).

The symptom burden of bone metastases increased. The symptom includes pain, hypercalcemia, pathologic fractures and spinal cord compression. It is striking that bone pain exists in MBC women with bone metastasis. Agents such as Bisphosphonates and Denosumab; and radiotherapy are implementing to control the disease (Rizzoli *et al.*, 2013). Utilizing the bisphosphonates contributed to better global QoL, physical, social and emotional functioning (Diel *et al.*, 2004). Bisphosphonates are widespread used among breast cancer women with bone metastasis. The side effects of bisphosphonates consist of fever, arthralgia, and gastrointestinal symptoms. Pain assessment and management among MBC women with bone metastases are necessary.

Lung metastases present symptoms encompassing pleuritic pain, dry cough, shortness of breath and exertional dyspnea. A part of women also has heaviness feeling or pain in the chest. All these symptoms caused by the metastases on lung tissue, pleural effusion or airway obstruction. And some of MBC women with early lung metastasis are surviving without obvious symptoms.

It is clear that the symptoms of liver metastases include abdominal fullness, pain, jaundice, pruritus, nausea, anorexia *et al*. Based on the specific symptom management, the administered drug were antiemetics, analgesics, and antihistamines. Obstruction of portal veins or liver failure resulting from liver metastasis could lead to ascites. It appears on some of MBC women, which may affect their QoL and leads to numerous symptoms such as abdominal distention, anorexia, nausea, vomiting, fatigue, lower extremity edema and shortness of breath (Tapping *et al.*, 2014).

Paracentesis and diuretics generally are used for mitigating the symptoms. The prognosis is poor when the ascites emerges (Stephenson and Gilbert, 2002).

It was reported that brain metastasis affects 10% to 15% of breast cancer metastasis patients (Lin *et al.*, 2013). Unfortunately, brain metastasis presents a poor prognosis. Symptoms of brain metastases include neurologic dysfunction and functional decline. Sometimes the brain metastasis affects the survivors' body controlling leading to movement imbalance (Mosher *et al.*, 2013b). A seizure happens on a small set of brain metastasis survivor (Feyer *et al.*, 2010). All these are difficult to control and can lead patients and caregivers to distress. It is necessary to palliate the headaches, nausea, vomiting, and reduce the brain swelling. Administering anticonvulsants to prevent seizure had been practiced to some extent even though the evidence is limited (Cleary *et al.*, 2013).

The treatment for MBC women is a complex and intricate result from the different metastatic sites, disease-free interval, medication taken and the pathology type. Regardless of MBC patients may have a good response to the medication effectively for a long time, it is also possible they have to move on to different regimens.

2.4 Comprehensive Cancer Care

According to the Education in Palliative and End-of-Life Care for Oncology (National Cancer Institute, 2015), comprehensive cancer care encompasses anti-cancer therapy, supportive care, palliative care and bereavement care (see Figure 2.1). Self-help, support, self-involvement, information giving, psychological support, symptom control, social support, rehabilitation, complementary therapies, spiritual support, palliative care, end-of-life and bereavement care should be involved in the

comprehensive cancer care. It is important and worthwhile to apply compassionate and palliative care for MBC women with health related problems early on.

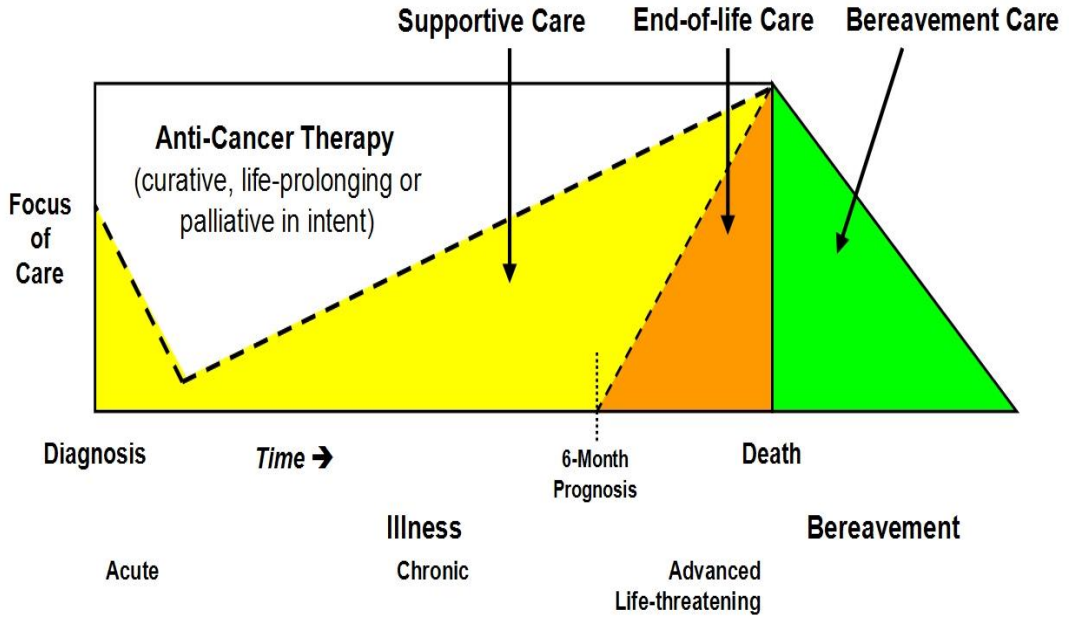

Figure 2.1 Comprehensive cancer care
Source: [http://www.cancer.gov/resources-for/hp/education/epeco/self-study/plenary-2/plenary-2.pdf]

The supportive and palliative care are indispensable parts of the comprehensive care for MBC women. There is an increasing argument that BC patients should be informed regarding support and palliative care services once a diagnosis of the advanced disease was made, or soon after the start of tumor- specific treatment (Cleary *et al.*, 2013). The definition of supportive care is care that helps the patient and their family to cope with cancer and treatment. It is from the disease diagnosis, through the process of diagnosis and treatment modalities, to cure, illness or death and into bereavement (Hui *et al.*, 2013). The implication of this supportive care is that it helps the BC patient to make the most of the benefits of treatment

modalities and to survive with the effects of the disease. Apart from that, a cancer patient was given an equal priority alongside diagnosis and treatment modalities.

Palliative care is an important approach to cancer care. This method is noted to improve the QoL among patients and their families when faced with challenges associated with life-threatening illness, prevention, and relief of suffering using early identification and impeccable assessment and treatment of physical symptoms especially pain, physical, psychosocial and spiritual wellbeing. Palliative care supports life and regards dying as a normal process. The care also offers a support system to help the family cope during the patients' illness and in their own bereavement. It was applicable in early processes of disease and in conjunction with other therapies intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications (WHO) and affordable for the MBC women at the beginning of the treatment course (Ganz and Stanton, 2015). Patients who were referred to palliative care early in the illness trajectory had better end-of-life care compared with patients with a later referral (Hui *et al.*, 2014; Zimmermann *et al.*, 2014). The integration of early palliative care and oncology care for metastatic cancer patients benefits their QoL and psychological wellbeing (Nipp *et al.*, 2016b). Decreasing aggressive medical interventions and hospital costs, reducing the inpatient admissions and increasing the satisfaction of hospital service result from the palliative care service as well (Meyers *et al.*, 2011; Parikh *et al.*, 2013; May *et al.*, 2016). Outpatient palliative care services are recommended to the gynecological cancer patients with severe symptom burden regardless of the stage or site of disease (Lefkowits *et al.*, 2014).

Approximately 40,000,000 people need palliative care every year, 78% of them are from low- and middle-income countries (WHO, 2015). The integration of supportive and palliative care for cancer patients are supported inadequately in China (Hu and Feng, 2016). In light of the findings from the Economist Intelligence Unit, China ranks 71st of 80 countries for palliative care and end-of-life health care programs. The effect of traditional view on death may be one of the reasons hinders patients to accept palliative care emotionally in China. Strong taboos against discussion of death were evidence in Chinese culture (Xiao *et al.*, 2012). One study conducted in Asia revealed that patients perceived the palliative care as death, hopeless, dependency and end of life comfort care for inpatients. The desperate feeling was engendered by receiving the palliative care among patients and their family. On the other hand, Chinese physicians provide inadequate end-of-life care may because of the undertrained palliative care education (Jiang *et al.*, 2011). The advocating and education relevant to early palliative care still need to be conducted on the public, patients and healthcare providers (Zimmermann *et al.*, 2016). Furthermore, the recommendations suggest integrating physical symptom management, pain management, administration of monitoring and documentation, psychosocial care, spiritual care for the patients. The researcher recommends that China should implement ambulatory palliative care programs for the sake of improving patients' QoL, consoling families and achieving cost-effective treatments course (Follwell *et al.*, 2009; Fan *et al.*, 2014).

2.5 Quality of life in Metastatic Breast Cancer Women

According to WHO Quality of Life (WHOQOL) group, QoL refers to an individual's perception of their position in life in the context of culture and value systems in which they live and to their goals, expectations, standards, and concerns.