# COGNITIVE CHANGES AND THEIR IMPACT ON FUNCTIONING AT WORK: A QUALITATIVE STUDY ON WOMEN WITH BREAST CANCER

# MARYAM HAFSAH BINTI MOHAMMED SELAMAT

# FACULTY OF MEDICINE UNIVERSITY OF MALAYA KUALA LUMPUR

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## MARYAM HAFSAH BINTI MOHAMMED SELAMAT

# DISSERTATION SUBMITTED IN FULFILMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICAL SCIENCE

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Name of Candidate: MARYAM HAFSAH

BINTI MOHAMMED SELAMAT

Registration/Matric No: MGN 120007

Name of Degree: MASTER OF MEDICAL SCIENCE

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#### ABSTRACT

BACKGROUND: Cancer-related cognitive impairment or chemobrain is an increasingly acknowledged after-effect of cancer treatment. It has occurred in 15 to 70 percent of patients. However, evidence of its presence is limited along with limited published articles on it. The aim of this study is to understand the phenomenon of chemobrain from qualitative perspectives. The objectives therefore are: i) to review qualitative studies that explored the lived experience of chemobrain among breast cancer survivors, with particular attention to its impact on daily living and quality of life; ii) to explore the perspectives from a) post-chemotherapy working women on the level of awareness and perceived impact of cognitive changes, and suggestions for suitable management b) health care providers (oncologists) on chemobrain issues. METHODS: This is a two-stage study to explore and to understand the phenomenon of chemobrain in cancer survivors. In stage one, a qualitative systematic review using meta-ethnography approach and conducted with selected keywords. 10 electronic databases were searched. Stage two involves a) four focus groups interview with breast cancer survivors (n = 17) and b) an in-depth interview with oncologists (n = 12). Thematic analysis and constant comparative method were used to explore the common and unique themes across participants. RESULTS: In stage one study: data was extracted from seven selected papers and concepts were analysed using a metaethnography approach. Final synthesis resulted in four new order interpretations: i) the chemobrain struggle, ii) the substantial impact of chemobrain on life domains, iii) struggling to self-manage, and iv) 'thankful yet fearful' representation. In stage two study: the focus group discussion with the survivor revealed five themes. These were: i) varying level of awareness, ii) debilitating impact on work iii) social climate at the workplace and iv) trying to self-manage. Meanwhile, the thematic analysis of in-depth interviews with the oncologists revealed three main emerging themes: i) lack of awareness ii) beliefs and attitudes on chemobrain and iii) future direction on chemobrain. DISCUSSION: Awareness of cognitive changes was context-dependent in healthcare settings and cultural contexts which appeared as strong determinants. Subjects verified the existence of chemobrain, but healthcare providers mis-recognised, under-recognised, and even negated it, perhaps due to its uncertain aetiology. Qualitative findings from the review as well as from focus groups with survivor confirmed that chemobrain brain impacted the work functioning of survivors. The lack of awareness, beliefs on the conception of the chemobrain between both patients and healthcare providers contributed to the poor acknowledgement and a lack of striving to address chemobrain in cancer survivors. CONCLUSION: The current literature on findings from the lived experiences of women's experiences of chemobrain and the indepth qualitative findings provided a consistent report that chemobrain is real and persistent with detrimental impacts on work functioning (manifested as constant struggles) and on the quality of life of breast cancer survivors.

#### ABSTRAK

LATAR BELAKANG: Salah satu kesan rawatan kanser yang semakin diberi perhatian ialah kemerosotan kognitif yang dikenali sebagai kemerosotan kognitif yang berkaitan dengan kanser atau 'chemobrain', berlaku dikalangan 15 hingga 70 peratus pesakit. Walau bagaimanapun, penerbitan artikel yang berkaitan dengan isu ini masih lagi terhad. Kajian ini bertujuan untuk memahami fenomena chemobrain dari sudut kualitatif. Oleh itu, objektif kajian ialah: i) mengulas kajian-kajian kualitatif yang meneroka pengalaman sebenar chemobrain dikalangan pesakit kanser payudara dengan perhatian kepada impak chemobrain terhadap kehidupan seharian dan kualiti hidup; ii) meneroka dari perspektif a) tahap kesedaran dan memahami impak perubahan kognitif selepas kemoterapi dikalangan wanita bekerja dan cadangan yang sesuai untuk menguruskan perubahan kognitif dan b) penjaga kesihatan (pakar onkologi) terhadap isu chemobrain. KAEDAH: Kajian ini melibatkan dua peringkat untuk meneroka dan memahami fenomena chemobrain dikalangan pesakit kanser. Pada peringkat pertama, satu kajian ulasan sistematik kualitatif yang menggunakan kaedah meta-ethnography dan menggunakan beberapa kata kunci. Sepuluh pangkalan data elektronik digunakan untuk carian. Pada peringkat kedua, a) empat kumpulan fokus bersama para pesakit kanser payudara (n=17) dan b) temu bual yang mendalam dengan pakar onkologi (n=12) telah dijalankan. Analisis tematik dan analisis perbandingan secara berterusan telah digunakan untuk mencari tema persamaan dan tema unik merentasi peserta kajian. KEPUTUSAN: Kajian peringkat pertama: data diekstrak dari tujuh kajian yang dipilih konsep-konsep telah dianalisis dengan menggunakan pendekatan metadan ethnography. Dapatan akhir sintesis menghasilkan empat peringkat interpretasi baharu: i) pergelutan *chemobrain*, ii) impak besar *chemobrain* terhadap domain hidup, iii) pergelutan untuk pengurusan diri, dan iv) menunjukkan sifat 'bersyukur dan takut'. Kajian peringkat kedua daripada perbincangan kumpulan pula menghasilkan lima tema utama: i) pelbagai tahap kesedaran, ii) impak lemah dalam pekerjaan, iii) perubahan sosial di tempat kerja, dan iv) cuba untuk menguruskan diri. Manakala, temu bual yang mendalam bersama pakar-pakar onkologi menghasil tiga tema utama: i) kurang kesedaran, ii) kepercayaan dan tingkah laku terhadap chemobrain, dan iii) hala tuju masa hadapan terhadap chemobrain. PERBINCANGAN: Kesedaran perubahan kognitif bergantung kuat dari segi konteks kawasan khidmat kesihatan dan budaya. Setiap subjek mengesahkan kewujudan *chemobrain* walaupun para penjaga kesihatan terlepas, tidak kenal pasti, dan menidakkan fenomena ini disebabkan oleh etiologi yang tidak dikenal pasti. Hasil ulasan kajian kualitatif dan juga kumpulan fokus dengan pesakit yang masih hidup mengesahkan *chemobrain* telah memberi impak terhadap kefungsian pekerjaan. Kurangnya kesedaran, kepercayaan terhadap konsep chemobrain antara para pesakit dan para perawat telah menyumbang kepada kurangnya tumpuan dalam menangani isu chemobrain. KESIMPULAN: Dapatan semasa mengenai pengalaman sebenar wanita yang mengalami chemobrain dan hasil kajian kualitatif yang mendalam telah menunjukkan laporan yang konsisten yang menunjukkan bahawa chemobrain benar-benar berlaku, berterusan dengan impak yang memudaratkan kefungsian pekerjaan (menunjukkan pergelutan yang konsisten), dan kualiti hidup dan para pesakit kanser.

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#### **CHAPTER 1: INTRODUCTION**

#### 1.1 Overview

The World Health Organization has alerted that cancer is the leading cause of death worldwide, accounting for 7.6 million deaths (around 13 percent of all deaths in 2008) (American Cancer Society, 2011). In fourteen Asian countries (Malaysia included), there were 3.6 million males and 4.0 million females living with cancer (Hertz, McDonald, & Lowenthal, 2008). Breast cancer is the second most typical cancer following lung cancer which affected both genders (Jacques Ferlay, Héry, Autier, & Sankaranarayanan, 2010) with 1.7 million women diagnosed within five years (WHO, 2013). There is a marked geographical difference in the worldwide incidence of breast cancer, with a higher incidence in developed countries compared to developing countries (Hisham & Yip, 2004). The burden of breast cancer load is increasing in the Asian region. About 82.5 percent of Southeast Asian women with breast cancer are at the early stages of breast cancer while 30.2 percent are at later, and advanced stages reported among (Bhoo Pathy et al., 2011). In Malaysia, National Cancer Registry reported, from 3242 females diagnosed with breast cancer, the highest incidence was among Chinese, where the standard age rate was 38.1 per 100,000 population, followed by Indian 33.7 per 100,000 population, and Malays were 25.4 per 100,000 populations (Zainal Arifin & Nor Saleha, 2011).

Nevertheless, the rate of women surviving breast cancer is on the rise (de Moor et al., 2013). There is an 83 percent rate for ten years of survival rate (Marin, Sanchez, Arranz, Aunon, & Baron, 2009). While 78 percent rate for 15 years of survival rate after diagnosis of breast cancer (American Cancer Society, 2013). The survival rates in the first, third and fifth year of breast cancer in Malaysia (n=13,060) was 70.8 percent, 56.9 percent, and 49.4 percent respectively, with median survival period of 68.1 months (Abdullah et al., 2013). Cancer survival rates tend to be poorer in developing countries

due to a combination of late detection, limited access and delay in receiving standard treatment (Jemal et al., 2011). Age wise, women with breast cancer aged below 50 years have shown a significantly better survival chance compared to those aged 50 years and above in Malaysia (Abdullah et al., 2013).

During survivorship, the advanced treatment regime and the aggressiveness of the intervention can affect multiple aspects of patients' functioning. In general, survivors are often affected by physical and psychosocial complications of cancer treatment. Complications from the treatment include pain, cognitive impairment, sexual dysfunction, weight problems, nausea (Ganz, Kwan, Stanton, Bower, & Belin, 2011; Schmitz, Speck, Rye, DiSipio, & Hayes, 2012), depression, anxiety and sleeping difficulty (Devi, 2013; Fiorentino, Rissling, Liu, & Ancoli-Israel, 2012; Reyes-Gibby, Anderson, Morrow, Shete, & Hassan, 2012). It has been reported that a combination of psychological and medical factors may contribute to cognitive decline, which is often associated with the adjuvant systemic therapy (Schilder et al., 2010).Current evidence suggests that combinations of drugs to treat cancer have neurotoxic effects, which have some association with diminished cognitive function (Staat & Segatore, 2005).

Cognitive impairment has been linked to post-chemotherapy symptoms in breast cancer survivors and is technically a deterioration of cognitive functioning (Dutta, 2011). It is widely known as cancer-related cognitive impairment (CRCI) or also known as *chemobrain*, that appears to occur in 10 to 40 percent of women complaining of cognitive domains deterioration (Jim et al., 2012; Matsuda et al., 2005; Wagner, Sweet, Butt, Lai, & Cella, 2009). Vardy (2008) reported that approximately a third of cancer patients experienced cognitive impairment before receiving chemotherapy. Meanwhile, possibly 20 to 30 percent (Jansen, Cooper, Dodd, & Miaskowski, 2011) have cognitive impairment after chemotherapy although the underlying mechanism was still unknown. Raffa et al. (2006) suggested that disease-related factors and patient-related factors, increase the risk of having cognitive impairment that is associated with malignancy prechemotherapy and the administration of chemotherapy. It has been hypothesized that potential mechanisms can be due to neurotoxic effects (Dutta, 2011; Staat & Segatore, 2005) such as oxidative damage, induced hormonal changes, blood clotting in a small vessel of the central nervous system (Vardy, 2008). In addition, the level of chemotherapy dose also affects the severity of cognitive changes. High-dose chemotherapy appears to impair cognitive functioning more than standard-dose chemotherapy (van Dam et al., 1998). The deterioration of cognitive function happens significantly over the course of chemo (Collins, MacKenzie, Tasca, Scherling, & Smith, 2013). In a comparative study of women with breast cancer who received adjuvant therapy and non-adjuvant therapy, women who received a combination of chemotherapy and hormonal therapy were reported to deteriorate more than women with only chemotherapy. The addition of tamoxifen may lead to more widespread memory deficits (Bender et al., 2006).

Survivors described issues with cognitive domains affect their daily functioning. The most common domains that affected are memory loss, working memory, executive function, verbal ability, visuospatial ability and processing speed (Jim et al., 2012; Vardy, Wefel, Ahles, Tannock, & Schagen, 2008). They had difficulties in word finding, reading, forgetting names or telephone numbers, difficulty with arithmetic, and to the extent of jeopardizing personal safety with driving hazards and medication mishaps (Myers, 2012; Thielen, 2008). Women showed significant decreases in their cognitive domains, particularly with visuospatial skills, attention, delayed memory, and motor function in six months post chemotherapy. Many survivors of breast cancer complained of increased difficulties with multitasking, which became more noticeable once they tried to resume their normal activities, in particular returning to work (Vardy,

2009). Breast cancer survivors had a cognitive limitation as part of the return to work problem on average three years post-treatment especially in memory and executive functioning (Calvio, Peugeot, Bruns, Todd, & Feuerstein, 2010). They displayed an abnormal pattern of sustained attention where they tend to wander away from the task and relevant information (Kam et al., 2015). These problems were more prominence for those in intellectually demanding occupations (Vardy, 2009).

#### **1.2 Background of study**

Cognitive impairment can be problematic to survivors as reported by them; it affects multiple domains in the cognitive aspect. There are several studies that report cognitive impairment in cancer patients and its relation to functional activities of daily living, Boykoff, Moieni, and Subramanian (2009) found that cognitive impairment significantly impaired a proportion of cancer survivors at great cost economically, emotionally and/or interpersonally. Mild impairments may impact survivor's ability to function both at home and work. From the insight of breast cancer survivors, the workability is determined by one's cognitive ability, awareness of cognitive failures which subsequently impact their confidence in carrying out daily tasks (Munir, Burrows, Yarker, Kalawsky, & Bains, 2010). Survivors indicating post-treatment decline reported greater difficulty in work-related activity, and they experienced either a decrease in functional ability or maintenance of functional ability levels (J S. Wefel, Witgert, & Meyers, 2008). According to Vardy and Dhillon (2010) in their commentary review, while for most people any cognitive symptoms are subtle and improve after completing treatment, for a subset of cancer survivors the impairment may be sustained and may have an impact on quality of life.

Although there is a series of studies that look into this phenomenon (Boykoff et al., 2009; Mitchell & Turton, 2011; Vardy, 2009), only a few studies focus on Asian

population, while none has focused on the Malaysian context. Some researchers have focused on the quantitative research instead of qualitative research. However, these women's experiences in cognitive impairment could be better studied qualitatively. Some of the reasons are detailed below.

The extensiveness of the burden of cognitive impairment has never been explored in Malaysian context yet. Thus, there is a need to understand Malaysians' reaction towards this issue, in particular, the subjective viewpoints on the term 'chemobrain' and its symptoms, consequences etc. There is also a general lack of attention on this issue from both medical team and patients, requiring an in-depth exploration of their perceptions. In addition, general lacks of support available for working breast cancer women persist and their qualitative feedback has yet to be explored and understood. Also, no study has highlighted the subjective views from the perspectives of health care providers in the Malaysian context. Therefore, a qualitative study is an appropriate design as it helps to illuminate the missing gaps. It is a key of interest to understand the phenomenon in greater depth from the both perspectives of breast cancer survivors and healthcare providers. Thus, to adequately answer these entire question, a systematic review and a qualitative study on i) breast cancer survivors and ii)oncologists was conducted to gain understanding about the awareness of cognitive impairment the perception of health care providers (i.e oncologists) and survivors in Malaysia regarding this issue.

#### **1.3** Research questions

This two-stage study was designed to answer the key research question:

What is the current literature, level of awareness, perception on cancer-relatedcognitive-impairment among breast cancer survivors and health care provider (oncologist) and, the self-management strategies utilised in relation to work functioning?

#### 1.4 Aim and Objectives

In order to answer the research question above, the study was designed in two phases. The phase one study aim to understand the phenomenon of cancer-related cognitive impairment or chemobrain from a qualitative systematic review of the qualitative literature. The phase two study aim to explore in-depth qualitative studies with two groups of stakeholder (breast cancer survivors and oncologists). Therefore, the objectives were:

- 1. To systematically review the current qualitative literature on the living experience of chemobrain among breast cancer survivors, with particular attention to its impact on daily living and quality of life.
- 2. To explore the qualitative live experience on the level of awareness of cancerrelated cognitive impairment, the impact of cancer-related cognitive impairment among employed breast cancer survivors, self-management strategies used at the workplace and the perspectives of health care providers (Oncologists) on cancerrelated cognitive impairment issue.

#### 1.5 Significance of study

This study is significant for several reasons:

Firstly, the study focuses on women with breast cancer, which is the most common cancer and leading cause of mortality among women worldwide (Jemal et al., 2011) with the highest incidence in seven countries in Asian (Japan, Indonesia, Malaysia, Philippines, Singapore, Taiwan and Sri Lanka) (Bhoo Pathy et al., 2011; Hertz et al., 2008).

Secondly, cancer survivorship is an emerging field, with a steep increase in numbers due to better chemotherapeutic regimens and better interdisciplinary collaborative care approaches (Marin et al., 2009; Meade & Dowling, 2012). Functioning and quality of life are becoming increasingly important as more people are living with it. The shift from the narrow symptom-based study into participation and occupation (self-managing of chores and roles) is in line with the unique field of occupational therapy.

Thirdly, the existence of a cancer-related cognitive impairment is now more universally acknowledged (Taillibert, 2010), despite the fact that there are still many grey areas on who, what and why it occurred. There is thus, a need for Clinical Practice Guidelines for therapists to enable the therapist to support patients to self-manage cognitive impairment in partnership with other health providers.

#### **1.6 Operational definition**

This study was conducted based on the definition of terminologies as follows:

Women with breast cancer: For this study, women with breast cancer refer to cancer survivors defined by National Cancer Institute as someone who remains alive and are still functioning during and after overcoming cancer from the beginning of the diagnosis until the end of their lifetime. (Institute of Medicine, 2005). To limit this study the researcher has narrowed down the selection criteria for women who have completed chemotherapy treatment after six months up to three years.

Awareness: According to the Cambridge dictionary, it refers to the knowledge or understanding that something exists, situation or subject at the presented time based on information and experiences.

**Cognitive changes:** Cognition is a complex, dynamic and organized system that allows our brain to function in the environment. It includes primary cognitive capacities (orientation, attention, and memory), higher level thinking abilities (reasoning, concept formation and problem-solving), and meta-process (executive functions and self-awareness) (Trombly & Radomski, 2002). In this study, it refers to the changes in

cognitive function from the premorbid status to the current state of cognitive impairment. Cognitive impairment is a condition where an individual has difficulty remembering, concentrating, learning new things or making decisions that affect their daily livings (Centers for Disease Control and Prevention, 2011) that might be due to receiving adjuvant chemotherapy as one of the breast cancer treatments (K.-A. Phillips & Bernhard, 2003). Another term that needs to be considered throughout this study that reflects the changes of cognitive impairment after treatment is chemobrain. American Cancer Society (2014) defined 'chemobrain' as mental fogginess or a decrease in mental 'sharpness' that occurred during cancer or cancer treatment. Other common terms used are cancer-related cognitive impairment, chemotherapy-induced cognitive impairment; cancer-therapy associated cognitive change or post-chemotherapy cognitive impairment. The term cancer-related cognitive impairment (CRCI) and chemobrain will be used throughout this study.

**Employed cancer survivor:** The term refers to female survivors who are working within three years after cancer treatment for at least one hour during the reference week for profit gain or family gain (as an employer, employee, own-account worker or unpaid housewife/family worker). The definition also goes beyond a person who did not work during the reference week due to the unfortunate event (environment or self-factor) but had a job to return to and/or temporary laid-off with pay and will return to work (Labour Force Malaysia, 2011). However, only women who have returned to work after treatment were considered for this study to focus on sharing their experiences on return to work.

**Professional Worker:** A person who is working based on tertiary education (university or postgraduate university degree, Malaysian skills advanced diploma), those with

supervisory occupations who are responsible for planning, organizing and directing work tasks in a group (MASCO, 2008).

**Non-professional Worker:** A person who is employed based on tertiary educational not equivalent to a first university level, Malaysian Skill Certificate; or secondary or post-secondary education, or primary education including technician and associate professionals, clerical support workers, services and sales worker, skilled agricultural fishery and forestry worker, craft and related trades workers as well as plant and machine operator and assembler (MASCO, 2008).

### **1.7** The organization of the thesis

This thesis was written following the conventional format. It has six chapters. In chapter one; background of the cancer-related cognitive impairment or chemobrain study was presented. Chapter two elaborates on the: literature review and the current knowledge. Meanwhile, chapter three: presents the methodology for both stages in a systematic review and in the main qualitative study to explore survivors and oncologists perspectives. Next, chapter four: presents the results of stage one and followed by stage two. Chapter five contains the discussion and details of the findings that reflect the merging of findings from both stages of the study. Finally, chapter six provides a summary of the findings with the implications and recommendations for future work.

#### 1.8 Summary

This study focuses on a qualitative review and in-depth qualitative exploration of a) the lived experiences of women with breast cancer who suffer from cancer-related cognitive impairment and b) the perception of oncologists who are the core health care provider liaising directly with them. Post-chemotherapy mild cognitive impairment is an area that still requires further investigation to address the unmet needs of the experiences and awareness of cancer-related cognitive impairment from the view of

women with breast cancer. Views from oncologists will help to bridge the gap and improve their quality of life. There is a lack of information that relates to the expression that gives meanings to human behaviours and action. Thus, qualitative research is vital to bring meaning and context to the study.

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#### **CHAPTER 2: LITERATURE REVIEW**

#### 2.1 Overview

This chapter on literature review presents the incidence of breast cancer, survivors' rates, cancer-related cognitive impairment (CRCI), its impact on daily living, functioning at work and the current clinical management and assessment in clinical practice. A literature review aimed to provide current knowledge and issue that has been highlighted and what was not known as to date.

#### 2.2 Breast cancer

#### 2.2.1 Prevalence, incidence, and mortality

According to GLOBOCAN (2012), cancer is one of the leading cause of death worldwide and is accounted for 8.2 million deaths. Generally, in the United States alone, most cancer death rates have declined 20 percent since 1991 (215.1. per 100,000 population) to 2009 (173.1 per 100,000 population) (Siegel, Naishadham, & Jemal, 2013). Four major cancers - showed a declination of death rates with 34 percent decline among women with breast cancer (Siegel, Naishadham, & Jemal, 2012). The declining of mortality rates among women with breast cancer has been observed since the early 1990s, which were influenced by state (poor areas), socioeconomic status and race or ethnicity (DeSantis, Siegel, Bandi, & Jemal, 2011).

For the last 50 years, the incidences of breast cancer were observed to have a constant rise with an estimated annual percent of change 1.03 (with 95 percent CI of 1.029, 1.031) (Mousavi-Jarrrahi et al., 2013).The breast cancer incidence rates were different across the ethnic group from 2006 to 2010; slight increase among African American women; decrease among Hispanic women; constant among whites, Asian Americans or Pacific Islanders and American Indians or Alaskan Natives (DeSantis, Ma, Bryan, & Jemal, 2014). However, in a recent study using a longitudinal approach,

the incidences rates were seen to be parallel between Asians and Western population with the rates rising until the age of 80 (Sung et al., 2015). About 55 percent of breast cancer is experienced in developed countries; yet, the incidence rates tend to be rapidly growing within developing countries (Jacques Ferlay et al., 2010). Breast Cancer incidence was predicted to rise for the next ten years among female Asian populations as it was associated with the increase of age and other risk factors as well as the screening programs (Shin et al., 2010).

In terms of the peak age onset of breast cancer, Asian countries recorded the age were between 40 to 50 years and it decreased and plateaued later, while western countries were between 60 to 70 years in the United States and 55 to 75 years in European Countries (Leong et al., 2010; Mousavi-Jarrrahi et al., 2013). In a multi-ethnic Asian study within Malaysia and Singapore, 72 percent of the women were Chinese, 16 percent Malays, 8 percent Indians, and the rest 4 percent were other races (Bhoo Pathy et al., 2011).

#### 2.2.2 Survival rate

6.3 million women with breast cancer survived in the previous five years in 2012 (WHO, 2013). In the United State alone, there are about 13.7 million cancer survivors and it is estimated to reach 18 million by 2022; 64 percent have survived 5 years or more, 40 percent within 10 years or more and 15 percent have survived 20 years and more after diagnosis (de Moor et al., 2013). The survival rate for breast cancer has been reported to be significantly different across the globe, with rates ranging from over 80 percent in North America, Sweden, Japan, Finland and Australia to 60 percent in middle-income countries (Brazil and Slovakia) and below 40 percent in low-income countries (Algeria) (Coleman et al., 2008). According to GLOBOCAN 2012, there were differences between 5 years survival rates among the more developed countries with 3.2

million women with breast cancer had survived and less developed countries with 3.0 million accounted (Jacques. Ferlay et al., 2013). The highest number of women surviving breast cancer after five-year post diagnosis was in Northern America and Europe while the lowest was in Africa and Asia (Jacques. Ferlay et al., 2013). In five years relative survival of breast cancer in relation to the stage of diagnosis, 99 percent is for localized disease, 84 percent for regional disease and 24 percent for distant-stage disease (American Cancer Society, 2013).

A study comparing presentation and outcomes of breast cancer between a middle income country (Malaysia) and a high income country (Singapore) in South East Asia indicated that the overall survival of Malaysian breast cancer patients were lower than Singapore with 60 percent more likely to die after five years of diagnosis (Saxena et al., 2012). Ethnic-wise, a Malaysian study (Abdullah et al., 2013) reported that for 5-year survival rate, the highest survival was among Indian women (54 percent), followed by Chinese (49 percent) and Malays (45 percent). Over the decades, the steep rise in cancer survivors across the globe was due to earlier detection, better chemotherapeutic regimens and multidisciplinary collaborative care approaches (Marin et al., 2009; Meade & Dowling, 2012; Siegel et al., 2013) and the rates are still rising.

#### 2.3 Breast Cancer Treatment

This section reviews the common treatment women with breast cancer have to go through, with potentially stressful moments at every stage of the treatment, and their potential consequences on cognition. Cancer treatment can prolong lives and improve survival rate among breast cancer patients. However, the advancement of treatment that prolongs the survival period has resulted in several complications on many body functions including cancer-related cognitive impairment (CRCI) (C. A. Low, Kalinski, & Bovbjerg, 2015). The cognitive changes have been acknowledged as one aspect of some of the cancer treatment complications which until today is still being debated with no effective prevention and treatment (Wang et al., 2015).

#### 2.3.1 Surgery

Women who were diagnosed with having breast cancer undergo surgery to remove the cancer cells. It is a primary treatment as one of the local region control that depends on the type of tumour, severity and stages (J. Lester, 2015) Women with breast cancer had options depending on the stages of cancer for breast conserving surgery (lumpectomy or partial mastectomy) or total removal of the breast (mastectomy) (Kummerow, Du, Penson, Shyr, & Hooks, 2015). Breast-conserving surgery involved removing some part of the breast or total mastectomy , which normally will be incorporated with other cancer treatment (eg: radiation, chemotherapy ) (Fajdic, Djurovic, Gotovac, & Hrgovic, 2013; Fisher et al., 2002; Schroeder, Lynch, Abu-Hejleh, Chrischilles, & Thomas, 2015)

Most women diagnosed with low grades tumour are potential subjects to consider breast conservation despite they need to be aware of the risk of recurrence or new cancer (Fajdic et al., 2013) especially for younger women (age less than 35 years), more than focally incomplete margins and treatment without radiotherapy (Nijenhuis & Rutgers, 2013). However, numerous studies (Fisher et al., 2002; Litière et al., 2012; Vila, Gandini, & Gentilini, 2015) have found that there are no significant differences in overall survival rate between total mastectomy and combining local excision or breast conservation surgery together with radiotherapy. Breast cancer patients experienced cognitive impairment with three to four-time risk compared to the control group after diagnosis and later after surgery (Debess, Riis, Pedersen, & Ewertz, 2009).

#### 2.3.2 Chemotherapy

Another breast cancer treatment that has been widely used since the 1950s is chemotherapy (Cardoso et al., 2002). It is used to stop the cancer cells from growing by killing or stopping the dividing process that is classified as one of the systemic treatment (Siegel, Ma, Zou, & Jemal, 2014). Based on the therapeutic goals, the administration of chemotherapy can be carried out in neoadjuvant (before surgery) to shrink the tumour, adjuvant (after surgery) to prevent possible recurrence and in palliative setting to manage the cancer-related symptoms (A. Lee & Moon, 2014). The use of chemotherapy treatment was significantly associated with age, tumour size, tumour differentiation and breast cancer subtype (Schroeder et al., 2015). Based on the independent factors that predict the use of chemotherapy, patients will receive regimens of first-line chemotherapy as a primary treatment; second line therapy if the first line treatment did not work (Younes, Pereira, Fares, & Gross, 2011) and subsequent lines if the primary and secondary line had failed. In patients with metastatic breast cancer, chemotherapy may prolong their survival (I. H. Park, Lee, & Ro, 2015; Younes et al., 2011). Agents used in chemotherapy consists of anthracyclines, taxanes, doxorubicin, paclitaxel, 5-flourouracil, epiricubin, cyclophosphamide, methotrexate and the mostly combination of these agents to improve the efficacy of the drugs used (Johnston, 2011).

Any cognitive deterioration occurring prior to chemotherapy can confound an investigation of chemobrain following chemotherapy (Biglia et al., 2012). Chemotherapy researchers are still mulling over whether it is due to the toxicity from chemotherapy agents particularly high dose treatment (Christie et al., 2012). It was reported that chemotherapy agents, administered systematically were unable to cross the brain, however, the changes in the brain structure, as well as toxicity due to the treatment was given, can cause inflammatory cytokines in peripheral tissues that may impact on the brain (Wigmore, 2013). High dose adjuvant chemotherapy has been

shown to be associated with long-term cognitive impairment (de Ruiter et al., 2011). Docetaxel has been shown to cause significant cognitive impairment in object recognition without considering the amount of dose intake after treatment. There is some evidence of a long-term effect on cognitive function after multiple doses of Docetaxel (Fardell, Vardy, & Johnston, 2013).

A study conducted by Krynetskiy et al. (2013) suggested that chemotherapy administration can damage the deoxyribonucleic acid (DNA), in rodents, where it may alter the neural cells and gene expression that leads to cognitive impairments. There was evidence of Tumour Necrosis Factor-alpha (TNF- $\alpha$ ) which may influence the manifestation of cognitive impairments in survivors. Findings of the study (Ganz, Bower, et al., 2013) showed that chemotherapy patients have a higher baseline of one of the pro-inflammatory cytokines tested, and it was connected with memory complaints and associated with diminished brain metabolism. Findings of an association between cytokines level and hippocampal volume have shown that the elevation of cytokines level and the reduced left hippocampal volume in breast cancer survivors implicated the verbal memory performance (Kesler, Janelsins, et al., 2013) that caused the memory impairment after treatment.

### 2.3.3 Radiotherapy

Radiotherapy is a local treatment that uses radiation to kill cancer cells. It can be used in initial stages, together with breast conservation (Fajdic et al., 2013); to reduce local recurrences after surgery among patients with several adverse features of increase risk of relapse. This is also used after systemic treatment if mastectomy could not be carried out and to relief cancer-related symptoms for metastatic patients (Bese et al., 2006). It can be administered through external beam radiation therapy, brachytherapy and intraoperative radiotherapy (Keshtgar et al., 2011) depending on the type and stages of breast cancer. Age, accessibility to designated centers, other comorbidities, treatment gaps, and surgical expertise also influence adherence and effectiveness of the radiotherapy treatment (Krotneva et al., 2013). After several months of exposure to adjuvant regional radiotherapy, there is tendency of breast cancer patients to develop cognitive impairment (Noal et al., 2011) which has been shown to be mediated by elevation of plasma Interleukin (IL)-6 levels (Shibayama et al., 2014). Breast cancer patients who undergone radiotherapy show significant less performance of executive functioning compared to healthy group women (K. M. Phillips et al., 2012).

#### 2.3.4 Hormonal therapy

Hormonal therapy is a systemic treatment that blocks the hormonal action by blocking the estrogen function or lowering the estrogen level. Thus, it preventing the growth of cancer cells (American Cancer Society, 2005). The options of hormonal therapy are dependent on menopausal status (De Vos et al., 2012). Premenopausal women in early stages or metastatic breast cancer would be given tamoxifen as a hormone therapy while postmenopausal women are treated with an aromatase inhibitor (Harold J. Burstein et al., 2014; De Vos et al., 2012). Tamoxifen is an anti-oestrogen that binds directly to the hormone-blocking its action can cause vaginal bleeding, uterine bleeding, the risk of developing endometrial cancer and blood clots. On the other hand, the aromatase inhibitors, reduce the oestrogen level by blocking the enzymes that result in producing small amounts of oestrogen which has lesser side effects than tamoxifen (American Cancer Society, 2005). Oestrogen and progesterone have a neuroprotective effect; however, when hormonal changes occur, it can alter the effects and lead to cognitive impairment. Changes in both hormones can deteriorate cognitive function and these changes of hormones (Sherwood, 2011) can be influenced by chemotherapy or hormonal treatments such as tamoxifen or aromatase inhibitors (A. T. Ahles & Saykin, 2007; Breckenridge, Bruns, Todd, & Feuerstein, 2012).

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#### 2.3.5 Targeted therapy

Targeted therapy is a drug that specifically targets cancer's specific tissues, genes or protein from growing and progressing. The therapy works in a few ways: - hormone receptor antagonists; monoclonal antibodies and inhibitors of the catalytic kinase (Wicki & Rochlitz, 2012). It included substances that affect directly to human epidermal growth factor receptor 2 (HER2), anti- vascular endothelial growth factor (VEGF), agents anti-tyrosine kinase which interfere with transduction pathways (Di Cosimo & Baselga, 2008). Targeted therapies are proven to improve the overall survival among advanced breast cancer patients, and the combinations with other cancer treatment and criteria of patients could influence a better outcome (Tripathy, 2005).

#### 2.4 Breast cancer survivorship

### 2.4.1 Concept of survivorship

Cancer survivorship is a term developed to describe the extensive experience on the continuum of cancer care. The National Coalition for Cancer Survivorship (NCCS) defines a survivor as a person who remains alive from the onset of diagnosis. This was reviewed, and family, friends, and caregiver were included in the definition. The definition of "Cancer Survivor" might represent someone who has fought his cancer but in the cancer terminology, it represents " *any number of things, from patient to someone who is post treatment, to a person who is cancer free but cares for a loved one with the disease*" (Twombly, 2004, p. 1414). Historically, cancer survivorship was defined as people who are "free" from any sign of cancer with a minimum of five years (Rowland, 2007). The definition was in debate to refer survivorship as a state of "free" or cured of cancer, even after five years without any sign of it, due to the chances of cure was a part of the uncertainty.(Surbone, Annunziata, Santoro, Tirelli, & Tralongo, 2013).

Phases in cancer survivorship have been documented as three distinct stages: that are: acute survival, extended survival and permanent survival (Mullan, 1985). The acute phase was during post diagnosis, aimed at surviving the treatment given. The second phase is extended survival or post treatment completion and it is aimed at managing the complications of treatments while the third phase is when survivors were considered 'cured' from a recurrence of cancer even though they are still managing the long-term effects of treatment. However, cancer is a complex disease, and its primary treatment might consist a variety of challenges which often distinctively depends on upon individual including the type of cancer, staged management, and the individual preferences for managing cancer.(Khan, Rose, & Evans, 2012; M. A. Morgan, 2009).

#### 2.4.2 Uncertainties during the period of survivorship

During the survivorship phase, breast cancer survivors were found to have anxiety about the recurrence of breast cancer together with unsettled emotions that disturbed their serenity, self-deprecation concerning the future, worries about treatment method and fear of metastasis, (Ashing-Giwa & Lim, 2011; Boonchoo, Linchong, Saipin, Pratum, & Hongsin, 2013; M. A. Morgan, 2009) which will impact survivors' quality of life. A significant area of an issue about most cancer survivors is the issue involving uncertainties of the cure from the illness. In all phases of survivorship, survivor, adolescents, and young adults experienced a high level of uncertainty which never diminished throughout these phases.(Decker, Haase, & Bell, 2007). Those who were in the third phase of survivorship have the greatest level of fear in survivorship phases. There was an association between survivorship and age, whereby, the younger groups were less fearful than, the older group. (Gibson, Thomas, Parker, Mayo, & Wetsel, 2014). The acute survivors experienced significantly greater uncertainty regarding longterm pain, the unpredictable illness course, staff responsibilities and issue concerning the ability to self-care independently. Survivors of more than five years upon diagnosis experienced greater uncertainty, and they had more unanswered questions concerning the likelihood of successfulness of the treatment. (Decker et al., 2007).

There were also significant differences between cultural background on the survivorship and health-related quality of life upon diagnosis of breast cancer. In a review among Asian American, (Wen, Fang, & Ma, 2014) it was found that there were unsettled overall quality of life that was associated with a cultural and socioecological system that lead to unmet physical, cognitive, emotional, social and occupational needs during the survivorship phase. These uncertainties could lead to stress that contributes to the lack of attention which can present as or complicates cognitive impairments. Therefore, it is important to manage survivorship among women with breast cancer as an individualized care as the quality of life among these women were impacted by age, race and years after diagnosis (Morrow et al., 2014).

### 2.5 Numerous after effects of cancer and cancer treatment

As the number of survivors increase, the after effects of cancer and cancer treatments can be seen in the aspect of bodily function as well as the psychosocial and occupational function. Studies found that there were several physiological and psychosocial aspect which were affected by cancer treatment (Stein, Syrjala, & Andrykowski, 2008). These impaired performance components have led to the deterioration of women' functional roles as a homemaker, partner and worker (Jones et al., 2015; Mackereth, Bardy, Finnegan-John, Farrell, & Molassiotis, 2015). It consequently resulted in poorer quality of life (Fenlon, Powers, Simmonds, Clough, & Addington-Hall, 2014; Grisold, Cavaletti, & Windebank, 2012; Meijuan, Zhiyou, Yuwen, Ying, & Xinzhong, 2013; Ridner, 2009). These women encountered multiple symptoms upon diagnosis and even after the completion of cancer treatment (Pachman, Barton, Swetz, & Loprinzi, 2012). The after treatment side effects can be influenced by other confounding factors such as
survivors' age of diagnosis, cancer stages and sociodemographic background (Kwan, Darbinian, Schmitz, & et al., 2010; Morrow et al., 2014; Ochayon, Tunin, Yoselis, & Kadmon, 2015), all of which can complicates the search for the reasons or causes for cancer-related cognitive impairments.

### 2.5.1 Depression and anxiety

The burden of chronic illnesses such as cancer seem to impact the brain function, in both mental (psychological) and physical (physiological) state which suggests that some effects of cancer treatment might be related to the indirect stressors rather than the pharmacological effects alone (Evenden, 2013; Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012). Women with breast cancer also experienced detrimental impact on psychological aspect after cancer treatment that can exist even after diagnosis.(Hill et al., 2011) There was a strong correlation at 18 months after treatment initiation between anxiety as well as depression with fatigue and pain. The pain was found to be the risk of developing anxiety while the risk factor of depression was found to be both pain and fatigue (Vahdaninia, Omidvari, & Montazeri, 2010). Moreover, one study had found that low social support, self-blame and shame have contributed to major depression and anxiety following a diagnosis of breast cancer (Hill et al., 2011). An experimental study on mice (Gandal, Ehrlichman, Rudnick, & Siegel, 2008) have shown a decreased ability of auditory stimuli associated with cognitive impairments when the experiment subjects were being exposed to chemotherapy. This complication has triggered a response of fear conditioning that suggests an emotional dysregulation, linked to chemotherapy administration and post-traumatic stress disorder (PTSD).

#### 2.5.2 Lymphoedema

During the early phase of survivorship, 13.3 percent of women with breast cancer tend to develop breast cancer-related lymphoedema (Kwan et al., 2010). Breast cancer

survivors were found to be at risk of getting lymphoedema following the first year posttreatment (Armer, Stewart, & Shook, 2009; Hayes, Janda, Cornish, Battistutta, & Newman, 2008; Schmitz, Ahmed, Troxel, & et al., 2010). The estimated incidence that occurred within 30 months of post-treatment is 87 percent and 94 percent 60 months after post-treatment (Armer et al., 2009). There were evidence of potential risk factors that contributed to greater consequences from lymphoedema such as age factor – older women with lymphoedema were found to have lower upper extremity functioning (J. E. Park, Jang, & Seo, 2012) and the extensiveness of surgery treatment and sedentary lifestyle which increased the incidence by three to six times (Hayes et al., 2008). Women with breast cancer started to experience pain, limited range of motion, numbness and weakness that affect their upper body function (Harrington et al., 2011; Hayes et al., 2008), self-care activities; impact on psychosocial factor due to loss of confidence (body image issue), psychological distress, sexuality concerns and financial issue on managing this problem. The psychological distress may indirectly contribute towards the cognitive functioning of women in breast cancer.

## 2.5.3 Neurological complications

Breast cancer survivors have also suffered from neurological complications (Pereira et al., 2014) such as persistent pain after breast cancer treatment (Smith & Wu, 2013). Several factors were associated with this problem including younger age (Meijuan et al., 2013), invasive surgery, acute pain after surgical and using less analgesia after surgical. (Bokhari, McMillan, McClement, & Daeninck, 2012). Physical exertion, stress, lack of physical activities and environmental forces were found to be aggravating factors that could worsen the pain experienced by them (Forsythe et al., 2013; Guerreiro Godoy et al., 2014). Majority reported having intermittent pain with aching, dull or pulling type of pain in the breast area, scar, and musculoskeletal area (arm, axilla and at the back of the body, knees, hip, wrist) (Fenlon et al., 2014; Meijuan et al., 2013). Peripheral

neuropathies are frequently reported by survivors due to the drugs intoxication by cancer treatment like chemotherapy and targeted therapy as well as other factors. Most of the clinical symptoms of neuropathies involved a sensory problem that caused the limbs to have paresthesia, dysesthesia, tingling or even pain that affect their motor function (Grisold et al., 2012). The onset of the peripheral neuropathies may begin several weeks or months after the first treatment and may subside after completion (Pachman et al., 2012). Hypotheses of the mechanism of cognitive-related cognitive impairment include vascular injuries and oxidative damages, inflammation, direct injuries to neurons and autoimmune responses (Nelson, Nandy, & Roth, 2007).

### 2.5.4 Fatigue

Cognitive performance can also be influenced by common problems faced by cancer survivors that may include pain, insomnia, depression and fatigue (Asher, 2011). Women with breast cancer often experience symptoms of fatigue even at the early period of diagnosis, and this can worsen during the post-treatment period up to eight months.(Bodtcher et al., 2015). The fatigue symptoms have been linked to the changes of autonomic nervous system (Vigo et al., 2015). The level of fatigue related to breast cancer treatment has been reported as genetically influenced whereby the severity of fatigue is associated with increased number of high-expression alleles, sedentary lifestyle, physical activity, the presence of anxiety (Bodtcher et al., 2015) or depression and other comorbidity (Bower et al., 2013). Those with significant fatigue experienced the burden of this symptom and were reported to have more moderate to severe disability compared with those without it (Jones et al., 2015).

#### 2.5.5 Sleep difficulty or insomnia

Perceived Cognitive Impairment (PCI) was related to poor global sleep quality (Von Ah & Tallman, 2015). Sleep difficulty or insomnia symptoms have affected a high number of women with breast cancer during cancer treatment. The symptoms of sleep difficulties reported while chemotherapy was estimated to be three times higher in the general population (Palesh et al., 2010). The onset of the problem could start at the perioperative phase and up to 18 months of post-operative, but it will decline over time (Savard, Ivers, Villa, Caplette-Gingras, & Morin, 2011). Women with breast cancer experiencing insomnia problem had significant symptoms of depression and fatigue as well (Liu et al., 2012; Palesh et al., 2010), as suggested by a study (Savard et al., 2011) that other cancer treatment reaction (e.g., fatigue, or menopausal symptoms) could trigger survivors to get insomnia.

## 2.5.6 Hormonal changes and menopausal status

One of the components that affect the brain function is the level of oestrogen hormone, where the study shows their significant effects on the brain (Morrison, Brinton, Schmidt, & Gore, 2006). Women with breast cancer were reported to have early menopausal symptoms (Del Mastro, Boni, & Michelotti, 2011) disturbances in menopausal symptoms and sexual dysfunction soon after receiving chemotherapy and endocrine therapy (Baumgart, Nilsson, Evers, Kallak, & Poromaa, 2013; H. Park & Yoon, 2013). After undergoing cancer treatment, some women experienced at least 12 months amenorrhea and some had menopause induced by the treatment (Scanlon et al., 2012) leading to vaginal dryness and painful or difficult sexual intercourse which affect their sexual interest, satisfaction and functioning (Baumgart et al., 2013; Morrow et al., 2014). There were differences in the prevalence of menopausal symptoms among Asian women where they experienced higher menopausal symptoms compared with women from different continents (H. Park & Yoon, 2013). Compared to premenopausal breast cancer survivors, the post-menopausal women are more prone to experiencing problems in cognitive function (Jeffrey S. Wefel, Lenzi, Theriault, Davis, & Meyers, 2004) as oestrogen plays a role in influencing cognitive skills (Sherwin, 2012).

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#### 2.5.7 Cardiotoxicity

Cancer survivors also have the tendencies to develop heart problems due to cardiotoxicity) (Feng et al., 2011; Ky et al., 2014). The symptoms started within five years after initiation of treatment and may last up to two to three decades (Darby et al., 2013). There are several risk of having cardiac problem:- exposure from radiotherapy related to the dose given (Darby et al., 2013) and radiation to the left-sided breast cancer have shown early cardiac toxicity (Cao et al., 2014) while chemotherapy treatment was dependent on the type of drugs used (Bowles et al., 2012). There is a high possibility for these women to develop pericarditis, ischemic heart disease, and valvular disease. It can aggravate uncertainties and anxieties that have an indirect bearing on attention and other cognitive issues manifested by a cancer survivor in their daily functioning.

## 2.5.8 Cognitive impairments

The phenomena of post-cancer cognitive impairment are gaining attention as one of the key foci of cancer survivorship research. Cognitive impairment, an increasingly acknowledged after-effect of cancer treatment, is also commonly known as cancerrelated cognitive impairment or 'chemobrain' and have been investigated for over a decade (Argyriou, Assimakopoulos, Iconomou, Giannakopoulou, & Kalofonos, 2011; H. J. Burstein, 2007; Jansen et al., 2011; Matsuda et al., 2005; Raffa et al., 2006; Weiss, 2008). Findings from a study (Rey et al., 2012) suggested that perceiving cognitive impairment was seen as a temporary phenomenon that occurred among women with breast cancer. After controlling the factors of intelligence, age and education, patients' undergone treatment and experienced, women with early menopausal status have more tendency to portray a decline in multiple cognitive functions (Jenkins et al., 2006). Nevertheless, many of the factors reviewed above can directly or indirectly impact the cognitive impairments of the survivors. Chemotherapy has been linked to the changes of behavioural and cognitive function (Gandal et al., 2008; Krynetskiy et al., 2013).

### 2.6 Cancer-related cognitive impairment

#### 2.6.1 **Prevalence and incidence**

There are multiple factors that contributed to the cancer-related cognitive impairment and one of the breast cancer treatment that has been implicated as the cause of this related cognitive impairment is chemotherapy (Deprez et al., 2011; Hutchinson et al., 2012). Studies have shown that the symptom of cognitive decline associated with chemotherapy is a common side effect among breast cancer patients (de Ruiter et al., 2011; Ganz, Kwan, et al., 2013; J S. Wefel, Saleeba, Buzdar, & Meyers, 2010). One in five breast cancer survivors who had undergone chemotherapy made complaints about the declination of memory and executive function (Ganz, Kwan, et al., 2013). Evidence suggest about 15 to 50 percent of patients with solid tumours experienced difficulty in cognitive ability after chemotherapy treatment (Hutchinson et al., 2012). Another study reported higher estimates of the incidence of cancer-related cognitive impairment from 15 and 70 percent for those who have undergone chemotherapy (Sherwood 2011). A Study conducted among breast cancer patients in Korean population found that 30 percent of the patients who have completed chemotherapy treatment showed a significant decrease of complex cognitive impairment when being measured by the Functional Assessment of Cancer Therapy-Cognitive Function test (Jin-Hee, Sun Hyoung, Yong-Sik, & Young-Mi, 2015).

## 2.6.2 Mechanisms and factors of cancer-related cognitive impairment

The cognitive changes after chemotherapy can be examined through multiple studies which identified the structural changes in the brain (Bruno, Hosseini, & Kesler, 2012; Deprez et al., 2012; Dumas et al., 2013; Koppelmans, de Ruiter, et al., 2012) which explained the cognitive impairment as reported by survivors. Based on a systematic review (Simó, Rifà-Ros, Rodriguez-Fornells, & Bruna, 2013) of structural and functional neuroimaging studies, a decrease in white matter volume and increased level of activation of the frontoparietal function prior to chemotherapy and early diffusion of grey matter were found. The result from Koppelmans, de Ruiter, et al. (2012) ha shown the decrease of local grey matter volume and an increase of white matter lesion in survivors on average of 21-year post chemotherapy treatment that might be associated with cognitive deterioration. A pilot study (Dumas et al., 2013) using a functional magnetic resonance imaging (fMRI) found a decrease in connectivity in dorsal attention network, which involved working memory and attention tasks. There were associations between cognitive function and the changes in white matter integrity after chemotherapy in which the fractional anisotropy value decreased implicating that the white matter tissue organization was affected (Deprez et al., 2012). MRI study using voxel-based morphometry to assess grey matter changes have shown a decrease in frontal grey matter density which was complemented with self-reported difficulties in executive functioning (McDonald, Conroy, Smith, West, & Saykin, 2013). A particular study conducted to examine the functional brain network topology among breast cancer survivors (Bruno et al., 2012), had demonstrated significantly lessened global clustering value, reduced nodal degree which affects executive control, memory and emotion regulation.

A validated study on the animal model in order to investigate long-term effects on links between chemotherapy and cognition found that regardless of the age, the administration of chemotherapy has induced selective executive functioning in association with a decreasing number of subgranular zone cells in the brain (Dubois et al., 2014). There were possible discrepancies between dosage intake and the effects on cognitive deterioration (Fremouw, Fessler, Ferguson, & Burguete, 2012). High dosage of chemotherapeutic agents administered in mice (Mondie, Vandergrift, Wilson, Gulinello, & Weber, 2010) resulted in long-term cognitive impairment (memory deficits) due to cell proliferation in the gyrus. An electrophysiological study to explore the effects of dosage between high-dose and conventional-dose on cognitive impact found that the reaction of times and the index of information processing was significantly reduced in breast cancer cases treated with high dose cyclophosphamide/thiotepa/carboplatin than those in the non-chemotherapy-treated group (Kreukels et al., 2006).

### 2.6.3 The onset of cancer-related cognitive impairment

In early breast cancer treatment, only a fraction of women was affected, with cancerrelated cognitive impairment, while the majority were either unaffected or recover over time (Jenkins et al., 2006). This side effects have been reported as occurring at one month post chemotherapy (T. A. Ahles et al., 2010), at around six months to one year (Reid-Arndt, Hsieh, & Perry, 2010) and even at up to 20 years after receiving treatment (Koppelmans, Breteler, et al., 2012). Cognitive function deteriorates over the course of chemotherapy treatment and worsens with the intensified treatment in women with breast cancer (Collins et al., 2013).

Cognitive decline manifestation occurred at a different range of timing from acute to later onset. 21 percent cases were reported before chemotherapy, 65 percent showed a cognitive decline in the acute interval, 61 percent occurred during post treatment completion upon long-term evaluation and 29 percent in new delayed cognitive decline (J S. Wefel et al., 2010). Some study reported that it can occur during the chemotherapy treatment with 27 percent showing cognitive decline towards the final treatment (Hermelink et al., 2007). However, it is in the debate due to other confounding factors. Subjective report from breast cancer survivors over their satisfaction of cognitive function decreased after undergoing treatment (Pullens, De Vries, Van Warmerdam, Van De Wal, & Roukema, 2013). Based on a total of 88 breast cancer survivors, 94 percent reported significant perceived cognitive impairment (PCI) after one year undergone treatment (Von Ah & Tallman, 2015).

### 2.7 Impact of cancer-related cognitive impairment

Cancer-related cognitive impairment might be subtle, but it affects patients in every aspect of life including a relationship with family, the social limitation as well as working life (Rönnängsgård, Önnerfält, & Glasdam, 2014). Survivors experienced cognitive changes in every domain of the cognitive function. Older breast cancer patients have the lower ability in processing speed (T. A. Ahles et al., 2010). Survivors showed significant differences in attention and concentration, psychomotor speed, and memory compared to baseline assessment (Deprez et al., 2012).Verbal fluency difficulties were associated with worse functional well-being after one-year chemotherapy (Reid-Arndt et al., 2010). The specific impact of cancer-related cognitive impairment is reviewed as below.

## 2.7.1 Impact of cancer-related cognitive impairment on ADL

According to Vearncombe et al. (2009), the greatest decline was experienced in verbal learning and memory with problems in concentration and memory functions, contributing to a decline in functional performance in daily livings. Cognitive dysfunctions were related to memory loss and inattention (Biglia et al., 2012; Matsuda et al., 2005), concentration difficulties, visual-spatial skills and motor function (Jansen et al., 2011). They also experienced detrimental consequences on work performance (75 percent) that required patients to utilize compensatory strategies (58 percent), with accompanying patient frustration (50 percent) as well as adverse impacts on family relationships (33 percent) (Wagner et al., 2009).

The ability to maintain attention is essential to daily function (Kam et al., 2015). Breast cancer survivors with difficulty in attention showed the significantly higher level of mind wandering (m=57, SD=16%) and presented slower reaction time when they were being observed in terms of neuronal response. A neuropsychological study (Chen et al., 2013) investigating two decision-making conditions under ambiguity and risk condition found a dissociation in decision-making under ambiguous conditions. However, decision making in risky condition remains intact in comparison to the group without chemotherapy treatment and healthy control group. Women described the impact of cancer-related cognitive impairment on themselves, their social relationships, working life and daily living (Von Ah, Habermann, Carpenter, & Schneider, 2013).

# 2.8 Breast cancer survivors and work functioning

### 2.8.1 Return to work

As the number of breast cancer survivors increased, the possibilities of them returning to work are high. In a study to investigates the predictors of return to work among early diagnosed with breast cancer, 59 percent of survivors have returned to work after ten months of surgery and the remaining 41 percent were on sick leave either part time or full time (Aina Johnsson et al., 2009). In a multiethnic mixed method study involving Malay, Chinese and Indian race done in Malaysia, 40 percent from 260 breast cancer survivors had successfully returned to work with 32.3 percent returning to work after 12 months of diagnosis (Tan, 2013). A return to work study (Tan, Loh, Su, Veloo, & Ng, 2012) conducted in Malaysia showed that 80 percent of the breast cancer patient return to the same employment with the same job scope and responsibility while the other 20 percent had changes in either employment or different responsibility and job scope. In a meta-synthesis review (Stergiou-Kita et al., 2014), there were nine key facilitators and barriers that contributed to the successfulness of return to work and it was divided into three categories of personal, environmental and occupational.

Many studies (Aina Johnsson et al., 2009; Lilliehorn, Hamberg, Kero, & Salander, 2013; Tan et al., 2012) has been conducted to identify factors that facilitate and hinder of return to work process among breast cancer survivors. For early diagnosed breast cancer patients without adjuvant intervention, women did return to work on average of  $7.2 \pm 5.2$  months (Balak, Roelen, Koopmans, ten Berge, & Groothoff, 2008). More women regardless of any adjuvant intervention return to work after some period of time after diagnosed of having breast cancer as their overall quality of life become better in time (Hedayati et al., 2013; Lilliehorn et al., 2013). Women with breast cancer were motivated to return to work due to several factors even that they were struggling to resume to working life. In a view from narrative experiences of early returners among women with breast cancer on factors of returning to work, the believe that it was because of the sense of normality and due to financial reason (McKay, Knott, & Delfabbro, 2012), even though they lost some of the meaning in work (A. Johnsson, Fornander, Rutqvist, & Olsson, 2010). In a qualitative research, the key facilitators were receiving social support from an employer as well as driven by financial pressure. Those who have returned to work were motivated as they perceived that work help to give a sense of meaning and purpose in life and they long to get back to work as they love the environment and the nature of the job (Lilliehorn et al., 2013).

Those with more advanced stage and involved with chemotherapy treatment were prone to take more leave, extended time return to work and end up not returning to work even after 12 months and up to six years upon diagnosis (Balak et al., 2008; Aina Johnsson et al., 2009). In a recent study, the key barriers were identified by the effect of physical-psychological, fear of potential environment hazards, job demands, negatives beliefs and overprotective family. Failure of returning to work was due to age, impact of treatment, the impact of cancer site, the severity of adverse side effects, occupational status and roles of others (Amir & Brocky, 2009). The sources of work challenges were encountered by breast cancer survivors and were reported to be physically and mentally overloaded, conflict among work team, job insecurity and insufficient qualifications (Noeres et al., 2013).

One of the key barriers for return-to-work complaints were reports about forgetfulness and processing speed (Tan et al., 2012).On the contrary, the result from Hedayati et al. (2013) showed that cognitive deterioration among breast cancer survivors has no significant association in term of return-to-work. However, survivor indicated that cognitive impairment affected their confidence in returning to work because it would highlight their problems further, and it became too challenging to continue working (Munir et al., 2010). Returning to work was a continuous process that involved a decision making which depends on survivor's readiness and how they manage the symptoms of functional impairments (Stergiou-Kita et al., 2014).

## 2.8.2 Impact on work functioning

In a study among breast cancer survivors (Calvio et al., 2010) on an average of three years post-treatment, cognitive limitation contributed to the work output performance in memory and executive functioning as to compare to the non-cancer group. This is especially evident when they returned to work and particularly for those in intellectually demanding occupations (Vardy, 2009). Significant correlations were found in breast cancer survivors treated with chemotherapy between decision-making performances and neuropsychological test where there were decreased in the information processing and working memory (Chen et al., 2013). Furthermore, it affects their decision-making where they were unable to retrieve some effective information by processing feedback prior choices made by them in which this cognitive ability was essential to work functioning.

Professional women reported that they needed more effort to perform tasks than previously and that as their jobs required several skill sets that incorporated multiple cognitive domains that created additional challenges. (Mulrooney Tamsin, 2007). Survivors found that they required more attention to complete work tasks to a sufficient standard (Boykoff et al., 2009).Munir et al. (2010) found that survivors sometimes hid cognitive difficulties from their employer. However, the findings suggest that good support from employers and colleagues helped survivors to regain confidence in returning to work. On the other hand, for women with existing background of social discrimination, the persistence of cognitive impairment may influence their ability to regain work function, the ability to return to social participation and might increase their social dysfunction (Rey et al., 2012).

## 2.9 Cancer-related cognitive impairment and management

As the progress of cancer-related cognitive impairment research is still ongoing over than decades, this issue is still being debated (Janelsins et al., 2012). It represents a real challenge in clinical practice due to its subtle presentation. It was found to have effects on selective cognitive function, aetiology of being unknown as well as other cofounding factors that contributed to the deterioration of cognitive ability (Ganz, Bower, et al., 2013). Lack ok standardized neuropsychological assessment in clinical practice hindered the practitioner from detecting cognitive impairment (Joly, Rigal, Noal, & Giffard, 2011).

Oncologist nurses were 100 percent aware of this side effects among cancer patient, and most of them have attended the educational program concerning cognitive impairment, however only 38 percent of them practices to assess patient and 44 percent educated patients and families on the issue (Myers & Teel, 2008). In assessing cognitive functioning, there are several screening tools and neuropsychological test that has been carried out by some researchers. It is important in clinical practices to make a screening as it would help the clinicians to choose appropriate therapy to enhance cognitive function (Lange et al., 2014). Most of the findings from studies to measure cognitive function using objective and subjective assessment have resulted in discrepancies between this two measurement (Hutchinson et al., 2012). On the other hand, in a recent study by (Von Ah & Tallman, 2015), there was a correlation between objective and subjective measurement of cognitive functioning. The subscales scores of Perceived Cognitive Impairment (PCI) and Perceived Cognitive Ability (PCA) were associated with verbal memory, delayed verbal memory, and executive function. Oncologists and oncology nurses estimated, on average, that 33 percent of patients in their practices (range, five percent to 75 percent) had reported symptoms of cognitive difficulties (Wagner et al., 2009).

Cognitive impairment might be managed using other than pharmacological strategies. Pharmacological treatments might not have confirmed value in the management of cognitive impairment. However, survivors might benefit from cognitive rehabilitation (Moore, 2014). The cancer-related cognitive impairment had become an important aspect of rehabilitation as it can affect patient's adherence to treatment and may advance as a long-term impairment (Janelsins et al., 2012). One of the strategies that were widely being investigated is cognitive training that was related to the significant improvements in executive functioning. In a randomized clinical trial conducted among 41 breast cancer survivors, using a computerized, home-based intervention program, it was found that this may improve cognitive function in verbal memory and fluency, processing speed and cognitive flexibility (Kesler, Hadi Hosseini, et al., 2013). In a review of benefits of exercise towards cancer-related fatigues, cognitive impairment, sleep problems, psychological problem and physical disability, generally, aerobic exercise, core strengthening training and other alternatives exercise

are helping survivors to cope with the side effects of their treatment, improve recovery and increase quality of life (Mustian, Sprod, Janelsins, Peppone, & Mohile, 2012).

### 2.10 Summary

The findings from previous studies suggest that there were mixed results in cancerrelated cognitive impairment (CRCI) or chemobrain where it has been found that there were many factors that contributed (directly or indirectly) to the cognitive impairment after breast cancer treatment. However, many studies linked to breast cancer treatment such as chemotherapy, and some have coined the term chemotherapy-associated cognitive impairment. The phenomenon and the impact on functioning at work are the core that funded the outcomes of the study. In view of the cognitive changes from the Malaysian health care providers (oncologists) and breast cancer survivors', it is valuable to investigate their perspectives on this phenomenon and the impact on survivors' functioning at work. This study reflects awareness need for future clinical guidelines and among survivors.

#### **CHAPTER 3: METHODOLOGY**

#### 3.1 Overview

This chapter presents the study in two stages. Stage one is a systematic review of the current qualitative studies on an aspect of cognitive impairment, and stage two study is the main study consisting of in-depth: qualitative studies that involved two groups of stakeholders, namely the breast cancer survivor and the oncologists. In-depth interviews were carried out with oncologists while focus groups interviews were conducted with breast cancer survivor to gain in-depth perspectives, views, and experiences of the cancer-related cognitive impairment or chemobrain phenomenon to them. This chapter reports the ethical consideration, research design for stage one – meta-ethnography review; and stage two qualitative studies on a) breast cancer survivors and b) oncologists, sampling design, participant selection, data collection, data analysis and the trustworthiness of the data collected. At the end of this chapter, a summary to reflect the overall content of this chapter was written.

### **3.2** Qualitative study for understanding cognitive impairment

The first stage of this study involved a systematic review using meta-ethnography because there is no study that was conducted in Malaysia; therefore a thorough systematic review was the best approach to accumulate latest evidence. This study chose qualitative study as a research design based on the following justifications.

- A qualitative study was designed to understand on experience and in-depth of a human phenomenon, based on personal knowledge, subjectivity and emphasizes the importance of personal perspective and interpretation (Lester, 1999)
- ii) The qualitative design is the best design to capture the actual phenomenon thoroughly from the participant's point of view; as quantified data are often

not able to explain a phenomenon. The techniques which involve interviewing, coding data into themes and drawing a conclusion based on the qualitative themes, enables the researcher to describe and interpret the participant's experiences.

iii) The interpretative nature of the qualitative study is best for enabling Occupational Therapy researcher to analyse their research as it aims to explore the insider views and perception (Cronin-Davis, Butler, & Mayers, 2009) in tandem with the discipline's client-centered approach. Occupational Therapy is a key service provider for cancer survivor as they improve survivor's self-efficacy in the performance of meaningful occupations in daily routines through the development of cognitive strategies. By acknowledging the importance of remediating this cognitive dysfunction and their effects on quality of life, the occupational therapist needs to understand how best to rehabilitate the clients and qualitative approach helps uncover the meanings of client experience.

In summary, the qualitative study design is the best suitable approach to generate an in-depth experience that presents a reality picture from participants which able to make interpretations that discuss meaning, cognition, affect and action (Reid, Flowers, & M., 2005).

### **3.3** Ethics approval

This study was approved by the University of Malaya Ethics Committee (Ref: 962.26) on 4th January 2013 (Appendix A) and Medical Research and Ethics Committee, Ministry of Health Malaysia (ref: NMRR-13-1006-17142) on 26 November 2013 (Appendix B) before the data collection process. The participants involved in both the a) focus groups with breast cancer survivors and b) in-depth interviews with

oncologists gave their consent. Participants were assured of the confidentiality to protect their identity and informed that participation was voluntary where they can withdraw at any point in time.

#### **3.4** Stage one study

### 3.4.1 Study design: Systematic review

The first stage of this study involved a thorough and comprehensive review which was extracted from multiple qualitative studies. The study chose to review qualitative studies only because there are a few review studies that have been published to collect quantitate data on cancer-related cognitive impairment (Hutchinson et al., 2012; Raffa et al., 2006; Simó et al., 2013). Moreover, the intention was to understand the rich and in-depth 'experiences and expression' of this phenomenon and to study the verbatim about their personal experiences and interpretation. A qualitative review is a relevant approach to evaluating the meaning that breast cancer survivor ascribes to cognitive changes and represents an area of concern not be feasible for examination using quantitative approaches. The meta-ethnography synthesis method can demonstrate cumulative knowledge and identify the absence of knowledge systematically by drawing some qualitative studies together which can produce a significant new insight (Campbell et al., 2011). Qualitative studies may be brought together to produce a comprehensive understanding of the phenomenon (Sandelowski, Docherty, & Emden, 1997).

### 3.4.2 Search strategy

This review undertook a systematic search of the literature for all published Englishlanguage articles from 2002-2013 that used qualitative methods to investigate cancerrelated cognitive impairments for women with breast cancer. The following databases were searched: CINAHL, Web of Knowledge, EMBASE, Proquest, OVID SP,

MEDLINE, Oxford Journal, Science Direct, PubMED, and Wiley. Researchers performed free text searches by using keywords of chemobrain OR (chemotherapy AND mild cognitive impairment) OR post-chemotherapy cognitive changes. Next, the term "breast cancer survivors" AND "qualitative" was added. The search filters were used at this stage to address the inclusion criteria for the study. The inclusion criteria were: 1) breast cancer and chemobrain. The terms used were chemofog, cognitive dysfunction, and cognitive changes. Chemobrain was referred to as any domain of cognition decline or dysfunction experienced by survivors who had cancer treatment; 2) qualitative study, including terms such as experience and qualitative experience; 3) studies published from 2002 to 2014, including all papers published within the last 10 years; 4) English language text; and 5) full-text publication. The exclusion criteria included the following: 1) study design other than a qualitative design methodology; 2) studies of patients with cancers other than breast cancer; and 3) non-English papers. The second step of the Noblit and Hare process involved deciding what studies were relevant to the research question and aims. In particular, the research team was interested in understanding women's lived experience of chemobrain.

### 3.4.3 Method and procedures

Using a meta-ethnography method, the interpretation of results from a range of original studies were compared and translated to acquire a greater understanding of the cognitive changes experienced by breast cancer survivors (Britten et al., 2002; Campbell et al., 2011; Dixon-Woods et al., 2006; Noblit & Hare, 1988). A seven step process of meta-ethnography by Noblit and Hare (1988) was implemented as follows: 1) developing a specific research question; 2) deciding what is relevant to the research question; 3) reviewing each study to identify key concepts and recording them; 4) determining how the studies are related, and comparing study approaches to the key concepts; 5) translating the studies into one another; 6) synthesizing the translation

outcomes, and 7) expressing the synthesis. Step five above has involved the researchers interpreting and translating the key concepts via 1) reciprocal translation (i.e. studies with similar findings were directly compared and synthesized); 2) refutational translation (i.e. studies rebutting each other with conflicts of findings); and 3) lines of argument (i.e. translation of the studies to build a final interpretation using both differences and similarities among studies) (Campbell et al., 2011).

Based on these steps, two researchers independently appraised the selected papers and undertook steps to extract the information and synthesize the findings. Further discussions took place between the reviewers when any discrepancies arose. Next, second order interpretations were identified, on the basis of which third order interpretations (based on key concepts and second-order interpretations) were constructed. These were all linked together in a line of argument (i.e. the final interpretation using both differences and similarities among studies) to present the interpretation of cognitive impairments experienced by women. This synthesis may be expressed as text as well as in summary tables, diagrams or models, which can produce significant new insights into the topic. Finally, a table synthesis of concepts and order interpretation was built to connect each of the papers.

### 3.4.4 Quality appraisal

Quality appraisal instruments are applied to qualitative research reviews in a consistent manner, to ensure credibility or trustworthiness of the findings (Toye et al., 2013). The 'Critical Appraisal Skills Program' (CASP, 2013) format was adopted to appraise each article to apply a valid, reliable and objective method prior to synthesis. The CASP checklist is a ten item tool to appraise qualitative papers without using a numerical score. This is to remind researchers of the importance of every criterion in a qualitative paper to reduce bias. Bias in qualitative research is usually related to the

influence of researchers and a lack of transparency in data collection and analysis, whereas, in positivist quantitative studies, bias is related to representativeness and generalizability. Therefore, qualitative studies are usually evaluated using agreed criteria about data collection and analysis processes that need to be fulfilled in order to contribute to a review of findings. The first two questions act as the core criteria in selecting qualitative reports (Campbell et al., 2003). Nevertheless, the process itself is useful as it may contribute to the richness and the focus of discussion. Appraisal of the selected studies contributed to the synthesis of the findings of the review, as any critique of the studies could be identified (Atkins et al., 2008) and incorporated into the review. The first two questions are screening questions. If the answer to both is "yes", it is worth proceeding with the remaining questions as mentioned in table 3.1.

**Table 3.1:** Quality appraisal criteria (Critical Appraisal Skill Program).

No	Question
1	Was there a clear statement of the aims of the research?
2	Is a qualitative methodology appropriate?
3	Was the research design appropriate to address the aims of the research?
4	Was the recruitment strategy appropriate to the aims of the research?
5	Were the data collected in a way that addressed the research issue?
6	Has the relationship between researcher and survivors been adequately considered?
7	Have ethical issues been taken into consideration?
8	Was the data analysis sufficiently rigorous?
9	Is there a clear statement of findings?
10	How valuable is the research?

### **3.4.5 Data collection and analysis**

Two authors (researcher and supervisor) were independently reviewed the identified studies from the search, appraised the selected papers and undertook the seven steps to extract information and synthesize the findings. Next, discussions took place between the reviewers and other authors where discrepancies arose from collecting and categorizing data of each selected study to form the primary dataset. During this early stage, the interpretation was avoided to maintain the original outcomes of each article. During steps three to five (Noblit & Hare, 1988), the research team identified key concepts through reciprocal translation (similar findings) and refutational translation (conflicting findings) and the interpretation of findings were taken together. This process of explicitly relating the papers occurs on three levels (Schutz, 1962) Schultz's process was systematically followed to interpret and explain the results via analysis of key metaphors and was careful not to reduce the qualitative accents but to retain the sense of the account of the women as reported in the papers. Schultz's concepts of firstorder refer to the daily perceptions of the common people; the second-order construct refers to the constructs of findings from the scientific view in the papers, and the third order constructs are final synthesis derived from the key concepts and second order constructs based on the interpretations of the review authors.

### 3.4.5.1 Theoretical framework for the review

To guide the synthesis for this review, the Model of Illness Representation by Howard Leventhal et al. (1997) was adopted. This allowed the study to capture individual perceptions of illness related to their lived experience of cognitive impairments. This framework propose seven components of illness representation: 1) identity - or the name or label of a threat; 2) timeline - the belief about the time trajectory of the illness; 3) consequences - the perceived consequence of a threat from the illness; 4) cause - the perceived causal mechanism of any threats; 5) control or cure - whether something can be done to control the threat; 6) illness coherence - whether a person thinks about the threat in a coherent way; and 7) emotional representation - the emotions associated with the illness experience. This framework is particularly relevant to the review topic and enabled the researchers to interpret and capture the reasoning and identify the self-management issues for women experiencing chemobrain.

### **3.5** Overview of stage two study: qualitative studies

This exploratory study used focus group approach and in-depth interview to explore the insight of health care providers (oncologists) and the perceived awareness and impact of cancer-related cognitive impairment or chemobrain in functioning at work among women with breast cancer with regard to this phenomenon. This stage involved two groups of stakeholder, including breast cancer survivors who have experienced the symptoms of cognitive impairment and participation from oncologists who have been treating patients diagnosed with breast cancer.

Both in-depth focus groups and interviews were conducted using a semi-structured interview (Appendix C and D) consisting of area or topics to be explored. With an extensive literature review, the topics for the semi-structured questions were developed. This flexibility in a semi-structured question enables the deeper exploration of information that might be important to the participants but may not have been known by the researcher (Gill, Stewart, Treasure, & Chadwick, 2008).

## 3.6 Stage two A: Focus group with survivor

Four focus groups were conducted on 17 patients who fulfilled the inclusion and exclusion criteria of the study. They were stratified into a group based on age and type of work. Focus group discussion was to generate information on views and the meaning in collective for understanding participants' experiences and belief (Morgan, 1998). A focus group is an approach involving an in-depth discussion with a target population

(Thomas, MacMIllian, McColl, Hale, & Bond, 1995), to obtain a range of information on the ideas and feeling on certain issues, and to reveal the different perspective between the group and individual (Rabiee, 2004). Focus group discussion was used among breast cancer survivors; to provide group cohesion and encourage participants to contribute freely to the topic discussed (Fern, 2001). The natural interaction among participants can produce essential data (Morgan, 1998) and provide them an opportunity to discuss and share personal issues and provide potential solutions (Duggleby, 2005). The dynamics of the interaction of a group produces rich and in-depth data (Thomas et al., 1995).

The focus group in this study has stratified the participants into a homogenous group, according to the age and socioeconomic (type of occupation) status, which is believed to generate rich data (Krueger, 1994). The study took place in the Clinical Oncology Unit in several Kementerian Kesihatan Malaysia (KKM) (Kuala Lumpur Hospital and Putrajaya Hospital), University Hospital of University Malaya Medical Center (UMMC), and University Putra Malaysia Cancer Care and several Non-Government Organization, upon ethical clearance from the UMMC and KKM medical ethics committee. These survivors were screened for cognitive impairment using questionnaires for subjective assessment and Montreal Cognitive Assessment (MoCA) (Appendix G) for objective assessment. Those who reported cognitive impairment and found to have cognitive impairment were invited to participate in focus groups to explore their awareness and perceived impact of cognitive changes in functioning at work.

#### **3.6.1** Recruitment and procedures



Figure 3.1: Flowchart of the recruitment process for breast cancer survivors.

This recruitment process was conducted from March 2013 to February 2014 as illustrated in figure 3.1. This involved four different places for data collection. The first eight months were from March 2013 to October 2013, started at the oncology clinic in University Malaya Medical Center. In August 2013, data collection was broadened to two other hospitals (Kuala Lumpur Hospital and Putrajaya Hospital) and in a cancer

care facility (University Putra Malaysia Cancer Care). A survey was made in the unit to get an estimated number of participants. Three methods were used to approach potential candidates: 1) flyers were printed and distributed to the appointed people and oncologists in the clinics (Appendix H) 2) researchers attended the clinic session and approached the survivors personally through their oncologists; and 3) through clinic databases, potential participants who were no longer coming for follow up sessions were contacted. Purposive sampling and snowball techniques were used to gain recommendation for other participants. Starting from the recruitment process up to the time to carry out the focus groups, communication was maintained monthly. The snowball approach was effective as some of the participants were able to identify other hidden survivors and it broadens the networking coverage.

All participants who were involved in the study were required to fulfil the following inclusion criteria: 1) women confirmed by physician diagnosis of stage I, II, or III breast cancer; 2) women who have returned to work after chemotherapy treatment; 3) women the age of 20 to 59 years old; 3) women who reported changes in cognitive function after receiving chemotherapy, such as forgetfulness, decrease in attention and concentration; 4) women who have completed chemotherapy that lasted 6 months and up to 3 years; 5) women with no history of seizures or other neurological disorders; and 6) women who are able to speak and understand English or Bahasa Malaysia. Participants who have a history of depression and anxiety disorders or on antidepressants or anxiolytics, current or past alcohol or drug and neurobehavioral risk factors, including neurologic, medical, or conditions known to affect brain structure of the function were excluded from the study.

Patients with breast cancer who fulfilled the inclusion and exclusion criteria were approached personally with the permission from oncologists or respective persons in charge in the clinic. Flyers were issued to the oncologists to help them identify potential participants as the oncologists work directly with breast cancer patients. This strategy gave the opportunities to contact and schedule an appointment with the participants for screening sessions. The flyers contained a brief description of the study, the inclusion criteria and the example of the presented symptoms of cognitive changes. Information about the researcher and respective corresponding person involved in the study were included as well. Participants interested to be screened were given a token of appreciation in the form of a bookmark which depicts information on body mass index measurements with brief tips on a healthy lifestyle. Participants, who agreed to be screened, were briefed about the background and the procedure involved in the study. Once they agreed to be part of the study, consent forms were signed, and participants were screened using MoCA. For those participants who were recruited using the snowball technique, or from the databases, a telephone call was made for verbal consent to be part of the study and to proceed to the screening session. Researchers maintained contact with participants until the day of actual focus groups session.

Screening was done via telephone calls using a list of questions regarding cognitive changes and to check for inclusion criteria. For those who fulfilled the criteria, telephone calls were made to confirm the date, venue, and attendance. After a collective number was achieved to form a focus group, participants were stratified to age group; between a young professional age group and a young non-professional age group (20 years to 39 years old); an old professional age group (40 years to 59 years old) and an old non-professional age group. Four focus groups were held with three to six people per group.

On the day of the focus group session, the confidentiality of each discussion was highlighted to the participants and regulations were outlined while the session took place. The information on the study background was explained during the screening process. The focus group started with an ice breaking session, including a brief self-introduction from members of the floor. The focus group sessions were carried out with a semi-structured guide developed by the researcher. Three people were responsible for recording the focus group session. The principal researcher was the moderator to ensure the smoothness of the discussion. Two note takers were appointed to document all the nonverbal communication and behaviour. At the end of the focus group, the moderator highlighted the key points made, and participants were allowed to make comments, add or omit the points.

All sessions took place approximately two hours and were conducted in the Rehabilitation Clinic University Malaya Medical Center and Keep Able building for Cancer Survivors in University Malaya, Petaling Jaya. Participants who attended the session were given a token of appreciation, including a breast cancer guide book and a book on brain training and exercises.

## 3.6.2 Data Collection

During data collection, written consent was obtained from the participants. A social demographic questionnaire was given to be filled up by participants. Other clinical data were obtained from medical records to document details of treatment received by participants. Participants were screened using an objective cognitive assessment. The MoCA was used to identify areas of affected mild cognitive impairment that could assist participants to highlight their cognitive difficulties and functional performances. This assessment was carried out in the form of an interview administered by the researcher which last about 15 to 20 minutes. Participants who subjectively reported having symptoms of cognitive changes were invited to be in the focus groups, regardless the result of the objective cognitive assessment. MoCA was used in this

study due to it sensitivity to detect mild cognitive impairment compared to other screening test and it has been tested in cancer population (Arcuri, Palladini, Dumas, Lemoignan, & Gagnon, 2015; Baxter, Dulworth, & Smith, 2011; Friedman, 2012)

Before the session started, questionnaires were distributed to gain information on the participants' current working status. The semi-structured interview was audio taped with permission from participants. They have been informed of the confidentiality of the focus group discussion. In the semi-structured interview, moderator provided neutral probes when necessary during the discussion to elicit full and rich description from participants. Moderator recorded the content to be summarized at the end of the discussion. One of the assistants was in charge of the recorder, and both assistants were required to observe and record all the non-verbal communication and gestures throughout the session.

During all sessions, observational notes and field notes were kept for further analysis. Every session ended with a discussion among moderator and two assistants to ensure the consistency of the recorded field notes. The researcher contacted participants for any raised issues. All sessions were audiotaped and transcribed. The interview was conducted once and a follow-up session for member check was organized to show the summary of the report to the participants in the group, which allowed them to give comments about the transcription data in order to ensure trustworthiness. All data will be destroyed at the end of the study to ensure participants' privacy and confidentiality.

#### **3.6.3 Data analysis:**

This study used thematic analysis approach as proposed by Krueger and Casey (2009). It began with listening to the recorded data for a few times and transcribing process. The process of analyzing the transcripts followed analysis guidelines, which were to use the word processor to cut and paste. The process was as follows: 1)

transcript were numbered in each line; 2) two copies of each transcript were made; 3) the working transcripts were arranged based on the category of participants, and 4) a new source files were created for each research questions and was further divided into groups of participants. During this process of categorizing, each quote was read and was constantly examined: 1) have the participants answered the question asked?; 2) does this comment answer different questions? 3) do the comments say something of importance about this topic? 4) has it been said earlier?. This step requires constant comparison and decision making in placing the comments at the suitable file. At this point, comments were placed in categories and subcategories. These categories were rearranged and combined when necessary. Next, each category was re-examined and a descriptive summary for specific groups written for each question, which was then it was compared and contrasted across the group. In the process of interpretation or recommendations, several factors were ruled out to put emphasis on certain comments and themes as follows: 1) frequency - the importance key insight was identified; 2) specificity specific details were emphasized; 3) emotion - comments showing emotion, enthusiasm, passion or intensity were given more weight; and 4) extensiveness - the amount and depth of info carried out.

## 3.7 Stage two B: In-depth interview with oncologists

In-depth interviews between the researcher and oncologists were carried out until data-saturated. The purpose of these in-depth interviews is to gain perception and insight from the perspectives of the oncologist in response to cancer-related cognitive impairment or chemobrain issue. A study using interviews conducted to explore the views, experiences, or beliefs of individuals in a selected area provide a better understanding of a phenomenon (Gill et al., 2008). Samples of oncologists were taken from University Malaya Medical Center, Kuala Lumpur Hospital, Beacon Hospital and Subang Jaya Medical Center.

### 3.7.1 Recruitment and procedures

A total of 12 oncologists from four different hospitals were recruited which involved government sector and private sector hospital. Purposive sampling and snowball techniques were used in the recruitment of participants. The samples of the population were recruited from June 2013 to January 2014. Oncologists involved in the study were expert oncologists and worked directly with or had experienced working with breast cancer survivors. Recruitment started with one qualified person in the unit, and he was asked to recommend other qualified participants. Oncologists were first contacted through emails before appointments were made. All the details regarding the researcher's background, estimated the time taken, the place to conduct the interview, and the purpose of the interview was sent to notify the potential participants to ensure a smooth-running interview. The participants were contacted twice before the actual interview upon confirmation to participate in this study. A day before the appointment date, a text message or email was sent to them to reconfirm the date and place. Participants were informed in the initial email that their participation in this study was private and confidential. They were given choices of preferred language to be used in the interview. Later, a summarized report was sent to participants to make any comments. The interview was conducted once, and any raised issues during analysis process were clarified back to participants.

## 3.7.2 Data collection

Before the interview took place, the participants had a brief introduction to the background of the study and a consent form was given to the participants. The interviews lasted approximately 30 to 40 minutes with a further interview for clarification and any issues raised during analysis. Most of the interview sessions were carried out at a convenient place as requested by participants, in the respective oncologists' clinics. The researcher acted as the interviewer in this process. A simple

social demographic questionnaire that experiences background of the participant was administered to the participant. An outline of the interview process was delivered to the participant to give them a clear idea of the flow of interview process. These interviews were conducted using a semi-structured interview guide, involving prompts and probes. Most of the data had early member check during the interview session by paraphrase and summarize the interview to ensure the understanding of the researcher reflected actual phenomenon from participants. The interviews were semi-structured to focus on the insight and perception of chemobrain; the concept of chemobrain, their experiences and what they think about the chemobrain issue. Field notes were used to record nonverbal respond during the interview session. Data reached saturation with the sample of eleven, and there was no new information found. Recurrent themes were noted. No new themes were a presence of the twelfth and last participants and the recruitment ended.

### **3.7.3 Data analysis**

Thematic analysis with constant comparison method was applied in the study. Thematic analysis is a useful research tool that is compatible with either method and is independent of theory and epistemology or theoretical and epistemology approaches, which provide rich and detailed data (Braun & Clarke, 2006). The recorded audiotape was transcribed verbatim, and the thematic analysis was used to identify and analyze interview with participants' content for themes. It is an ongoing process occurring in a continuum before, during, and after the interview and a recursive process that often requires the researcher to check constantly back and forth in all stages. The stages involved were as follows:1) familiarizing data: the transcribe interview together with the field notes from note takers and moderators summarizes notes after interview was read repetitively to search for meanings and patterns; 2) generating initial codes: the data was coded in via the use short phrases, sentences, words that bring meaning to the

phenomenon. This was done manually using a word processor, where the transcript was divided into columns. Each line was numbered, the sentences and words highlighted, and the different columns marked with potential codes; 3) searching for themes: the codes were reviewed to group them into potential themes. A brief description of each code was named in different files of a word processor; 4) reviewing themes: a process to review all the combined codes, refined them, separated or discarded. All the transcribed data was read again to ensure the representation of the data throughout the entire set of data; 5) defining and naming the themes: the themes were defined together with the available subthemes and name given that represented what it was all about; and 6) producing the report: to give examples of quotes by participants and each theme needs to be reflected in research questions. Using a constant comparative analysis principle, the interview data was analyzed as soon as the conducting interview began by comparing the results in a recursive manner. This approach was able to determine that the study had reached data saturation.

#### **3.8** Trustworthiness of data

Steps to ensure the trustworthiness of the data was carried out to ensure the outcome have the truth value. The step taken included was to address credibility, transferability, dependability and confirmability of the data. (Lincoln & Guba, 1985). Credibility was achieved through member check via the discussion with fellow assistant upon the completion of the interview and validation of finding by returning the summarized report or transcripts to participants to make comments or corrections. Transferability referred to either the research data or processes being able to be used by others. It was achieved by using purposive sampling to ensure that all participants had experienced the phenomenon. Dependability and confirmability are used to refer to the stability of finding over time. It was met by having an audit trail of the study process. In this study, this consisted of audiotaped interviews that were transcribing verbatim, the notes taken during the interview process, and the process of conducting the analysis. The data presented were all elicited from the original data.

## 3.9 Summary

This chapter has provided a detailed explanation of the methods used for both stages in this study. Using a systematic review, it enables the study to produce a significant new insight coherent with the cumulative existing knowledge and the current gap between studies. Two in-depth qualitative studies from two stakeholders; breast cancer survivors, and oncologists provided the means to explore their perspectives and experiences to understand this phenomenon of cancer-related cognitive impairment.

#### **CHAPTER 4: : RESULTS**

#### 4.1 Overview

This chapter presents the findings from both stages of the study. The results will be reported in three sections. Section one (stage one), covers findings from a systematic review. The result of stage one will be used to inform the formulation of semi-structured research questions that guided the stage two studies. While section two (stage two) study comprises of two subsections: Stage 2a reports the focus group discussion with breast cancer survivors and the last section Stage 2b reports the in-depth interview with oncologists. The results and analysis of these qualitative studies comprising of a) four focus groups discussion with breast cancer survivors, and b) face to face interviews with 12 oncologists in order to explore the awareness and perceived impact of cognitive changes in their functioning at work will be reported. At the end of this chapter, a summary of current research findings will be provided.

## 4.2 Stage one: systematic review

#### 4.2.1 Qualitative studies identified for review

A total of 3628 papers were identified electronically following the search using the keywords "chemobrain" and "chemotherapy" and "mild cognitive impairment". These papers were further scanned for their relevance, and this process reduced the number to 457 articles. Next, the criteria for inclusion were applied to the abstracts, and this resulted in 83 articles. Further examination of the full versions of these papers, according to the boundaries set by the focused research aim for this study resulted in seven papers that met the inclusion criteria for the review. Some of the qualitative papers did not include the study design in the titles of the publications, so it was necessary for the researchers to read and screen the methodology sections to ensure that a qualitative design was used. The full text for each of these seven papers was obtained and each study was appraised. Figure 4.1 outlines the search results for the review.



Figure 4.1: Identified qualitative studies.

## 4.2.2 Quality appraisal

Based on the CASP checklist table 3.1 as outlined in the methodology section, five of the seven papers were considered to have met all the quality criteria as judged by the reviewers. Table 4.1 below showed the result of the critical appraisal skill program (CASP)'s quality appraisal for the seven selected papers. The researchers record a Y =" yes", N ="no" or C = "cannot tell" to each question and then discuss to reach a consensus. Two studies did not meet one quality criterion, which concerned the adequacy of consideration of the relationship between researchers and survivors. These
two studies were still included in the review since the unmet criterion was judged to be a minor issue and did not adversely affect the relevance of the studies to the objectives of this review.

CASP Criteria	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]
Mulrooney Tamsin 2007	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Von Ah et al. 2013	Y	Y	Y	Y	Y	Ν	Y	Y	Y	Y
Cheung et al. 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Munir et al. 2010	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Myers 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Boykoff et al. 2009	Y	Y	Y	Y	Y	Ν	Y	Y	Y	Y
Thielen 2008	Y	Y	Y	Y	Y	Ν	Y	Y	Y	Y

Table 4.1: Quality appraisal for selected papers.

# 4.2.3 Data extracted from qualitative review

Table 4.2 outlines the summary of each of the selected papers for review and identifies the themes from each study. Based on the synthesis-of-order process, this table summarizes the first order constructs that reflect the understandings of the participants from each study and are usually summarized in the results section of each article. Four themes emerged from the analysis of the seven selected papers-: i) the chemobrain struggles, ii) the substantial impact from chemobrain, iii) the struggle to adjust and self-manage and iv) the 'thankful yet fearful' attitudinal representation. Four-second order interpretations were identified, on the basis of which four third order interpretations (based on key concepts and second-order interpretations) were constructed. These were all linked together in a line of argument that accounts for survivors struggle to self-manage the chemobrain impairment that impacted their activities of daily living. The summary of seven steps of meta-ethnography was presented in appendix I page 153.

Table 4.2: Summary characteristics of selected studies.							
	Aim	Sample & method	Findings	Conclusion	Limitation		
Von Ah et al. (2013) USA.	To obtain a better understanding of breast cancer survivors' experiences of perceived cognitive impairment, its trajectory, and its impact on the relationship, daily functioning, work and overall life satisfaction after breast cancer diagnosis and treatment.	n=22 breast cancer survivors who reported cognitive impairment at least one-year postchemotherapy treatment. Interview and content analysis approach.	Expressed concern in 6 major domains of cognition: short term memory, long term memory, the speed of processing, attention and concentration, language and executive functioning. Chemobrain is frustrating, affects self-confidence and social relationships. Difficulties in work and adapt using compensatory strategies. Validation of perceived cognitive impairment is important for adjustment.	Perceived cognitive deficits have broad implications for wellbeing. The study provides direction for theory development, measurement selection, and additional targets. Greater understanding leads to the development of effective treatment of these symptoms.	Limited by sample characteristics (geographic area and homogenous). Self-report might be influenced by previous participation in the cognitive behavioral trial.		
Myers, (2012) USA.	To provide an in- depth description of the experience of chemotherapy- related cognitive impairment for women with breast cancer and identify related information that women would find useful prior to chemotherapy and cognitive changes	n=18 breast cancer survivors who reported cognitive changes within 6 - 12months postchemotherapy. Focus group discussion, semi- structured interview and content analysis approach.	Survivors describe the difficulty of cognitive changes and the impact on daily living. Survivors share their coping skills strategies. Survivors want to get information prior to initiating chemotherapy and psychosocial education.	It provides a framework for better understanding regarding the changes that can be used as a guide for patient and family education and generates questions for additional research.	Coding was performed by a single investigator and as such may be biased. Interpretation by only one individual poses bias.		

# Table 4.2: Summary characteristics of selected studies.

 Table 4.2, continued

	Aim	Sample & method	Findings	Conclusion	Limitation
Cheung et al. (2012) Singapore.	To gather descriptions from multiethnic breast cancer survivors on their experiences and impact of chemotherapy- associated cognitive changes on daily lives and the coping strategies.	n=43 breast cancer patient receiving chemotherapy- Focus group discussion and thematic analysis.	Survivors were unfamiliar with the term's chemobrain' and viewed it as a result of physical and psychosocial adverse effects. Encountered memory loss, difficulty in decision making, speech problems. Married women claimed frustrations that limited their role as a homemaker. Self-identification of coping strategies.	This phenomenon is unfamiliar to most Asians yet it impacted their daily lives. Results suggested that a culturally relevant approach should be adopted to evaluate and manage cognitive changes in these patients.	Selection bias due to nonrandomized sample recruitment and response rate was low. No baseline assessment was conducted. Heterogeneous group. Priming effects and preexisting knowledge of chemobrain.
Munir et al. (2009) UK.	To investigate women's awareness of chemotherapy- induced cognitive changes, their perception of cognitive limitations in carrying out daily tasks and subsequent return to work decision and perception of workability.	n=13 breast cancer survivors who completed chemotherapy between 12 months to 10 years ago who have returned to work. Semi-structured interview with two focuses groups. Using template analysis.	Survivors noticed decline lasting about a year or longer in concentration, confusion and lack of clear thinking. Chemobrain negatively affects self- confidence in the cognitive ability and return to work, but support from colleagues and employers increased confident in cognitive skills. Impact related to work ability: poor memory, concentration, difficulties in thinking quickly, organising information, and decision making. Insufficient information regarding cognitive side effects from oncology team or support groups.	Chemotherapy-induced cognitive impairment affected returning to work and subsequent workability. Return to work and ability to manage work were influenced by three interrelated factors: 1) actual cognitive ability the following chemotherapy, (2) awareness of cognitive failures by the women and their families, & 3) subsequent impact on their confidence in carrying out daily tasks including work tasks.	This study does not explore issues in sufficient depth.

Tabl	le 4.2,	continued
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Table 4.2, con	tinued				
	Aim	Sample & method	Findings	Conclusion	Limitation
Boykoff et al. (2009) USA.	To document in- depth the effects that cognitive impairment has on women's personal and professional lives.	n=74 white and African American breast cancer survivors who experienced side effects at least one year beyond completion. Focus group/in-depth interviews and content analysis approach	Cognitive impairment can be problematic for survivors. Survivors reported it the diminished quality of life and daily functioning. Survivors suggested a range of coping strategies to manage social and professional lives.	Chemobrain impacts survivors' economically, emotionally and interpersonally. More research needed on the psychosocial aspect of post-treatment symptoms to inform the efforts of medical and mental health communities	This study was non randomised and participants self-nominated for the study.
Thielen (2008) USA.	To explore the lived experiences of the neurological changes women describe while undergoing chemotherapy for breast cancer	n=13 breast cancer patients are undergoing or completed adjuvant chemotherapy within 12 months. Interviews. A Descriptive Phenomenological Method guided analysis	Validated the existence of chemobrain phenomenon Women described it affected daily living. These findings may be useful for designing questionnaires, educational products, and interventional strategies.	A decrease in cognitive function is multifactorial in origin. The women's' feelings, meaning, and perceptions contribute to the fundamental of the lived phenomenon.	Small sample size: Participants were not of mixed ethnicity: sample were from Caucasian women. Inexperienced researcher
Mulrooney Tamsin (2007) USA.	To describe lived experiences of self-reported cognitive impairment in a sample of women who were treated with chemotherapy for breast cancer.	n=10 women with breast cancer – treated with chemotherapy within last 15 – 52 months. Interviews. A descriptive and interpretative Gadamerian phenomenological theory	Survivors described problems with memory, learning, concentration, language and multitasking. Incidents of chemobrain could occur at any time and affected activities at home, work, and relationships with friends and family Chemobrain caused by treatment of breast cancer.	The experiences of chemobrain can impact all aspects of life including work. Despite the belief of chemotherapy as a cause, other factors should be acknowledged.	Small numbers, homogenous participants with the similar demographic background, educational levels.

Table 4.3 outlines the meta-ethnography process that utilizes the Schultz notions of first, second, and third order constructs as the follow-up analysis. The findings from the synthesis (third order interpretations) are reported under each heading in the next section.

Concepts	Second order	Third order
Experiences of cognitive changes: Trajectory of cognitive changes, types of cognitive changes, cognitive domains affected, experiences of cognitive changes, awareness of cognitive changes Call for help and support: Healthcare providers to inform of possible cognitive changes, respond to medical community, how to teach me, Looking for answers in all the wrong places, underwhelming information for an overwhelming experience	<ul> <li>(a) Patients want validation that it is real and to be prepared for cognitive changes; want health staff to be proactive in addressing the issue; a strategy viewed as able to reduce tension and frustration of family members</li> </ul>	(b) The chemobrain struggle
Impact of chemobrain: Self and social relationship – how I changed, daily functioning, working life, psychosocial, financial, overall life satisfaction, change in all aspects of functioning	<ul> <li>(c) The significant impact of chemobrain phenomena on self, family, social circle, daily living and work performances</li> </ul>	(d) The substantial impact of chemobrain across life domains
Coping: Trying my best to fit in, coping strategies, adjusting to fit in, prior needs of information on cognitive side effects	<ul> <li>(e) Ways of coping derived by survivors with multiple strategies to help themselves to overcome the phenomena.</li> </ul>	(f) Struggling to self-manage
Reflect on survivorship: Thankfulness - I am still alive, Apprehension - what the future holds.	(g) Reflection on survivorship to attain normality and regain function	(h) Thankful for life, yet fearful of the future

**Table 4.3:** Synthesis of concepts, with second and third order interpretations.

#### 1. The chemobrain struggle

Chemobrain or cancer-related cognitive impairment was reported consistently as a real experience. The signs and symptoms were noticed by women with breast cancer, who described them in various ways. The term chemobrain offers a quick reference to a concept that may easily encapsulate a range of experiences and enable women to attribute their experiences to a concrete term. However, the phenomenon of chemobrain was experienced as a struggle, whereby the manifestation of the signs and symptoms triggered the survivors to question continually its existence and to question if their experience was real. There was a need to seek confirmation through various means, yet the conflict remained unresolved as there was no clear answer to their question, leading to a persistent struggle within themselves and with significant others.

Most women felt that chemobrain was an outcome of cancer and its treatment, and perceived themselves to be "chemobrain victims" (Mulrooney Tamsin, 2007) Studies used indirect probes to gain descriptions of the experience of chemobrain. These validated the cognitive changes by providing descriptions such as not being 'as sharp or quick' as before or feeling 'foggy' or 'spacey' after treatment (Von Ah et al., 2013). In a study involving Asian women, participants were only able to identify the term chemobrain or describe the symptoms when they were indirectly probed about their experiences (Cheung et al., 2012). Survivors noticed cognitive changes during and after chemotherapy treatment (Munir et al., 2010). Most of the breast cancer survivors reported changes in the cognitive domains of short and long-term memory, processing speed, attention, concentration, language, verbal memory and executive functioning (Mulrooney Tamsin, 2007; Munir et al., 2010; Myers, 2012; Von Ah et al., 2013).

Although other confounding factors (e.g. cancer-related fatigue, mood changes, lack of mental and physical activity, the cancer condition, ageing, hormonal therapy, lack of social support and menopausal status (Cheung et al., 2012; Von Ah et al., 2013), have been found to induce or worsen sustained cognitive issues, many survivors disagreed with this. They justified that they had problems with attention and concentration, although they agreed that they may be more easily distracted when they were tired (Cheung et al., 2012; Von Ah et al., 2013). Multi-tasking, in particular, seemed to cause concern and often resulted in feelings of anxiety and frustration (Mulrooney Tamsin, 2007; Munir et al., 2010). Survivors often described chemobrain as "frustrating", "upsetting" and some were frightened by problems in processing new information. This phenomenon was perceived to affect their emotions as they struggled to understand the changes occurring.

#### Timing of onset of Chemobrain

The onset of chemobrain has been reported at different times across the illness trajectory. Survivors had difficulty giving an exact time of onset of the chemobrain symptoms; however they seemed to lessen over time but not fully resolve (Mulrooney Tamsin, 2007; Myers, 2012). Some survivors reported they experienced changes in cognitive functioning after diagnosis, during chemotherapy or after one to two months of treatment (Cheung et al., 2012; Myers, 2012; Von Ah et al., 2013) with most reporting that they continued to experience it after the completion of chemotherapy. A rationale offered was that during chemotherapy, many other acute physical symptoms (such as nausea, vomiting, and fatigue) could not be ignored, and so survivors did not focus on the subtle cognitive symptoms. Women tend to be overwhelmed by having to suddenly adjust to the reality of a cancer diagnosis, starting chemotherapy and having a potentially life-threatening illness, so that they initially disregarded changes in memory or attention (Thielen, 2008; Von Ah et al., 2013). The present information suggests that cognitive changes can remain a long-term problem for breast cancer survivors.

Dealing with the symptoms or side effects of cancer treatment is a challenge that requires support from others. Family and friends were regarded as good social support systems that encouraged survivors to engage in activities and return to their role in the community. Healthcare providers were also seen as a potential source of support since they work closely with survivors. It has been reported that many healthcare providers are more nonchalant about the phenomena of chemobrain. Survivors reported that their health care providers did not discuss any issues relating to chemobrain (Myers, 2012; Thielen, 2008; Von Ah et al., 2013) and some were insensitive when survivors made complaints about their experiences of cognitive deficits. It seemed that the survivors were dissatisfied as they wanted professional validation of their experience of chemobrain symptoms, but they were largely ignored.

Healthcare providers often assumed that reported cognitive changes were due to other variables such as stress or the natural ageing process (Boykoff et al., 2009; Thielen, 2008). Conversely, some women reported that they did receive general information about the possibility of cognitive side-effects from chemotherapy from the oncologists or oncology nurses (Boykoff et al., 2009), although conversations were usually initiated by the survivors as they sought explanations (Mulrooney Tamsin, 2007). Women felt that early warnings and validation of these changes from healthcare providers with patient information could help them cope proactively with these changes (Boykoff et al., 2009; Myers, 2012; Von Ah et al., 2013). Support groups may help survivors to identify or recognize cognitive changes and to be better prepared (Myers, 2012).

#### 2. A substantial impact of chemobrain across life domains

Women described the impact of chemobrain on themselves, their social relationships, working life and daily living (Von Ah et al., 2013). Survivors reported

that family and friends ranged from being supportive of being unconcerned about their chemobrain experiences. Some women reported that the cognitive changes had affected their psychological well-being, and they lost self-confidence and self-esteem in the company of family members and friends. Survivors were often confused by their cognitive changes and then felt misunderstood or embarrassed. Survivors who were homemakers described memory difficulties adversely affecting their roles in the family, and that some family members had a lack of awareness about these changes. Some suggested their difficulties maintaining their homemaker roles were related to their own expectations about what they should be able to achieve (Boykoff et al., 2009; Cheung et al., 2012; Thielen, 2008). Some families provided considerable support as they understood the issues and were aware of the cognitive changes, and this was related to positive cultural values. For instance, Cheung et al. (2012) reported that the Asian value of living in communities and having a kindred spirit meant that members of the community became a source of support.

Cognitive changes often impacted on working life and school related activities. Survivors indicated that cognitive impairment affected their confidence in returning to work because returning to work would highlight their problems further and be too challenging (Munir et al., 2010). Survivors who had returned to work reported that they were struggling to perform and complete tasks. Their job performance had decreased due to an inability to maintain attention or focus at work, to maintain their thoughts during conversations and inability to comprehend a text without reading it more than once. As a result, work tasks required more time, and they were less productive. For some, this difficulty contributed to the loss of employment and difficulties finding work (Myers, 2012; Thielen, 2008; Von Ah et al., 2013). Professional women in jobs that required a high level of cognitive functioning were more negatively affected by chemobrain (Mulrooney Tamsin, 2007).

3. Struggling to adjust and to self-manage

While struggling to overcome cognitive changes, often without real support or acknowledgement from health professionals, most survivors developed their own strategies to overcome the effects of chemobrain, to prevent further complications and to help them cope with daily living and work functioning. These are listed in table 4.4.

Coping strategies	Mulrooney Tamsin (2007)	Cheung et al. (2012)	Munir et al. (2010)	Myers (2012)	Boykoff et al. (2009)
Pharmacological				U	
Nutritional products		Х			
Complementary and		Х			
alternative medicine					
Non-Pharmacological					
Healthy lifestyle		Х	X		
Physical activities		Х	X		
Mental activities	Х	Х	Х	Х	
Psychosocial	Х	X	Х	Х	Х
management					
Practical Reminders					
Written reminders	Χ	Х	Х	Х	Х
Technology	Χ	Х			

**Table 4.4:** Coping strategies adopted by survivors.

The majority of the survivors used non-pharmacological strategies such as mental activities, psychosocial management, and practical reminders while some survivors trained themselves in memory strategies to remember things more easily. In the Asian study by Cheung et al. (2012), the use of complementary or alternative medicine was more popular than pharmacological intervention as participants perceived these remedies would enhance energy and improve blood circulation to the brain. Coping strategies for some survivors meant avoiding situations that required them to remember names and engage in social conversation. Many survivors decided not to focus on their disabilities and adapted their environment to cope with chemobrain by sharing with others about their cognitive changes (Thielen, 2008) Other survivors relied on their

family members and co-workers to remind them about important things (Myers, 2012; Thielen, 2008).

## 4. Thankful for life, yet fearful of the future

In spite of the challenges of daily living activities and the psychosocial impact, during the chemobrain experience, these factors did not cause women with breast cancer to withdraw from chemotherapy treatment. Survivors appreciated receiving chemotherapy as it reduced their risk of mortality. Most were grateful that they had survived, and some took their diagnosis as a turning point in their life. They worked towards personal goals for self-satisfaction and some women placed a higher priority on developing relationships with family and friends and contributing to wider society (Cheung et al., 2012; Von Ah et al., 2013). "Life isn't guaranteed, and I try not to be real pessimistic, but it is a wake-up call. You are not guaranteed that tomorrow will come" (Mulrooney Tamsin, 2007, p. 122).

However, Thielen (2008) reported that survivors were still living in doubt about their cancer prognosis and the likely duration of their chemobrain symptoms. They were apprehensive about the situation as they had received little information about chemobrain. This created additional stress for survivors who were attempting to self-manage what they saw as obvious impairments. This also led them to adopt the belief that they should be grateful (to be alive), and 'downplay' cognitive impairment as a lesser issue to self-manage their return to their normal state.

## 4.2.4 Illness representation theory to inform interpretations

The line-of-argument synthesis using the Leventhal model enabled us to frame the significance of the burden of cognitive impairment in cancer survivors. In table 4.5 attempted to present each dimension of Illness Representation Theory (Leventhal et.al, 1997) in the context of the experiences of chemobrain from the reviewed studies. The

cognitive and emotional processes experienced by women were captured and may influence their mental image of potential threats attributable to chemobrain. The interpretation that chemobrain is a relatively small issue (in comparison with death for example) may underestimate the threat of the debilitating effect chemobrain can have on everyday functioning and quality of life. The burden of cognitive impairment in cancer survivors appeared grossly underestimated. This warrants it to be addressed promptly as studies have shown that illness perceptions have associations with a number of negative outcomes in the experience of chronic illness including self-management behaviors and quality of life (Petrie, Jago, & Devcich, 2007), and this can be anticipated within the breast cancer population.

Dimension	Potential Manifestations (per illness representation theory)
Identity	Matching or nonmatching of cognitive symptoms to the chemobrain experience (e.g:matching symptoms like feeling foggy, not as sharp, not as quick referring to the chemobrain syndrome; or rationalizing it as 'deficits are unimportant compared to getting through treatment, surviving from cancer)
Timeline	Beliefs about the expected onset/duration of it (e.g., acute vs. chronic or cyclical). Increasing reports of survivors' belief that chemobrain starts after they resume work, but most are unsure of exact timing. Some believe it is transient, but others fear its persistent impact. There will be some degree of struggle- transient to persistent.
Consequences	The perceived and anticipated impact of chemobrain (e.g., reversible vs. static vs. progressive or permanent). Subjects highlighted that chemobrain affected their daily functioning, economic status, and their social relationships. Some believed these impacts might get better while others feared that the cognitive deficits may be a permanent loss. The underlying finding is that they will have to struggle with it.
Causes	They perceived the contextual factors or antecedent causes (e.g., aging, stress of having cancer and treatment, rather than from treatment since there is no evidence on the mechanism and since their health providers did not validate chemobrain) leading to a constant struggle
Controllability	An expectation that chemobrain symptoms can be somewhat controlled via coping strategies, but may not be cured and may even be permanent damage. Survivors were struggling to adjust. A belief that they should just self-manage since "it does not seem to be a significant according to the health providers.'
Illness coherence	The subjects' perceived understanding of the chemobrain phenomena – (i.e., vague, subtle, foggy, and space) but the health team did not validate it, suggesting a period of uncertain struggle.
Emotional representations Based on the 1	Panic and frustrated in response to chemobrain experience. The sense of dissatisfaction and anger that they were not forewarned. Neutral or matter-of-fact emotional state (for some). Again manifesting a constant struggle within themselves and with significant others.

 Table 4.5: Interpretation based on illness representation theory.

Leventhal, 1984; Howard Leventhal et al., 1997).

# 4.2.5 Formulation of focus group guide

The result from stage one: The new syntheses is involved in the formulation of focus group guide for stage 2(a) study based on the results of the systematic review in stage one. Below are the end results from the third order interpretations:

1. The chemobrain struggle

- 2. The substantial impact of chemobrain across life domains
- 3. Struggling to self-manage
- 4. Thankful, yet fearful of the future.

There is three topics that arose based on the comprehensive review from stage one, based on the results, it demonstrated patients, experiences, impact, and management of chemobrain. From this major topic that emerges from the studies, the researcher used it as guidelines to explore the lived experiences of cancer-related cognitive impairment in a particular related to functioning at work place.

# 4.3 Stage two: Qualitative studies

# 4.3.1 The aim of the qualitative studies

In this stage, it presents the findings from both groups of stakeholders in this study. It comprises of results and analysis from a) 4 focus groups discussion of breast cancer survivors and b) face to face interview with 12 oncologists to explore the awareness and perceived impact of cognitive changes of work functioning among with breast cancer and health care providers. It based on aim of this study to explore the perspectives of cognitive changes from healthcare providers and the impact of cognitive changes in functioning at work as experienced by women with breast cancer who have completed chemotherapy:

#### 4.3.2 Focus Group Discussion (breast cancer survivors)

#### **4.3.2.1** Demographic data of participants

36 respondents who underwent a brief cognitive screening and subjective assessment from the earlier phase, however only 17 breast cancer survivors turned up to participate in four focus group discussions that consisted of two groups of professional background and another two groups of non-professional background. Participants were recruited within six months to three years of post-chemotherapy treatments. All 17 breast cancer survivors subjectively reported having cognitive changes upon receiving chemotherapy treatment and had returned to work after receiving chemotherapy treatment regardless of the changes of current work status. The group participant's age ranged from 27 years old to 56 years old. 12 participants were Malay breast cancer survivors, and the remaining five participants were Chinese. Prior to the diagnosis, 15 of them were fulltime workers, and the other two were part-timers. All those women returned to work on average of eight to twelve months after chemotherapy, but there few of them made some changes in their work status. The participants underwent chemotherapy treatment, and most of them had undergone other treatments to manage breast cancer, for instance, radiotherapy, hormone therapy, and surgery. One patient had quit the job one year after returning to work, three patients returned to same organisations but have to scale down their work, two patients changed the organisations and had scaled down, and one has changed the work status to part-time, while the rest returned to the same organisations with some amendment on working hours. All participants were screened using a screening tool for cognitive impairment using MoCA. 10 out of 17 participants scored below 26, which indicated that they have mild cognitive impairment. Table 4.6 show the demographic data of the breast cancer survivors.

* <b>P</b>	Age	Education	Ca.	Occupation	Occupational	MoCA
_	_		stage	_	status	
1 <b>B</b>	45	Graduate	II	Business	Scaled down work	21/30
		school		manager		
<b>2B</b>	42	College	II	News	Flexible hours	28/30
				presenter		
3B	45	Graduate school	II	Teacher	Flexible hours	25/30
<b>4B</b>	42	Graduate school	II	Accountant	Part time	27/30
5B	51	High school	Ι	Clerk	Flexible hours	22/30
6B	44	College	1	Sales assistant	Flexible hours	24/30
7B	56	High school	III	Personal assistant	Flexible hours	25/30
<b>8B</b>	54	High school	III	Clerk	Flexible hours	26/30
9B	47	Graduate school	II	Administrator	Different post.	27/30
10B	51	High school	Ι	Clerk	Quit after one year RTW	22/30
11 <b>B</b>	34	Graduate school	II	Teacher	Reduced hours	29/30
12B	37	Graduate school	Π	HR officer	Flexible hours	23/30
13B	39	Graduate school	Π	Teacher	Scaled down work	23/30
14B	29	High school	II	Clerk	Flexible hours	27/30
15B	27	High school	Ш	Production operator	Different post	25/30
16B	36	College	III	Sales	Scaled down work	25/30
17B	27	Graduate school	II	Clerk	Flexible hours	29/30

 Table 4.6: Demographic data of Breast Cancer survivors

\*P: participant; Ca stage: Cancer stage; MoCA: Montreal Cognitive Assessment; RTW: Return to work



# 4.3.2.2 Analysis of findings with breast cancer survivors

Figure 4.2: Themes from the perspectives of breast cancer survivors.

Figure 4.2 summarizes the themes from the perspectives of breast cancer survivors. Findings from the analysis of the study are reported under each thematic heading, and it is presented together with participants quotes.

#### 4.3.2.3 Varying level of awareness

• Lack of information on chemobrain

Awareness of cognitive changes issue among breast cancer survivors varies across the participants' groups. Response from the participants was ambiguous, where most of the participants from non-professional background have never heard of the term used for 'chemobrain' as an opening remark of the topic discussion or even 'cognitive changes' to represent the phenomenon among this group. Most of the participants have a lack of awareness on chemobrain issues; on the other hand, only a few survivors from professional background seem to be alert to this issue.

"Chemobrain? No, I never heard of this". (15B)

"I know about cognitive. It is something that is related to our brain. But that is all I know". (8B)

"After the chemo, I experienced a lack of focus and forgetfulness,. I asked questions, someone answered but two hours later, I asked again. These were things that I experienced, but I didn't know it was called chemobrain. I had experienced this symptom; I know it is related to chemo, but I didn't relate it as chemobrain". (1B)

Some participants experienced and noticed the symptom but were not aware of the phenomenon. They only realised the existence of the phenomenon once they approached and were screened by the researcher.

"I started to realise about it when you ask me to participate in the study and during the screening process, I noticed that I have the symptom especially when I started working". (7B) Participants expressed that they were never told about the cognitive side effects from any health care provider that they have gone to. Despite experiencing the symptom in daily life and due to lack of information given, participants are however unable to voice out the issue to the healthcare providers, especially the doctors care. They knew that the problem affected their life, but they forgot to make complaints about it when they have the opportunity to meet the doctors. Furthermore, the information from the pamphlet given by the hospital has not included cognitive side effects.

"Like what I said, I don't even remember to complain about this. It's not that I don't want to complaint, but I don't remember!". (17B)

• Significant time -lapsed before realisation

Few of the participants experienced the onset of cognitive changes during the chemotherapy treatment, but for most of them, the onset came later after chemotherapy and experienced significant changes after returning to work.

"I had this symptom during the third cycle of chemotherapy, I could remember to multitasking on errands, manage bills and all. But now I am missing a lot of things". (17B)

"So the first year, my concern is more on my physical aspect, I focus on the pain, fatigue and so on. The mental issue was still manageable. I don't seem to have a problem organizing my unit, but there's a huge difference in my second year after returning to work. I have no idea what to say in meetings. My mind was blank". (9B)

On average, most of the participants experienced and started noticing the onset six months after chemotherapy treatment. They seemed to be unclear on the changes occurred and were struggling to cope with earlier acute adverse side effects, which are more related to physical side effects. ".... six months or more than six months. I think I focused more on the physical changes at first because we need time to recover. But other side effects like the mental and cognitive parts, these are after six months". (2B)

Participants reflected that it was a slowly progressive symptom for them to realize; however, it was getting better in time when they started to pick up a better way of handling the problem.

"These cognitive symptoms, I felt that they appeared gradually. It's not just once we don't remember things. Eventually, we notice that we are getting slower and blur, my mind was not sharp". (5B)

"Yes. It took me a while to notice the symptoms." (7B)

• "Stumbled upon it."

For some survivors, the fact that they have breast cancer made them more alert and curious on the side effects of the treatment, hence making them realise that chemotherapy treatment affects their cognitive as well. Some of them who had noticed the cognitive changes earlier on had the initiative to self-search on the information regarding the side effects and they gained the information upon general search on the side effects. They found the information through the internet, reading the newspaper, and discovered the issue via a casual conversation with other breast cancer patients during clinic follow-up. Conversation with other survivors revealed to the participants that it was normal for them to get or have cognitive impairment.

"... I came across this term in the newspaper, through a Chinese newspaper because normally I flip through Chinese newspaper. So I came across this Chinese newspaper, and for those people like us who have gone through chemotherapy, we get very sensitive about chemotherapy, what it is and all about chemotherapy. So I came across this term and mainly it is about the side effects following chemotherapy. To a certain extent, damages have been done to your brain cells, causing something like being forgetful, having a problem in focusing and even the way you think. Somehow, it affects the way you make a decision. It is very hard for you to explain, and you can't remember. So I just read through, and it matched with my own experiences". (2B)

"I googled it on the internet after I was diagnosed with breast cancer and before I had my chemotherapy. So I wanted to know what are the side effects of chemotherapy but suddenly I saw the word chemobrain, so I wonder, what is chemobrain? Is it something that is related to my brain? So I just googled and read what it is all about. But after I had my chemotherapy, I felt something in my brain... foggy". (3B)

"I had talked with other survivors during our radiotherapy treatment and, they admitted to having the same problem. So previously, I thought I was the only one having a speech problem, but then they all have it. At first, we all assume that no one has this, but when we all admitted, it is real then". (17B)

The sharing session between survivors who had gone through the same experience and combined with personal research on information related to cognitive changes allowed the participants to be at ease knowing that what they are going through is normal.

"It is quite a relief you know because I feel like 'ooh... it's normal actually'. Because I have gone through this therapy, chemotherapy, so I don't have to worry so much because it is part of the side effects and is considered normal". (2B)

#### • Misconception about chemobrain

When asked about the terminology; 'chemobrain', those who never heard of the term started to assume that it might be related to the cancer being spread to the brain and required chemotherapy for treatment, while other participants thought that there is something wrong with the brain. When the groups were asked how they perceived the word chemobrain or cognitive impairments, the first thing that always comes to their mind is memory related.

# "It's the brain, (administering) chemotherapy onto the brain". (16B)

However, there is still uncertainty about the causes and mechanisms of cognitive changes after undergoing chemotherapy treatment. The existence of forgetfulness and other cognitive impairment created a subtle perception of cognitive changes after chemotherapy. Most women expressed that they did experience the cognitive changes, but they did not acknowledge the cause from the treatment and perceived it as a sign of biological (aging) process. Most participants relate it to psychological effects.

"It gets worst (cognitive changes), and I thought it is because of my age". (10B)

"I'm so worried when I was diagnosed. I think a lot felt worried and stressful. So I tend to forget a lot of things". (13B)

"When I first realized I had the symptom, oh, now what? Alzheimer?". (2B)

#### 4.3.2.4 Debilitating impact on work functioning

• Lowered self-esteem and low confidence

Participants discussed their view of the impact of cognitive changes on the emotional aspects. Participants expressed that they lost confidence and started to underrate their workability.

"I can't perform, I'm not conscious, I cannot work, I cannot present. I don't even know which way I'm going, where I am now, why I'm lost. Where is the toilet, where am I now, where am I going to go, what I'm going to do,- Blank".(2B)

"I feel that it lowers my self-esteem. At the office, I start to compare myself with my colleagues, I feel inferior to them". (15B)

They started to have a fear of making mistakes in front of clients; they rejected the promotion was given and communication in front of people, giving the anxiety of the occurrence of 'mental block'.

"I try to stay in my comfort zone rather than scale down. Even when the opportunity comes; I just leave it because my confidence is affected... half an hour before I went on air. My mood was totally affected. I have no confidence because it's like being traumatised you know". (2B)

"Where I work, there are a lot of international students. But after returning to work, it is hard for me to communicate with foreigners. I tend to forget even though I have done this for a long time, but after chemo, not anymore. I lost confidence; it is hard for me to communicate; I have the fear of doing it wrongly". (5B)

They constantly feel frustrated that they could not achieve and fully contribute to the team. They expressed their concern about the ability to contribute to the teamwork in former organizations and their work performances were affected. Failing to achieve the expected job demand has caused an emotional impact on the participants. They were under a lot of stress and frustrated with the job output when they were unable to keep up with the tasks.

"I'm in charge of the complaint unit; I need to go through reports from my colleagues and send it to the higher board meeting. To present the data, I need to know all the information. I feel very stressful because it was very hard for me to pick up certain things". (9B)

"...I noticed that my work output was terrible, that is why I didn't dare to take a fulltime job anymore. To me, I felt guilty if I take the payment". (8B)

Being supervised on work constantly had put them under a lot of pressure; it lowered their confidence in doing work independently. These utterances suggested that participants were battling on psychological and emotional issues.

• Changed of role or job or early retirement

Upon returning to work, all women were overwhelmed with cognitive changes. On average of those who return to work, it took at least 6 months to re-establish their work function and some still struggled to adapt to the changes even during the second year after they have returned to work.

"When I started to work, handling work tasks... Oh my God! Even to switch on the computer was confusing to me. I have no idea that steps come first. It took me about one month to re-establish my skill. My brain... it is so bad". (10B)

Participants with professional working background have experienced greater burden on related job demand and resulted in the transition of work status. The higher demand for work functioning linked to critical decision making makes them different from participants with the non-professional background.

"Now, I don't remember the workflow, to which I deal with, I don't remember. When my boss follows up with me, I try to recall but I couldn't". (9B) Non-professionals have described their work as something that they keep repeating every day. This routine type of job assisted them to regain the work function and help to reduce the burden impact. Moreover, non-professionals worker work together hand in hand with other colleagues, whom they can rely on during the state of difficulty period.

"I do a lot of reports. It was the same task every day, so I knew what to do". (6B)

"But for me, I have not encountered many problems in work. I work as a factory operator. I keep repeating my work every day. Sometimes I'm a bit lost but I can still finish my work task". (15B)

"It's been two years sinceI was on leave. But it doesn't matter if I can't recall my work tasks, it's a routine work. So I just need to re-establish with the help from my colleagues". (7B)

The quantity and the quality of the work caused some to decide on making a job transition. One of the participants found that the working environment and pressure due to the effect on cognitive have led to the decision of early retirement. Most of the participants have changed their work status, scaled down and opted for working hours to cope with the existence of cognitive changes.

"I decided to quit my job because I could not remember a lot of things." (10B

"This year I have changed for 'pool post'. I requested for the post, so other people can replace my job that requires a lot of decision-making. It allowed me to have time to recover". (9B) Hence, performances in work functioning were affected, as participants discussed that their key performance index did not reach the expected marks. They kept getting a lower score in examination and test, and they needed to repeat sitting for an exam. Also, some of them have found a new job that they felt was suitable for their condition. They chose to work in an environment that is personal to them, for example, starting an online small business and working with a family business that is believed to reduce their work burden and stress related to work.

"Because the thing is, I pull myself out from a full-time job. I'm currently only supervising as a part-timer. So for me, I don't have to do it on a daily basis like I don't really have to deal with it but as I said, my other daily routines doesn't affect me so much".(1B)

• Extra effort/time taken to complete task

Most participants, with either professionals or non-professionals, have experienced cognitive changes, which impaired their functioning at work. However, severity often happens within the group of people with a professional background. It was more obvious when participants have difficulties focusing attention and concentration to tasks. They reflected that they had to put in extra effort to finish tasks at work. It took several attempts to get the job done. Some of them work for extra hours to accomplish the work given on that day. Participants reflected that it was time-consuming to finish one-hour work task as it can drag up to two or three hours as compared to before.

"It is something that I did over the years: it's very simple. But then after you do it for some time, it's like, it's getting a bit difficult. You just want a break, you don't want to do anymore, let's just put this aside. So it gets slower". (4B) "That time when I was still working as a full-time worker, I tried to compensate by staying back very late. I was in a private sector, so I end up stayed long hours to compensate". (8B)

"...I used to complete my work in a day but now, it took me three days to complete it." (9B)

# 4.3.2.5 Social climate at workplace

• Positive support from colleagues and employer

Prior to returning to work, employers were supportive towards the participants. Most of the women received an offer from their employer to have flexible working hours or reduced working hours, especially after seeing participants struggling with the cognitive issue.

"At work, my employer has reduced my work responsibility. Other colleagues were responsible for handling a few of my work task, and I was given working hours reduction. He understands my condition. That's it". (5B)

Colleagues were always reliable when they sought for help. They received personal coaching from their colleagues, and some were supportive enough to help them in handling and managing work tasks. Common mistakes that they have done were corrected by their colleagues before proceeding to other work tasks. The supportive working environment helped participants to cope with their emotions on fear of unable to achieve work expectations.

"In managing computer problem, I will seek help from my colleagues. They will help me with the work process, and I write down all the steps". (5B) "Luckily I have a lot of colleagues, so when I lose focus, I told them the important matter, and they will do it". (16B)

# 4.3.2.6 Trying to self-manage

• Acknowledge and acceptance (rationalise)

In managing the adverse cognitive side effects, all participants reflected that the most important way to manage this symptom at work was by accepting their current ability in handling the task at work. Forcing themselves to the idea of "return to normal/former work functioning" is unacceptable, in which they felt it did not assist them in managing their emotion to cope with the struggle.

"I supposed to a certain extent, instead of saying it's totally gone, actually we found a way to go around it". (4B)

"I learnt to deal with my job tasks one by one. I told my boss; I can do this, but I need to do it at my own pace". (9B)

Some participants found that confronting their colleagues and employer about their cognitive changes gave them a chance to rebuild their confidence in work, as it helps others to be more understanding of the problem. Hence, it established a good working environment.

"Sometimes it can be useful as well. I just highlight to people around me, because I do get assistance from them. Because of the forgetfulness, so I just let people around me know that I have this problem. It's the same thing where I might repeat this problem again and again because I forget. But because I did mention it earlier, so they just bear with me". (2B) "Initially, I gave my responsibility to my colleagues, until I gain my confidence to work independently". (17B)

• Reliance on technological devices and applications

Technology devices and working aid tools promote their independence in work functioning. They often forget an appointment, names, and even work deadline. Therefore, they often rely on their best companion of all time – smartphones and tablets with applications that will always remind them of all important events at work as they can always refer to their smartphone if they happened to have forgotten something. Some felt that to write everything in little book memos is quite struggling for them.

"Because I cannot remember, where did I put down my memos? I noted it, but I can't even find it, so I use the phone". (2B)

"I just spare time on myself, everywhere I go I will bring my handphone and make sure that the GPS (Global Positioning System) in my car is functioning". (3B)

Nowadays, there are a lot of mind-stimulating games, such as Sudoku and puzzles that they can download to their gadgets. They frequently use them as a method to keep their brain active as they believe it enhances and improves their cognitive abilities.

"When she said [referring to 7B], playing application games, I also started to play games. It's a memory game. The farming game, I need to memorise a recipe, and I have to farm the ingredients in the recipe. I'm new to the game, I started a few months back, but it helps me to increase my memory". (9B)

"I think it has a lot do with our mind. I practiced with Sudoku, games that are mind stimulating". (14B)

• Use of problem-solving strategies

Changing the way you perceived things to accept current condition is one thing, and taking action towards it is another, as self-managing provides the participants a sense of self-control over the condition that occurs among them. Most patients felt that they experienced mental exhaustion and were unable to give focus and concentration at the workplace. They now plan earlier ahead and prioritise their work. Delegating work among members maximizes their ability to accomplish work given. Taking break consistently from time to time helped some to manage the problem, and for some, they required a nap between 10 to 15 minutes during working hours.

"Now, I have started to write my plan today and for tomorrow. I'm doing a checklist". (9B)

"I had to take a walk and take a deep breath and come back and do it". (1B)

"When you are unable to concentrate, all you need is to relax. You can't even think, so you need time to rest. Sometimes take a nap for a while". (5B)

They overcome the memory issue by selectively picking the most important thing to remember and always keep memo or notebook at all time to record every instruction and particulars of the tasks given. Table 4.7 outlined strategies management that has been adopted by working breast cancer women.

"I obviously have to write everything in the office, for all the things I can't remember. Bank account numbers, phone numbers, everything, is here you know. I write it down and put it somewhere that I can find". (4B)

"I wrote all the things for work, I made a copy and put it in a file, I have a daily file, fail timbun". (9B)

No	Technique
1	Work simplification techniques
2	Energy conservation techniques
3	Paper-and-pencil techniques
4	Smartphone applications and technology devices

# Table 4.7: Management strategies at workplace

• 'Work' as a mean of recovering

These are the common points that emerge consistently throughout the focus group participants. Be it they have successfully returned to work to the same organization and responsibility, changes of responsibility, reduce workload, change job, or even early retirement, they all expressed that works are seen as the solution to cognitive changes. Through work process, they felt it 'polished' their mind and gave them sharp and quick response towards challenges. Those who have retired and scaled down reported that cognitive changes were more prominent prior to unemployment and during work transition.

"We need to work. The more I use the brain, the better. Previously, I didn't know how to go back home but now, not anymore".(3B)

"For me, during my medical leave, staying home, not working causes my brain to be inactive. Every day watching television, there... it makes it worse". (6B) The strategies management adopted by breast cancer survivors based on both stages of this study (other studies in systematic review and current qualitative study) are presented in appendix J page 155.

#### 4.3.3 In-depth interview (oncologists)

# 4.3.3.1 Demographics of the participants

Participants of this study comprised of 12 oncologists, six of them were female and six were male. In terms of ethnicity eight of the participants were Malays, three of them were Chinese and one was Indian. The participants' age ranges from 37 to 55 years old. The participants are qualified oncologist as they have served in their field range from 1 year and up to 21 years. Estimated cancer population treated by these participants' are approximately 500 to 4000 patients annually. All parting oncologists have experience in managing breast cancer patients. Table 4.8 show the demographic data of the oncologists.

	Age	Gender	Race	Training	Patient	Years of
					Population	experiences
					served	
<b>1H</b>	37	Female	Malay	Local	600/year	3 years
<b>2H</b>	55	Male	Malay	Local &	1500/year	25 years
				abroad		
<b>3H</b>	52	Male	Malay	Abroad	4000/year	20 years
<b>4H</b>	34	Male	Indian	Local	2000/year	6 years
<b>5H</b>	37	Female	Malay	Abroad	520/year	8 years
<b>6H</b>	39	Male	Chinese	Abroad	560/year	10 years
<b>7H</b>	38	Female	Malay	Local	3000/year	13 years
<b>8H</b>	39	Male	Chinese	Abroad	500/year	10 years
9H	40	Female	Malay	Local	450/year	10 years
<b>10H</b>	40	Female	Malay	Local	900/year	13 years
11H	38	Female	Malay	Local	800/year	9 years
<b>12H</b>	37	Female	Malay	Local	1000/year	5 years

 Table 4.8: Demographic data of oncologists.

#### 4.3.3.2 Analysis of findings with oncologists



Figure 4.3: Themes from the perspectives of oncologists.

Figure 4.3 summarizes the themes from the perspectives of oncologists. Findings from the analysis of the study are reported under each thematic heading, and it is presented together with participants quotes.

#### 4.3.3.3 Lack of awareness

• Lack of related knowledge on chemobrain

When oncologists were asked about the term 'chemobrain', the quick response from them was quite definite that it was a misnomer and did not explain the phenomenon. Most of the oncologists have come across the terminology but have not studied it indepth now. However, among oncologists, there are a few who have never heard of the existence of this phenomenon. It was further probed to review what they think of cognitive changes after chemotherapy. A few oncologists felt that it was not on top of their priority and. some felt it is real, but it is not a well-defined phenomenon.

"I don't think I can... I mean, to go into details, because I do not know what chemobrain is because I have heard, but I don't know". (11H)

"I don't know because the term doesn't explain to you what you are talking about. When you say 'chemobrain', nobody has heard of that term. So what are you talking about?". (3H)

"I'm aware of it being a decline in cognitive function with time due to the direct effect of chemotherapy. So it has been observed in a number of malignancies, and I think it is very well established in the paediatric population, also I think that recently, there are a lot of attempts to look into it in an adult patient. I'm aware of some publications, but I'm not sure of the findings. I haven't looked into it yet". (1H)

• Low scientific evidenced on chemobrain

They reflected that there was still a lack of evidence to show the existence of chemobrain or to relate chemotherapy with mild cognitive impairment. Regarding the causes, the oncologists kept on enquiring and questioning the evidence of chemotherapy leading to mild cognitive impairment, as they believe that from their experiences, chemotherapy drugs does not cross the blood-brain barrier. Also, there is no available prevalence of cognitive changes that occurred among cancer patients reported in Malaysia, as well as the lack of any in-depth research that suggest the existence of the phenomena. Some of the participants believed that alkylating agent is the potential culprit that causes the cognitive changes.

"As I said, it's very difficult to generalise because we do not know how bad it is in the local population. We know from studies on chemotherapy and radiotherapy, Asian response differently as compared to Westerners. It could be very different in a positive way. So that the instance could be very low, or the incidence can be extremely high but until now, we don't know what it is like in our population. It's difficult to make any conclusive decision about that". (4H)

New cases of breast cancer take up 1/3 of the cancer patient population that they received each year. Most of the breast cancer patients were middle age and beyond, ranging from 45 to 70 years old. Cognitive issues could be due to biological responses. According to the oncologists, it is difficult to comment on the cognitive issue for the elderly as most of them would either have the symptoms because of biological aging process or they are retired or unemployed. The oncologists stated that there were other confounding factors that may contribute greatly to causing cognitive changes instead of the changes resulting from side effects of chemotherapy alone. They strongly feel that the psychological aspects may also contribute to the problem due to the overwhelming reaction to diagnosis, which can cause the patients to have cognitive impairments. They often link it to the physical aspect, as the patients will experience fatigue and weakness, which they believe will affect their focus, concentration and slowing down the thinking process. Upon diagnosis, they received patients with a degree of depression, as well as experience societal pressure. This could potentially mask some of the symptoms that they have experienced. However, some of the Oncologists viewed it as the results of toxicity of the drugs and treatment, as well as changes in the structure of the brain that cause cognitive declined.

"I think there will be some differences on side effects according to the treatment given, So I would say chemotherapy can cause a decline in cognitive function, but it may not be the only reason for it". (1H) "Chemobrain started even before chemotherapy. So the term 'chemobrain', maybe it's just not the chemo... after diagnosis, even the diagnosis itself might cause some level of depression, that might affect the slowness in thinking and other treatment as well that is involved in the management of the patient. Although the term is chemobrain, it is just not about the chemo, it is a multifactorial caused". (5H)

"...I'm not convinced that chemo crosses the blood-brain barrier... so how does it cause something like that? So there are a lot of confounding factors involved. The patient's psychological background, the impact of the diagnosis, and impact of having treatment. All this is confounding factors". (10H)

• Under-experience with chemobrain issues

Most of the oncologists have not come upon patients that came to the clinic and subjectively reported the symptom to them. For oncologists that received complaints from patients, those reports were negligible from the total amount of cases that they have received each year. From their experience, patients, especially those who worked in government sectors, were entitled to two years of leave starting from the time they were diagnosed. Furthermore, they received a frequent demand from patients to take leave, and some patients would even opt for early retirement and therefore, having cognitive impairment was not a major concern for them. It is a long-term effect that would not have much burden or impact on retired and unemployed patients. One oncologist did notice through his observation and during a few sessions of a follow-up interview with his patient. He noticed that the patient was not as sharp as before when handling questions from him, as well as began having difficulty expressing herself in words. Loss of memory is a common complaint that most oncologists received. Patients have difficulty remembering new information and recalling information. Most
complaints came from people with working experienced, as well more educated patients and aware of this phenomenon.

"So the effects of having declining cognitive function are not a problem; it becomes something that helps them decide that they are not going to work for the next two years. We have that a lot. Early stage I breast cancer already asked for ILAT, ILAT is a retirement scheme, and they asked for two years medical leave". (10H)

"I do see that among teachers. I think the two patients that have made a complaint to me; in the past few months, both were teachers, where memory places a very important part in their work. So the inability to recall certain things causes a lot of stress to them. I hardly or never heard any complaints from a housewife, but always from working patients". (4H)

"Cognitive changes, the only thing that the patients tell me are, they are having some memory problem. They don't tell me anything else. Some people have difficulty sleeping while on the chemotherapy, and these changes continue for a while after that, maybe for a few months or a couple of years. They go back to normal. Occasionally, when we hear it, the patients tell us that they notice some changes. Usually, it's memory". (3H)

Time restriction is the primary argument for the oncologists to assess patients on the cognitive issue, as it is time-consuming to conduct the test in the clinics. Furthermore, they receive a large number of patients per day in the clinic; therefore, accommodating cognitive screening is challenging due to lack of manpower to conduct the test, and it is not practical to implement testing without knowing the extent on how severe it impacts cancer patients beginning with chemotherapy. Oncologists do not routinely inform or suggest any screening for cognitive impairment practice in the public clinic at the

moment unless the patient initiated the question. Oncologists reported that most of their patients did not actively complain about the issue and some of the oncologists or the treating doctors were not even aware of it. It is a broad aspect to be looked into, and they have never been documented well in their reports. Some of the self-administered questionnaires were not culturally adapted to suit the Malaysian context, making it difficult for patients and health care providers to use the questionnaires locally.

"Yes, of course, it is important. At least if she knows that chemotherapy causes it, she will be less anxious about it. But again, it is something that is not very well studied. Not well proven. Not something that a patient and the doctor look at". (3H)

"I don't think the clinic can adjust to an additional 30 minutes or one-hour session just to screen this thing. Of course, we need to know what the prevalence is because, in any screening procedure, we need to know whether it's worth doing. Therefore, if the prevalence is very high, then, of course, we should screen our patients for that, but if the prevalence is very low, we might as well wait for the patient to complain to us".(8H)

"Yes, the questionnaires are there but sometimes the questions are not worded in a way where our local patients can understand. It's probably not been validated. Even those questionnaires that have been validated, it depends on patient's educational level and understanding, and some are not even educated. So they need someone to help them translate". (4H)

### 4.3.3.4 Beliefs and attitudes on chemobrain

• Terminology is vague and has negative connotations

The term 'chemobrain' can cause misconception to health care providers, patients, and our society. It gives a quick interpretation that chemotherapy damages the patient's brain. The brain has multiple functions other than cognitive, which involve motor function, psychological function, hormonal function and a lot of other things. Using this term will not reflect directly on cognitive ability. However, they suggest that the term used should be more scientific and words that describe the phenomenon should be something to do with declining cognitive function without relating directly to chemo.

"It's not suitable... chemobrain. It's not nice to call this as chemobrain like something is wrong with the brain". (2H)

"It could create a principle that chemo damages the patient's brain. And even you might use the term in public or media...I think is going to cause a lot of misconception. You know, to the already misconception, about chemotherapy. This will give more negative impression". (4H)

• Fear of patient's withdrawal

Most oncologists perceive the issue in cognitive changes as something that needs to be treated with caution as it may cause unnecessary fear cancer patients leading to withdrawal from treatment. The information provided to patients during the consent for chemotherapy session includes acute side effects such as nausea, weaknesses, vomiting, lost appetite and also some late effects. These are all established adverse effects that related to chemotherapy. Based on oncologists' experience, most cancer patients, and our society already have a negative perception on chemotherapy; hence, the subtle cognitive issue may add more negative perception on chemotherapy.

"We got to be a little bit careful about how we see this thing, because if we are going to make this as a big issue, patients are going to say 'if I'm going to forget things, then forget this, and I don't want to have chemobrain. I'm not going to have treatment'. I think that's going to have a very negative impact, so I think we have to be a bit careful on how we address this problem. If we make this a big issue, patients are going to start defaulting treatment and they are going to die from cancer". (2H)

"You know that chemotherapy has lots of side effects. If we make this issue as a big problem, some people will take it negatively. They think to a greater extent of the chemotherapy effects, especially those who really feel that the brain is important. So they become afraid if they lose all the cognitive function, they cannot work better and so on, maybe they will refuse chemotherapy. It gives a reason they don't want to do chemotherapy. That is the most common concern if we raise this issue". (7H)

"Because patients have a certain perception on chemotherapy and it's normally really a negative perception to the extent that sometimes they are scared of chemotherapy and think the worst of chemotherapy. But chemotherapy can improve the quality of life in some patients, especially the metastasis stage. So using chemobrain might add some negative perception to the patient". (5H)

• 'Chemobrain is not a major issue.'

Oncologists were more focused on the existing and obvious symptoms such as acute and physical side effects. They emphasized more on acute side effects such as neutropenia, which can be life-threatening. They are more concerned with patient's survivorship and adherence to treatment rather than cognitive issues that seem to be insignificant to them.

"I don't think it is a health concern. It's just patient, forget certain things. Yes... not a major issue". (2H)

"So the focus now you know how to get patient to present early, to have the treatment early, to have the surveillance, screening, and everything early. That is the issue. This chemobrain to me is last on the list. I'm sorry about that but to me, that's

the real thing happening here that we have to focus on the big issues and the big picture". (12H)

"As a doctor, we don't make this such a big point to them before we are considering of getting consent for chemotherapy from them. We are not really into this cognitive failure due to chemo and did not discuss more detail with them". (7H)

### 4.3.3.5 Future direction on chemobrain

• More research on prevalence/statistical data

Most of the participants expressed that without incidence rate of chemobrain and lack of patients complaining about the symptoms, they disprove of the need of addressing chemobrain issue at the moment.

"If we are going to make an active intervention, screening looking out for it and then doing early intervention, I think we need to have numbers first". (9H)

"Probably it is better to look at the evidence or outcome of a patient who had undergone chemotherapy and saw how it affects our population before we come out with intervention". (11H)

• The need to create awareness on chemobrain

However, at this point of time, an improvement in the accessibility to the current educational effort is a step to create awareness among both patients and health care providers.

*"Educate the doctor that there is such a thing call chemobrain phenomenon because of chemotherapy. That would be better than screening thing". (8H)* 

# 4.4 Summary

This chapter reported findings from both stages of the study. From the systematic reviews of a qualitative study, it revealed a new synthesis of to help understand and capture the current knowledge that emerges from the synthesis of multiple qualitative studies on the impact of cancer-related cognitive impairment in daily living and quality of life. The follow-up stage two qualitative in-depth findings from the stakeholders a) breast cancer survivors and b) oncologists, the researchers was able to capture the real perspectives and experiences on this issue, so as to provide a better understanding how it affects the cancer survivors' population. This helps to provide more information about the field and within a Malaysian context.

#### **CHAPTER 5: DISCUSSION**

#### 5.1 Overview

Cancer-related cognitive impairment or Chemobrain is consistently reported by breast cancer survivors. From both the perspectives of oncologists and breast cancer survivors, they believe that the cognitive changes are strongly influenced by other factors such as; - psychological and biological factors. There is a growing body of research, but the incidence and causes remain uncertain due to inconsistent methods of objective assessment of cognitive changes and subjective reports from survivors (Castellon & Ganz, 2009; Shilling, Jenkins, Morris, Deutsch, & Bloomfield, 2005) although many studies suggest that chemobrain is related to cancer treatment such as chemotherapy. This is the first study that explores the cognitive impairment issue among breast cancer survivors in Malaysia and among a few which was conducted in Asia. There are limited evidence and data on cognitive impairment in the Asian population. Moreover, the results of this study provide an overview and perspectives about cancer-related cognitive impairment or chemobrain among healthcare providers (oncologists) and working breast cancer survivors. This chapter merges the key findings from both stages. It writes up the summation and synthesis of the major results and themes from the findings. This chapter also tries to draw possible explanations through a comprehensive discussion based on the research questions. The implication for healthcare practices is also highlighted in this chapter followed by a discussion on the strength and limitations of the study.

## 5.2 The presence of cancer-related cognitive impairment is real.

The meta-ethnography method facilitated the synthesis of seven qualitative research studies, and the creation of a preliminary notion to highlight the perceptions of women with breast cancer about their experience with chemobrain. The application of the Illness Representation Theory to the findings allowed further interpretation of the meanings attributed to the chemobrain experience. Although our analytical approach was inductive in nature, it was helpful to consider a theoretical framework that addressed meaning such as the construct of illness representation. The Illness Representation Theory informed the analysis about the 'vague but real' cognitive symptoms experienced by breast cancer survivors, portrayed as broader health problems involving identity, timeline, consequences, cause, control, illness coherence, and emotional representations (Howard Leventhal et al., 1997). The idea of illness perceptions is derived from self-regulation theory (H. Leventhal, 1984). This theory proposes that individuals form common-sense beliefs about their symptoms to cope with any potential health threats. The review and result from the current study suggest that the breast cancer survivors were actively trying to find some meaning in their chemobrain symptoms that became more confronting when they resumed their daily activities and worked. The current study has shown that participants were struggling to cope with the impairment that affects their work functioning.

### 5.3 Awareness and information on cancer-related cognitive impairment

There is a lot of established early information on acute and physical side effects, and patients were initially more concerned with the established issues. Oncologists were more concerned about acute management side effects rather than psychosocial issues (Pirl et al., 2007). In a medical model, health care providers often tend to emphasize the aspects that can be measured, but patients are exposed to issues outside of the framework, which causes patients to struggle in cognitive changes (Mitchell & Turton, 2011). The absence of information leads to the anxiety of not knowing the aetiology of the symptom. Some of the patients were relieved when they had validated the problem from other resources such as electronic and mass media, as well as sharing session with other breast cancer survivors. It became easier for them to go on with life. But for those who were not, they were always wondering about this issue and questioning the changes

that have been occurring; thus, it keeps them in an anxious state. Early information and validation from health care providers would provide survivors with readiness to the adverse side effects. Further evaluation using valid and reliable assessment, as well as subjective reports from patients are important to identify potential reasons for any inconsistencies (Hess & Insel, 2007).

Information seeking behaviour is a common strategy that is suggested to have positive outcomes (Smith-McLallen, Fishbein, & Hornik, 2011). They all emphasized that early information is important during the early phase of survivorship. For those who received adequate information, they were able to manage their emotional changes and had better coping skills at work. However, Asians showed less action on health efficacy which they reported having lack of knowledge about breast cancer and the treatment related as well as the lack of resources in handling survivorship (Tam Ashing, Padilla, Tejero, & Kagawa-Singer, 2003). This has led to a lack of assertiveness in decision making. Asians were depending on the physicians in terms of decision making of the treatments even though they expressed to be more involved in the process of decision making (S. Lee, Chen, Ma, & Fang, 2012).

## 5.4 Beliefs and attitudes about cancer-related cognitive impairment

Some of the beliefs of both patients and health care providers have contributed to this unacknowledged cognitive complication. Oncologists believed that the term can be misleading to the patients because of the term itself did not explain the phenomenon and gave a negative meaning to the patients, which may lead to patient's withdrawal to treatment. On the other hand, survivors received a lack of information, which causes false interpretation and will later generate misconception of the phenomenon. Coupled with the unusual terminology of 'chemobrain', survivors have expressed that their health providers are negating its presence and are therefore not validating its existence. The aetiology of cognitive changes remains debated. Oncologists and participants believed that other confounding factors, especially psychological and biological effects were the reasons for mild cognitive impairment. This was supported by a study of perspectives from oncology's practitioners, that oncologists are less likely to agree that chemotherapy is the main factor of chemobrain (Cheung et al., 2013). Their belief of the symptoms hindered them to acknowledge this phenomenon. The existence of this phenomenon should be educated to them. Increasing awareness and information will provide better empowerment on decision making among participants.

### 5.5 Impact of cancer-related cognitive impairment on work functioning

Our review identified a lack of self-awareness about when changes in cognitive functioning became obvious for survivors. It seemed to be most apparent when they struggled to get work done, engaged in their role as a homemaker, socialized and tried to cope with being less productive at work. Inability to perform functional tasks that required constant effort for survivors had resulted in emotional frustration, mood changes, and higher anxiety.

Based on the outcomes of the current study, cognitive changes have a tremendous impact on participants' work functioning. It can be seen from the struggle to adjust to their working environment from the first day they return to work. Cognitive changes had emotionally affected and impacted their work task. They reported of having deterioration of memory functioning, ability to multitask, difficulty to sustain attention and concentration and had difficulty for decision-making and problem-solving. Survivors tend to have a higher level of mind wandering which influences their ability to sustain attention, where they are more prone to be immersed in their inner thoughts due to their concern referring to the difficulty in daily livings (Kam et al., 2015). In the view of experiences of symptoms severity of cognitive changes on work functioning

from survivors in this study, it has similar outcomes to other studies where there were self-reported cognitive deterioration has affected their work performances (Boykoff et al., 2009; Groeneveld, de Boer, & Frings-Dresen, 2013; Kennedy, Haslam, Munir, & Pryce, 2007; Munir et al., 2010).

To manage the work burden and load, survivors decided to change their role and function at the workplace, scaled down their skills in doing tasks, changed job and chose to opt for early retirement. This is to help participants reduce their work burden as it lessens work stress as well. Participants with professional working background have expressed greater burden related to job demand, which results in changes of work position and responsibilities. The higher demand for work functioning on critical decision making makes them different from participants with the non-professional background. They reported that they needed more effort to perform tasks than they did previously and that as their jobs required several skill sets that incorporated multiple cognitive domains, this created additional challenges. Professional women in jobs that required a high level of cognitive functioning were more negatively affected by chemobrain (Mulrooney Tamsin, 2007). There was evidence that level of job stress, depression, anxiety and fatigue contributed to global and work-related cognitive limitation among breast cancer survivors (Ottati & Feuerstein, 2013). The result of this study was found to be coherent with findings from a study in Sweden (Rönnängsgård et al., 2014), which indicated that the cognitive changes have a great impact on their ability to work which required an adjustment to tasks, working hours and some settled for early retirement.

Even though survivors had lost confidence and low self-esteem because of cognitive changes, most of the survivors received support from colleagues and employers. They received support in terms of moral support and help to regain work function. Other studies have shown that survivors did not receive any pressure from employer upon return to work (Groeneveld et al., 2013) and have been supported by colleagues which help them boost their confidence level to complete work tasks (Munir et al., 2010). It is important to get social support at the workplace for a successful return to work. In some findings among women who had a lack of support, they were struggling to resume the work functioning and hence the difficulty to return to work was more prominent (A. Johnsson et al., 2010). Besides the positive support from people at workplace, there were other contrary findings that stemmed from colleagues or employers who have expectation that survivors have fully recovered and can perform as usual, which has led to misunderstanding and has complicated the process of successfully returning to work (Tamminga, de Boer, Verbeek, & Frings-Dresen, 2012). A good communication between survivors and employers or colleagues would facilitate better outcome of quality in the workplace (McKay et al., 2012).

Apart from the personal difficulties experienced, our review found that the impact of chemobrain is extended to affecting survivors' social relationships. Survivors reported that they withdrew from social situations to avoid feelings of embarrassment about the effects of their chemobrain symptoms, and this caused changes in their social relationships among family members, friends, and colleagues. If they had been prepared and had some self-management guidance, these social consequences could have been lessened or prevented.

# 5.6 Self-management on the symptoms

Representation Theory dictates that illness representations are mediated by influencing factors that have not been adequately explained by the biomedical model of illness. A strong thread of 'struggling' with the 'why', 'how' and 'when' of chemobrain is manifested cognitively and in survivors' self-management behaviour. There is thus, a

real gap in survivorship care, as chemobrain becomes a consistently reported phenomena associated with the rise in breast cancer survival rates. Common sense reasoning is then left to fill the gap so that cognitive issues are attributed to stress or aging or other potential contextual factors. This leads the survivors to arrive at a state of problem-solving where they struggle to self-manage an 'unknown' but the real issue. The idea that women should just manage as well as they can suggests a constant struggle to cope. In this qualitative study, accepting the condition helps survivors to let go of some of the things that are beyond their control. The changes are there, so thinking positive is needed to deal with the problem. Their spiritual beliefs and practices have become a source of positive coping behaviors (Boonchoo et al., 2013).

Findings from this study have shown that these survivors expressed their participation in work contributed to the recovery of cognitive changes. Consistent with other studies, women who have returned to work have a better quality of life compared to those who are still on sick leave (Hedayati et al., 2013; Lilliehorn et al., 2013). Most of the survivors used self-management strategies to overcome their difficulty as a personal action to perceived barriers in cognitive deterioration. This action strategies that involved emotional and problem coping management incorporated stress, appraisal and coping strategies as an individual reaction to a stressful event (Lazarus & Folkman, 1984).

In terms of self-managing cognitive impairment, cancer survivors struggled and tried many ways to cope with impairments. Most of the selected studies found that psychosocial interventions and practical reminders were good sources of coping strategies. There appeared to be some cultural differences in coping strategies for chemobrain. Asian women were more likely to use a complementary and alternative medicine such as traditional Chinese medicine to improve their cognitive function (Cheung et al., 2012).

## 5.7 Addressing cognitive impairment

### 5.7.1 Cultural differences: Asian vs Westerners

Based on the qualitative papers available in the review, the researchers found emerging differences in the approach to their chemobrain experience between the Asian and Western subjects. Our review suggested that Asian women are less familiar with the chemobrain phenomena than their Western counterparts; however, this needs to be interpreted with caution as it was based on only one paper with a small sample size (Cheung et al., 2012). Asian cultures were emotionally less expressive (Hirokawa, Nagata, Takatsuka, & Shimizu, 2004). It has been suggested that Asian women are more focused on completing their treatment rather than being concerned with survivorship issues (Cheung et al., 2012). Nevertheless, the uniqueness of the perceptions of Asian women should be taken into account in any discussion on the issue of chemobrain.

These women clearly verified that chemobrain was not a myth, but a real daily experience for them, which became apparent when they resumed daily duties. Many expressed that they were thankful to be alive, and had adopted the belief that chemobrain was just one of the changes that they need to adapt to since survival was the ultimate outcome in overcoming breast cancer. This tolerance of chemobrain symptoms may be best explained by the medicalization of cancer treatment, and this has contributed to the lack of recognition of chemobrain from the medical fraternity. For both Asian and Western cancer survivors, the medicalization of the cancer journey is focused on efforts to battle the disease and at the same time is a reminder to survivors that there is a risk of cancer recurrence. '... undermining efforts at self-determination and self-care; and, keeping the patient's life suspended by continual reminders that death is just around the corner, and that all the time and energy left must be devoted to ferreting out and killing the disease' (H. Leventhal, 1984, p. 53).

### 5.7.2 Clinician versus patients' perspectives

The final dimension of illness representation is a cognitive representation of the issue, and this amounts to chemobrain being considered insignificant compared to surviving cancer, despite dissatisfaction with the situation and having to live with the consequences. The patient's unvoiced needs have led to the unaddressed issues in health care (Barry, Bradley, Britten, Stevenson, & Barber, 2000). Few responses have been received on this chemobrain issue from their oncologists, which was a query initiated by the participants. Oncologists received no minor complaints on cognitive changes as patients did not remember to voice their concerns due to memory deterioration. However, patients felt that cognitive problem is significant to be acknowledged by health care providers as the cognitive function is the biggest asset for them to return successfully to work.

Frequent changes of doctors or oncologists, limited time per follow-up session and a long gap period of follow-up have caused the issue to be unacknowledged. These results are similar to the unvoiced needs study by Low et al., (2008) in which the reasons were due to i) forgotten issues, ii) perceived health care providers' attitude, iii) expecting health care providers to enquire and iv) did not want to waste health care providers' time. Patients also did not know who to seek for to receive professional help. The unvoiced needs occurred about 1.4 to 4.6 times more among patients who were unsure on the category of health care providers they had consulted (Low et al., 2011). This has

caused an absence of understanding between patients and health care providers, which disempower patients (Mitchell & Turton, 2011).

The refusal or reluctance by some medical practitioners to acknowledge the cognitive issues experienced by survivors may lead to a lack of referrals to allied health professionals to address issues like chemobrain. Lack of attention to chemobrain means that the measurement of chemobrain symptoms is neglected. This means that the extent of impairment cannot be defined, and may decrease the impetus to develop effective interventions for outcomes cannot be evaluated. This is a particular issue for the management of return to work for survivors.

### 5.8 Reflexivity

## 5.8.1 The context of study from a personal view

Occupational therapy is a discipline offering services and works with multiple diagnosis and conditions which have debilitating effects on one's functional performance in either the physical, cognitive and/or psychosocial domains. This will eventually affect their activities of daily living, work, and leisure. Embedded in the Occupational Therapy Process Framework, is a practice that calls for a partnership between practitioner and client in the evaluation, intervention, and the outcomes to enhance the services provide to the client. The defining contribution of Occupational Therapy is the application of core values, knowledge, and the skills to assist clients (people, organization, and population) to engage in everyday activities or occupation that they want and need to do in a manner that supports health and participation (AOTA, 2008) which is more holistic and client centred approach.

The Oncology rehabilitation worldwide has a limited evidence and to result in an inconclusive method to improve psychosocial and cognitive area based on a systematic review (Loh & Musa, 2015). There is a general lack of evidence and support on the

importance or significance of cognitive impairment in oncology rehabilitation. In the Malaysia healthcare practice, there is still a lack of involvement of occupational therapy with a general lack of good quality of training for more occupational therapists to be involved in the various areas, including oncology rehabilitation.

Early detection of breast cancer and treatment regimen has resulted in the longer life span of breast cancer women. The probability of these survivors to return to work is high. However, the lack of acknowledgement of cognitive impairment which is an essential component to work has caused these women performances deteriorate. There were still grey areas between survivors and healthcare providers regarding this issue. Thus, as a researcher, exploration of perspective towards cancer-related cognitive impairment from both patients and health professionals is needed to inform the future therapy in terms of management of cognitive impairment. During the analysis process, the researcher explore participants' experiences subjectively and collectively as a group, so that a better understanding can be reached after making sense of the phenomena by linking in pre-knowledge and clinical viewpoints, to provide an overall view of this issues, which is then captured for the aim of this study -ie to understand the live experiences of human nature in our context.

Using a client centred practices in occupational therapy; we empower the decisionmaking from the patients. Thus, it is important for the patients to receive information and knowledge pertaining to the diagnosis and the side effects of the treatments that they received. The information can influence patients in treatment goal selection, which contributes to the success of the therapeutic process (Maitra & Erway, 2006).

Until to date, there is almost no study (to the researcher knowledge) conducted on cancer-related cognitive impairment in the Malaysian context. In our healthcare system, doctors are still the key decision maker for patient care including rehabilitation needs. They are the first line that influenced patient's decision making on a treatment plan. Until the Malaysian healthcare becomes more collaborative with doctors and healthcare professional collaborating autonomously at the same level, it is crucial to explore the doctors' perception regarding this rehabilitative aspect of 'cognitive impairment' among breast cancer population.

# 5.9 Implications for health services

Based on the outcomes of the current study, cognitive changes have a tremendous impact on participants' work functioning. To enhance the quality of life of survivors, healthcare providers other than oncologists or physician such as counsellors, psychologists, occupational therapist and nurses should be reliable sources of information about cognitive changes. Chemobrain or mild cognitive impairment associated with chemotherapy treatment is consistently reported by breast cancer survivors. A proactive inter-disciplinary team approach comprising of the oncology medical staff and allied health professionals is essential to ensure a holistic partnership to provide better care, and to address the participation needs of cancer patients (Vearncombe et al., 2009).

A consistent evaluation of potential causative factors by health professionals can help to explore the main causes and mechanisms of chemobrain as well as assist in developing interventions for survivors. While the debate continues, women with breast cancer may face dilemmas about continuing treatment that may lead to worse adverse effects (Raffa et al., 2006). Nevertheless, there are no data to suggest that fears about chemobrain are likely to lead to withdrawal from chemotherapy. In fact, the majority of participants indicated that they were willing to undergo chemotherapy despite the side effects. However, most of the participants stressed the importance of getting early information regarding potential cognitive changes. This needs to be a component of the informed consent process prior to treatment. It was both found in the review and current study that there is a need to highlight this issue; hence, the patients can get the information that they need.

## 5.9.1 Implication for Occupational Therapy practice and research

Cognitive impairment is a significant issue that needs to be highlighted for cancer survivor as well as professional health providers. There is a pressing need to address this issue because most survivors are not even aware of these post-chemotherapy symptoms that can hinder their functional performance. Finding implications can be seen in the progress of Occupational Therapy in Malaysia, as Occupational Therapy may provide or implement rehabilitation such as cognitive therapy or behavioural therapy that can enhance functional performance. Occupational Therapists will be able to carry out early detection (through cognitive assessment) and subsequent rehabilitation. Furthermore, this can assist the field of Occupational Therapy to progress and integrate into the field of oncology in the form of cancer rehabilitation in Malaysia. It may also provide information that can be used by other health care professionals, cancer patients who are undergoing treatment and caregivers so that they are aware of the signs and symptoms of cognitive impairment.

As Occupational Therapy is involved in improving the quality of life and functional activities including physical and mental dysfunction, as so Occupational Therapists can play a role to improve the level of understanding. Furthermore, Occupational Therapists can be involved in the cognitive relearning process of cancer survivors as this has been part and partial of their duties. Occupational therapy and oncologist's support play an important role in enhancing breast cancer survivors' quality of life by providing the best treatment plan including medication, counselling, therapeutic remediation and self-management. By acknowledging the importance of cognitive function and their effects

on quality of life, occupational therapists can involve in the remediation process of cancer survivors prior to mild cognitive impairment. Occupational Therapy has the potential to provide services to cancer survivors in facilitating and increasing survivor self-efficacy in the performance of meaningful occupations and daily routines through the development of cognitive strategies. Professional health providers play a vital role to educate patients about breast cancer to provide the best treatment plan and enable self-management strategies to ameliorate the impact on daily living.

# 5.10 Strength and Limitation of study

# 5.10.1 Strengths of the study

The strengths of the studies were:

- 1. This is the first study in Malaysian setting that confirms the presence of cognitive impairment after treatment of breast cancer survivors.
- 2. The unique study design where a detailed systematic review (to gather evidencebased findings from published literature across the world) was used to inform the decision-making of the in-depth qualitative study focusing on work functioning of women with breast cancer.
- 3. Synthesizing the data from the review and the two groups of key stakeholders helps the researchers identify the scope and depth of the cognitive impairments experienced by cross-cultural cohorts, time periods, cultures and health settings.
- 4. Complementary sources of information gathered from extensive qualitative review and extensive in-depth interviews converged to confirm the findings of chemobrain from the review and two stages qualitative studies.

#### 5.10.2 Limitations of the study

The limitations of the studies were:

- 1. The inclusion criterion of published sources with full-text availability may have omitted the inclusion of other potential sources such as unpublished theses or published book chapters, and this may have reduced the richness of the data.
- 2. This was a small, in-depth study that is limited to the study participants. The findings cannot be generalized to all women who have undergone chemotherapy. However, it is subjected to the concept of applicability where they were selected because of their knowledge and experiences in the studied issue (Burrows & Kendall, 1997).
- 3. The use of focus groups as a means of interviewing subjects has its inherent weakness whereby it can inhibit some participant's responses and while others dominantly participate in the focus groups. However, this was overcome by facilitation of the dialogue by the researcher. Also, follow-up during the clarification of the data can generate participants concerned.

### **CHAPTER 6: CONCLUSION**

#### 6.1 The summary

This study was conceptualised to explore the phenomenon of chemobrain or cancerrelated cognitive impairment to address the lack of research evidence in CRCI. It was also designed to support the current findings regarding the impact of cognitive impairment on functioning at work among breast cancer survivors and the possible management strategies at the workplace which they found useful and effective to assist them in managing work tasks. Moreover, this study was conducted to fill the gap between the view from local healthcare professionals and survivors regarding the cancer-related cognitive impairment or chemobrain. The subjects in this study were two groups of stakeholders which were the survivors of breast cancer and oncologists who attend women with breast cancer.

This study found clear verification and consistent reports in which breast cancer survivors' experiences of cognitive impairments are real, with a reported disparity between health professional and survivor's viewpoints across different healthcare settings. A continuous experience of chemobrain clearly has a detrimental impact on the economic, emotional and interpersonal status of breast cancer survivors. Subjective selfreport were validated by the consistent findings based on the current study and across the studies from the systematic review, and it is likely that the severity of difficulties experienced was underestimated.

Women may downplay the effect of these impacts because of the lack recognition from health providers. Cognitive impairment is considered less important in a healthcare setting as it does not threaten lives. Hence, it has been neglected causing lack of awareness among oncologists. There is a gap between the needs of breast cancer survivors and what oncologists perceived as important. The issue that needs to be considered is, that as a developing country, we are still leaning towards the fundamental healthcare system that focuses on having access to treatment, follow up with the patient on treatment and an essential part in oncology is losing a patient to traditional therapy. This issue probably is at the front line compared to the long-term complication of treatment such as cognitive impairment. Cognitive dysfunction is seen to be more of a problem in the first world country.

This is the first study that explores the in-depth experiences of women with breast cancer who are experiencing chemobrain and the impact on functioning at work, and further complements the findings from the in-depth interviews with a group of oncologists in Malaysia. The deterioration of cognitive changes affected women's work functioning and influences the outcomes of their work performance, and this struggle continues among these survivors due to a lack of awareness and recognition from key stakeholders in care provision. The findings of this study provide a crucial view from real experiences of women with breast cancer in terms of cognitive changes and the impact on functioning at work. It provides the insight into different working background (professional and non-professional). Moreover, this study is directed to the possible management strategies at the workplace that might benefit other cancer survivors who are still struggling to cope and the most importantly, it creates awareness to highlight this issue to gain a better understanding of the cognitive impact on work ability among breast cancer survivors.

The finding of this study may provide a better quality of life for breast cancer survivors. The insight into survivors and healthcare providers may be useful for designing screening tools, intervention or strategies to manage the symptoms in the future. The current study on the live experience of chemobrain symptoms by women with breast cancer provides (manifesting as a constant struggle on their daily life domains) the evidence that chemobrain is real, persistent and has substantial and detrimental impacts on functioning at work, daily lives and quality of life.

## 6.2 Implication for future studies

The findings of the study have shown a wide range of live experience of breast cancer survivors. Current data showed that patients have reported deterioration of functional performance as the result of cognitive, physical and emotional problems that are thought to be secondary to the neurotoxic effects of cancer therapy. It is important to highlight cognitive impairment as it integrates with humans' mind that will result in goal-directed action. The significance of cognitive impairment may lead to the interruption of functional performance in daily living as well as job satisfaction.

Breast cancer is the most common cancer among Malaysian women and it is the main cause of cancer deaths. These study findings contribute to both theoretical and empirical implications for future research and to the development of practice to address the cognition in cancer survivorship. There is a possible implication of the study towards the country. This research might benefit the society, whereby the government or NGOs' should be taken into consideration regarding the financial allocation to create the awareness among health care providers and cancer survivor or to help the survivors to be independent in the society.

Cognitive impairment is said to be one of the factors that cause a big impact on survivors' functional performance as well as their quality of life. Further studies are needed to provide the insight into the clinical significance and treatment-related to cognitive impairments and a review study that include both qualitative and quantitative findings to update current knowledge on cancer-related cognitive impairment. There is a potential for some psychological consequences of perceiving a threat from chemobrain that may be induced by the provision of information about it. Some of the health care professionals do acknowledge cognitive changes as the issue the survivors, although there is a lack of scientific data regarding the aetiology. Thus, future research is needed to investigate this phenomenon from a baseline study to identify the aetiology and to exclude other confounding factors. Furthermore, a study can be conducted to link on the effects of other factors such as age, stage of chemotherapy, cancer treatment to the cognitive function.

Further studies are needed to explore how cultural beliefs and health setting models can influence health early intervention and the coping strategies of survivors. Research exploring how ethnicity or cultural background can affect how someone faces chemobrain symptoms - and how they deal with the situation, is a viable and timely topic to minimise the gap in this field of cancer survivorship studies.

# 6.3 **Recommendations**

On the basis of the key findings discussed above, we recommend the development of information resource to create an awareness of potential cognitive changes associated with breast cancer treatment among patients, family caregivers and, perhaps most importantly, among healthcare providers. A more objective testing and monitoring of neurocognitive function in survivors complaining cognitive changes is warranted. Also, studies evaluating cognitive testing should be derived from reliable, functional and ecologically valid assessments that are culturally defined, rather than depending only on pen and paper assessments. Optimisation of some of the self-management strategies used by some breast cancer survivors can be used for the development of educational information for survivors, and for enhancing the awareness among healthcare providers.

Further quantitative research is required to confirm the extent of the issue. Future research that includes systematic, longitudinal investigations of illness representation and its impact on health behaviours among survivors with cognitive impairment is needed. Greater awareness and culturally-specific therapy are critical to enhancing the ability to perform daily tasks and for the quality of life during cancer survivorship phase, especially related to return to work. Our study findings contribute to both theoretical and empirical implications for future research and the development of practice to address the cognition in cancer survivorship.

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## LIST OF PUBLICATION AND PAPER PRESENTED

## **Publications (Appendix M)**

Selamat MH, Loh SY, Mackenzie L, Vardy J (2014) Chemobrain Experienced by Breast Cancer Survivors: A Meta-Ethnography Study Investigating Research and Care Implications. PLoS ONE 9(9): e108002. doi:10.1371/journal.pone.0108002

## Paper presented (Appendix K and L)

Chemobrain Experienced by Breast Cancer Survivors: A Meta-Ethnography Study Investigating Research and Care Implications. The Malaysia Occupational Therapy Association Competition of Innovation and Academic Research, 23<sup>rd</sup> to 24<sup>th</sup> May 2014, Kolej Sains Kesihatan Bersekutu Sungai Buloh, Kementerian Kesihatan Malaysia.

Chemobrain and the Impact on Functioning at Work: A Qualitative Study among Breast Cancer Women. Malaysian Occupational Therapy National Conference 2015, 15<sup>th</sup> to 16<sup>th</sup> May 2015, Puri Pujangga, Universiti Kebangsaan Malaysia.