Diet, Weight Change, Treatment-related and Psychosocial Challenges in Women Treated with Chemotherapy for Early Stage Breast Cancer

by

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A thesis presented to the University of Waterloo in fulfillment of the thesis requirement for the degree of Doctor of Philosophy in Health Studies and Gerontology

Waterloo, Ontario, Canada, 2012

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AUTHOR’S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.
ABSTRACT

Background: Weight gain, fat gain and loss of lean tissue are common among a growing population of breast cancer survivors. These unfavourable changes in body composition are distressing for many women and may lead to metabolic disturbance, increased risk of obesity-related disorders and poorer prognosis. Although data are accumulating on the adverse health effects of obesity and weight gain in this population, relationships between acute and chronic effects of treatment, dietary change and weight gain after diagnosis are poorly understood.

Objectives: The purpose of this thesis was to gain an appreciation of the experience of food intake and body weight over the treatment trajectory, from the perspective of women who have received chemotherapy for breast cancer. Study 1 was designed to explore the unique challenges associated with chemotherapy in relation to diet and weight management and to investigate possible relationships among psychosocial and treatment-related factors, dietary intake and weight gain during treatment. Study 2 was a follow-up to study 1, within the same study population. The purpose of study 2 was to investigate relationships among persistent side effects of treatment, diet and weight gain since the completion of chemotherapy treatment.

Methods: Twenty-eight early stage breast cancer survivors, who were within 12 months of completing chemotherapy, were recruited from four regions in southwestern Ontario, to participate in comprehensive qualitative interviews, identify changes in diet since diagnosis, provide 3-day food records and complete validated surveys to assess current (past week) symptoms of physical and psychological distress. Demographic, medical, treatment and weight history were collected via questionnaire. Current weight was measured at the time of interview.

Results: The mean weight change during treatment (mean = 15±4 weeks) was +0.8± 4.6 kg (range = -12.3 - +9.1). Among women who gained (n=11) or lost (n=6) >2.0 kg during
treatment, the mean weight change was +5.1 and -5.2 kg, respectively. Based on the recalled experiences of women, who were on average 6.4±4.4 months from completing chemotherapy treatment, food intake during treatment appears to be highly responsive to treatment day, with most women reporting lower food intake and irregular eating patterns for the first few days after treatment. Women who lost weight during treatment tended to report more severe and persistent side effects of treatment, leading to a more prolonged reduction of food intake after each cycle. Increased appetite, food cravings and intake of energy dense comfort foods seemed to be more common among women who gained weight during treatment. In these women, changes in taste, nausea and emotional distress were central in promoting these dietary responses. Most women reported a reduction in physical activity during treatment.

The mean weight change from the completion of chemotherapy treatment to the time of interview was -0.4±3.2 kg (range = -6.0 - +5.2), with six women gaining (mean=3.5 kg) and seven women losing (mean=5.1 kg) >2.0 kg during this time frame. Most women (84%) reported changes in diet after diagnosis. Dietary changes were largely consistent with current recommendations for cancer prevention, however some women were still above the guidelines for total and saturated fat and many were below recommendations for vegetables/fruit and milk/alternatives. Based on the EAR cut-point method, the prevalence of inadequate calcium and vitamin D intakes from foods was high (47-96%). Although symptoms were highly variable, the mean levels of physical and psychological distress in this sample were similar to previous reports among early stage breast cancer patients in active treatment and appear to be markedly higher than previous reports of distress among cancer-free adults. Fatigue duration (proportion of daytime) was negatively correlated with weight change after treatment (r = -0.46, p<0.05).
Conclusions: While the etiology of weight change in this population is complex, findings from this study suggest that food intake and dietary patterns may play an important role for some women. A theoretical model based on qualitative analysis supports several pathways by which psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight change during treatment. Relatively high levels of physical and psychological distress after treatment suggest that these symptoms may persist for many breast cancer survivors in the first year after completing chemotherapy, and may associate with weight change during this time frame. Data on dietary change and current dietary habits highlight several possible targets for intervention in this population. Understanding the unique challenges related to diet and weight management after diagnosis, in the context of psychosocial and treatment-related factors, may serve to inform future research and to guide the development of effective diet and weight management interventions after diagnosis.
ACKNOWLEDGEMENTS

Completion of this thesis involved the collaborative efforts of so many others who offered their time, expertise and support over the last three years. First and foremost, I extend my sincere gratitude to my supervisor and mentor Dr. Rhona Hanning who has been so instrumental in guiding this achievement. Your knowledge, leadership and commitment to academic excellence have provided so many incredible learning opportunities and made my time as a graduate student such a rewarding experience. Most of all, I appreciate your integrity, kindness and generosity and I look forward to continuing our relationship as collaborators, colleagues and friends. To my advisory committee, Dr. Marina Mourtzakis, Dr. Sharon Campbell and Dr. Linda McCargar, thank you so much for your advice, encouragement and helpful suggestions throughout. Special thanks also to Dr. Bette Caan for your interest in this research and for your willingness to serve as external examiner.

I would also like to acknowledge the assistance and support of many others who helped along the way: Pete Driezen who provided valuable guidance around statistical issues, Renata Valaitis for her helpful review and feedback on qualitative components of this research and Betina Butler for her always professional and timely transcription services. I have also had the good fortune to work with many exceptional graduate students in the School of Public Health and Health Systems and the Department of Kinesiology over the last few years: Renata, Kelly, Michelle, Allison, Katie and Kirsten - it has been a privilege and I wish you all the best as you continue your graduate studies.

To my family and friends, thank you for your unwavering show of confidence that helped to bring me ever closer to the finish line. Brenda, Laurie, Sarah and Cathy, your kind words of encouragement helped to keep me motivated but also served to remind me, when I needed it, to
keep the balance in my life. To my Mom & Dad and Janet & Jerry, thank you for always being there, for your unconditional love and support and for helping me to believe I could manage this major undertaking at this point in my life. To my amazing children Michael, Jennifer and Stephen, who cheered their mom on with steadfast enthusiasm - I am so proud of all of you. I hope you will always be happy and that you will reach for your dreams with confidence and creativity. And finally to my best friend, confidant, number one cheerleader, IT supporter and husband Rob, who helped me day in and day out in every possible way. Thank you for your patience, encouragement and eternal optimism, without which this pursuit would not have been possible - I share this accomplishment with you.

I would also like to acknowledge financial support for this research through a grant from the Canadian Foundation for Dietetic Research and a Doctoral Research Award from the Canadian Institutes of Health Research.

Last but certainly not least, I am especially grateful to the wonderful women who shared their personal stories with me. Their willingness to participate fully in this study, with a clear passion to “give back”, added a richness to this emerging area of research, that will assist our efforts to improve the lives of breast cancer survivors.
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INTRODUCTION

1.1 Statement of the Problem

Weight gain is a common and persistent problem for many breast cancer survivors, both during treatment and in the months and years after diagnosis (Vance, Mourtzakis, McCargar & Hanning, 2011). Furthermore, with or without weight gain, unfavourable changes in body composition including fat gain and loss of lean tissue have been observed in this population; changes which may lead to a body composition phenotype known as sarcopenic obesity (Demark-Wahnefried, Peterson, Winer et al. 2001; Kutynec, McCargar, Barr, & Hislop, 1999).

Emerging data suggest that obesity, and weight gain associate with increased risk of disease recurrence and breast cancer mortality (Nichols, Trentham-Dietz, Egan et al., 2009; Ryu, Kim, Nam et al., 2001). Weight gain is also known to impact negatively on quality of life (Halbert, Weathers, Esteve et al., 2008; Knobf, 1986) and to increase the risk of developing co-morbid conditions (Brown, Brauner & Minnotte, 1993; Wingo, Gloeckler Ries, Parker & Heath, 1998). Loss of lean tissue might further exacerbate the problem of weight gain and, combined with gains in adipose tissue, may lead to metabolic disturbance, treatment complications and poor clinical outcomes (Carmichael, 2006; Prado, Baracos, McCargar et al., 2007).

Although data are accumulating on the adverse prognostic effects of sarcopenic obesity and weight gain, the underlying mechanisms of energy imbalance in the post-diagnosis period are not well understood. Diet and exercise patterns after diagnosis and possible treatment-related reductions in resting energy expenditure are areas of active research, however the extent to which these individual components of energy balance contribute to weight gain is not yet clear. Diet has clearly been implicated in weight gain among breast cancer survivors, but there are significant gaps in available knowledge and the limited data base suffers from important methodological flaws.
1.2 Study Rationale

Breast cancer is the most common female malignancy in the world, accounting globally for 16% of all cancers in women and more than 500,000 deaths each year (World Health Organization, 2011a). In 2011, it was estimated that 23,400 Canadian women and 230,480 American women would be diagnosed with breast cancer (Canadian Cancer Statistics, 2011; National Cancer Institute, 2011). Improved screening, combined with advances in treatment, has resulted in a decline in breast cancer mortality however, with more than 250,000 new cases expected in North America each year, an increasing number of women are living with a diagnosis of breast cancer. This growing population of breast cancer survivors, currently estimated to include at least 152,000 Canadian women (Canadian Breast Cancer Foundation, 2011) and 2.6 million American women (National Cancer Institute, 2011), underscores a critical need to investigate modifiable risk factors that will promote overall health, disease remission and long-term survivorship.

Given the adverse health consequences of weight gain after diagnosis, further efforts to investigate dietary factors relating to energy imbalance are warranted. These findings will help to identify women who may be most at risk of weight gain, and may assist in the development of nutrition guidelines and diet/weight management interventions targeted towards the diet-related issues experienced by women during or following breast cancer treatment.

There are several hypothesized mechanisms by which breast cancer and its treatment might influence diet and eating behaviours in ways that promote weight gain, but little empirical evidence at this time. Although nutrition-related side effects are well documented, relationships between acute and chronic effects of treatment, dietary change and weight gain
after diagnosis are poorly understood. Previous research, however, is limited by imprecise
dietary assessment methods, small sample size and limited data over the treatment trajectory.
The timing of dietary measures in the current literature is especially problematic. Many studies
have relied on pre-chemotherapy measures of dietary intake as the baseline, raising the
possibility that important changes in dietary habits between diagnosis and the initiation of
chemotherapy may have been missed. Moreover, most studies have used before and after
chemotherapy measures only, which will not detect fluctuations in intake over the course of
treatment and within treatment cycles. This limitation likely reflects the significant challenge
in recruiting women in active treatment to a study of this nature, and reluctance to place
additional burden on patients. This however, is an important component of dietary assessment
in this population. Given the stresses of a cancer diagnosis and the known gastrointestinal side
effects of treatment, food intake and eating patterns would be expected to be highly variable
across treatment and within treatment cycles. Data from our pilot study (n=6) support this
supposition, revealing a mean energy intake at baseline (onset of chemotherapy) of 1857 kcals,
which drops to 1612 kcals at 8 weeks and returns to baseline by 16 weeks (p<0.05). When the
data were analyzed by weeks from treatment, the mean energy intake for diet records
completed in the first week after treatment was 1424 kcals, increasing to 1958 kcals and 2019
kcals in the second and third weeks, respectively (Appendix A). This pilot work suggested high
intra and inter-individual variability in intake over treatment as expected, but was limited by
small sample size and did not specifically address factors influencing dietary intake across
treatment. Furthermore, the precision of food records and other self-reported dietary
assessment methods may preclude the ability to detect small changes in dietary intake over a
short period of time.
Comparison of diet and eating behaviour between women who gain weight versus those who remain weight stable has not been reported, suggesting that the role of dietary intake in post-diagnosis weight gain has not yet been adequately characterized. Lastly, there are very limited data on dietary changes in the post-treatment period, with no studies reporting these changes in relation to persistent treatment effects or in the context of dietary intake in the first year after diagnosis.

The current research was designed to explore these gaps in the literature; to gain an appreciation of the experience of food intake and body weight over the treatment trajectory, from the perspective of women who have received chemotherapy for breast cancer. Use of a mixed method design was based on the premise that incorporating both qualitative and quantitative analysis may help to circumvent some of the research gaps and methodological challenges and would provide important insights on food intake and weight change that have not been previously explored.

Our pilot work with patients in active treatment suggested that post-treatment interviews would be preferred over data collection during treatment and might allow for a larger, more representative sample. Furthermore, follow-up consultations suggested that most women had vivid recollection of the influences that affected their eating patterns during treatment (gastrointestinal disturbance, fatigue, family support), which might have been missed by midtreatment food records, but could be captured as a whole using qualitative interviews.

1.3 Objectives and Research Questions

1.3.1 Study 1

Study 1 was a qualitative analysis, based on comprehensive interviews with 28 breast cancer survivors within 12 months of completing chemotherapy treatment. The purpose of
study 1 was to describe the unique challenges associated with chemotherapy in relation to diet and weight management and to explore possible relationships among psychosocial and treatment-related factors, dietary intake and weight gain during treatment. Study 1 was based on the following objectives:

**Objective #1**: To describe food intake and eating patterns in relation to the experience of chemotherapy.

**Objective #2**: To identify common psychosocial and treatment-related factors associated with changes in food intake and eating patterns during treatment.

**Objective #3**: To describe similarities and differences in food intake and eating patterns in relation to the experience of chemotherapy, among women who gained weight during treatment compared to women who did not gain weight.

**Objective #4**: To develop a theoretical model based on grounded theory, to explain how psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight gain during treatment. This model was considered within the context of changes in physical activity.

**Research Questions**

1. Are there common themes around diet-related issues and supports/barriers to healthy eating and weight management among women treated with chemotherapy for early stage breast cancer?

2. Are there apparent differences in diet and eating patterns in relation to chemotherapy treatment among women who gained weight compared to women who did not gain weight?

3. Are there relationships between psychosocial factors and treatment-related side effects, diet and eating patterns, and weight gain during treatment?

**1.3.2 Study 2**

Study 2 was a follow-up to study 1, within the same study population. The purpose of study 2 was to investigate relationships among persistent side effects of treatment, current dietary intake, changes in diet and weight gain since the completion of chemotherapy treatment. Study 2 was based on the following objectives:
Objective #1: To describe current (past week) symptoms of physical and psychological distress and global quality of life using the Rotterdam Symptom Checklist and the Distress Thermometer.

Objective #2: To conduct a comprehensive assessment of the intensity and duration of current fatigue (past week) and to describe the extent to which fatigue has interfered with daily living (e.g., activities, concentration, relationships) using the Fatigue Symptom Inventory.

Objective #3: To investigate changes in diet after diagnosis based on self-reports of having “introduced, increased, reduced or eliminated” specific food groups or dietary constituents.

Objective #4: To describe current dietary intakes based on 3-day food records, relative to the Dietary Reference Intakes (energy, macronutrients, fibre, calcium and vitamin D), and Eating Well with Canada’s Food Guide (recommended number of food guide servings). Mean intakes were also described relative to the Canadian Community Health Survey, Cycle 2.2, Nutrition (2004) (energy, food groups, % energy from macronutrients, calcium, vitamin D).

Objective #5: To examine relationships between weight change (kg, gain vs. stable or loss) since the completion of treatment and composite scores for physical and psychological distress, intensity of fatigue, duration of fatigue, level of interference associated with fatigue, current dietary intake (energy, carbohydrate, protein and fat intake) and self-reported changes in diet (number of positive changes) after diagnosis. Small sample size may limit statistical power to detect significant correlations, but this objective will serve to generate hypotheses and power calculations for future studies.

Research Questions

1. Based on responses to standardized surveys, what is the level of physical and psychological distress in early stage breast cancer survivors after chemotherapy treatment, and how do these scores seem to compare to previous reports of distress (*) among early stage breast cancer patients in active treatment and comparison groups of cancer-free adults?
   * based on published normative data from the Rotterdam Symptom Checklist and the Fatigue Symptom Inventory

2. What is the nature and extent of self-reported changes in diet in early stage breast cancer survivors, after diagnosis?

3. How do current intakes of energy (kcals), carbohydrates (g, %), protein (g, %), total and saturated fat (%), fibre (g), calcium (mg), vitamin D (ug) and servings of vegetables & fruits and milk & alternatives, in this sample group of breast cancer survivors, compare to age and gender specific dietary recommendations?

4. Are there relationships between weight change since the completion of treatment and each of physical and psychological distress, self-reported changes in diet and current dietary intake?
1.4 Study Components

Figure 1.0: Study components for Study 1 and Study 2.

1.5 Organization

The first chapter of this thesis is a review of the literature, providing an overview of nutrition-related issues during chemotherapy treatment and a review of weight gain, health consequences and potential mechanisms of energy imbalance in breast cancer survivors. A conceptual model of possible and probable factors promoting energy imbalance after diagnosis summarizes and integrates these findings. Chapter 2 provides a comprehensive description of the research methods. Chapters 3-5 are presented as three manuscripts, representing the results of three distinct areas of the thesis. Chapter 3 is based on the qualitative analysis from study 1. Chapters 4 and 5 are based on the dietary change, 3-day food record and survey data (persistent treatment effects) from study 2. Chapter 6 is a general discussion providing a summary of the
key findings and contributions of this thesis, clinical applications and recommendations for future research and is followed by a list of references and appendices.

Sections of the literature review have been published as follows: (Appendix Q)


A second paper has been submitted and is currently under review:

Vance, V., Mourtzakis, M., McCargar, L., & Hanning, R. Weight gain in breast cancer survivors: The role of diet, resting energy expenditure and physical activity.

The content of chapters 3-5 will be submitted for publication as follows:

CHAPTER 3:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. The voice of experience: a qualitative analysis of food intake, psychosocial and treatment-related factors and weight change in women treated with chemotherapy for early stage breast cancer.

CHAPTER 4:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. Dietary changes and food intake after a breast cancer diagnosis.

CHAPTER 5:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. Weight change, physical distress, psychological distress and food intake among early stage breast cancer survivors.
CHAPTER 1: LITERATURE REVIEW

1.1 Breast Cancer, Chemotherapy and Nutritional Status

A breast cancer diagnosis and chemotherapy treatment can profoundly impact dietary intake, dietary requirements and nutritional status. Normal dietary patterns may be altered by stress and the burdens of active treatment, changes in physical activity and by several possible nutrition-related side effects of chemotherapy agents.

Chemotherapy drugs target cancer cells that are dividing rapidly, however some normal cells including skin, hair, nails, blood cells and the lining of the digestive system also divide rapidly (Cancer Research UK, 2008). The process of killing cancer cells therefore, also damages healthy cells, producing “nutrition impact” symptoms that can lead to inadequate intake and nutritional deficiencies (Doyle, Kushi, Byers, Courneya, Demark-Wahnefried, Grant, McTiernan et al., 2006). Common nutrition-related side effects of breast cancer chemotherapy include nausea, vomiting, anorexia, changes in sense of taste or smell and bowel complications including both constipation and diarrhea. Damage to the mucous membranes of the upper gastro-intestinal tract can also produce mucositis (mouth sores), esophagitis (inflammation of the esophagus) and heartburn (Doyle et al, 2006; Eldridge & Hamilton, 2004; Grant & Byron, 2006; National Cancer Institute, 2006). General information from the Canadian Cancer Society (2002) and the BC Cancer Agency (2011) suggests that individual responses to treatment are highly variable, however many breast cancer patients who receive chemotherapy experience difficulty eating for several days after treatment. In addition, fatigue, reported in 96% of women in active treatment (Demark-Wahnefried, Rimer & Winer, 1997b) and the psychological impact of cancer and cancer treatment (Halbert et al., 2008) can interfere with the desire to eat and the ability to plan, shop and prepare healthy meals (Eldridge &
Hamilton, 2004; National Cancer Institute, 2006). These common treatment effects can present significant challenges to healthy eating that may vary between women and across the treatment trajectory (BC Cancer Agency, 2011).

Cancer and its treatment may also produce alterations in energy, macronutrient, micronutrient and fluid requirements. Nutritional needs for breast cancer patients vary widely as a function of age, physical activity level, nutritional status at diagnosis and individual response to chemotherapy agents and may change significantly over the course of treatment. Adequate energy intake is especially important during cancer treatment to help resist fatigue and assist the body to withstand the effects of treatment (Canadian Cancer Society, 2002). Stress on the body caused by cancer may produce changes in amino acid metabolism and an increase in need for dietary protein. Additional protein is recommended during treatment, to preserve lean tissue, promote healing, re-build tissue and maintain immune function (Hurst & Gallagher, 2006; National Cancer Institute, 2006). Protein requirements can be determined using urinary urea nitrogen balance studies, but are more commonly estimated, based on grams of protein per kilogram of body weight. The recommendation for early stage, adult cancer patients is 1.2 g/kg (Hurst & Gallagher, 2006); 50% higher than the current dietary reference intake (0.8g/kg) for the general population (National Academy of Sciences, 2005). Adequate carbohydrate and fat calories are needed to spare protein and preserve lean muscle mass (Hurst & Gallagher, 2006). Carbohydrate and fat recommendations for cancer patients are the same as current guidelines for healthy individuals (carbohydrates-45-65% of total energy with an emphasis on fruits, vegetables and whole grains, fat-20-35% of total energy with an emphasis on mono and polyunsaturated sources) (National Academy of Sciences, 2005). Fibre intake may have to be adjusted, based on individual gastrointestinal response to treatment.
Cancer patients may be at risk for micronutrient deficiencies due to physiological stress, changes in vitamin and mineral metabolism, poor diet and gastrointestinal complications. While reliance on a healthy balanced diet is strongly encouraged over supplements, a low dose multi-vitamin supplement ($\leq 100\%$ of the Recommended Dietary Allowance) is sometimes recommended (BC Cancer Agency, 2011; Hurst & Gallagher, 2006). There is no scientific evidence to date, that supplements will help to prevent or fight cancer and in fact some evidence to suggest that high dose antioxidant vitamins and minerals, in particular, may be harmful and/or interfere with anti-cancer medications (BC Cancer Agency, 2011; Doyle et al., 2006).

Lastly, hydration status may be compromised during cancer treatment by inadequate intake or treatment-related nausea, vomiting and diarrhea (Eldridge & Hamilton, 2004). Hydration is especially important during treatment, to protect the bladder and kidneys from the effects of chemotherapy drugs (BC Cancer Agency, 2011). Breast cancer patients are encouraged to drink 8-10 cups of liquids per day and to eat foods that contain significant amounts of fluids (soups, popsicles, jello, puddings) in order to achieve and maintain adequate hydration.

1.2 Weight Gain in Breast Cancer Survivors

1.2.1 Frequency and Magnitude of Weight Gain

Weight gain is a common problem among breast cancer survivors. First reported in the 1970’s (Dixon, Moritz & Baker, 1978), this finding was initially unexpected given the known gastrointestinal-related side effects of treatment and because many forms of cancer are more typically associated with weight loss (Demark-Wahnefried et al., 1997b). Weight gain in this population has since been well documented.
Two extensive reviews of weight gain among breast cancer survivors were conducted during the 1990’s (Demark-Wahnefried, Winer & Rimer, 1993; Demark-Wahnefried et al., 1997b). At this time, combined results suggested that 50-96% of early stage breast cancer patients experience significant weight gain during treatment. Weight gains in the range of 2.5–6.2 kg were most commonly reported but gains of 10 kg or more were not unusual. Since 1997, many additional studies have reported on weight gain during and after breast cancer treatment; 30 studies (1997-2011) are summarized in Table 1.1 (pg. 53).

While there appears to be a general trend toward a reduction in the magnitude of weight gain since the mid 1990’s (Ingram & Brown, 2004), the majority of recent investigations continue to show a high frequency of weight gain among women with early stage disease (Campbell, Lane, Martin et al., 2007; Costa, Varella & del Giglio, 2002; Cheney, Mahloch & Freeny, 1997; Del Rio, Zironi, Valeriani et al., 2002; Goodwin, Ennis, Pritchard et al., 1999; Halbert et al., 2008; Irwin, McTiernan, Baumgartner et al., 2005; Lankester, Phillips & Lawton, 2002; Makari-Judson, Judson & Mertens, 2007; McInnes & Knobf, 2001; Rock, Flatt, Newman et al., 1999; Gordon, Hurwitz, Shapiro & LeBoff, 2011).

A 2002 retrospective chart review of 100, stage I-III breast cancer patients for example, found that 64% of women gained more than 2 kg during six cycles of adjuvant or neoadjuvant treatment (Lankester et al., 2002). The mean weight change across all participants was 3.78 kg (range = -8.4 - + 17.9), with one-third of patients gaining more than 5 kg. Del Rio et al. (2002) measured weight changes prospectively in stage I-II breast cancer patients during chemotherapy treatment and reported significant weight gain in all 30 participants, with a range of 2.0 - 5.5 kg and a mean gain of 2.8 kg. Defining “significant” weight change as a gain or loss of greater than 2.5 kg, Ingram and Brown (2004) concluded that only 34.2% of
Premenopausal women (n=76) gained weight during chemotherapy treatment. The mean weight change among all women was 1.4 kg (±3.4 kg), however, those who were classified as “gainers” (>2.5 kg) experienced a mean weight gain of 5 kg (±1.4 kg).

Some of the more recent investigations have not reported significant weight change during active treatment, possibly owing to shorter duration chemotherapy regimes (Demark-Wahnefried, Hars, Conway et al., 1997a; Freedman, Aziz, Albanes et al., 2004; Kutynec et al., 1999) however, longer follow-up data in these studies and others have reported progressive weight gain after the completion of treatment. Investigating weight, body composition and components of energy balance in women with early stage breast cancer, Kutynec et al. (1999) found that, while body weight was unchanged over 12 weeks of adjuvant chemotherapy (n=8) or radiation (n=10), follow-up data for 13 participants revealed that four out of seven women treated with chemotherapy (mean follow-up 66 weeks) and four out of six women treated with radiation (mean follow-up 103 weeks) had gained an average of 4.7 kg (range = 3.0 - 7.5 kg) and 4.1 kg (range = 1.9 - 8.2 kg), respectively. Likewise, Demark-Wahnefried et al. (1997a) found no significant difference in mean body weight among 18 premenopausal women before and after treatment, however at a one year follow-up found that 14 of the 18 women for whom weight data were available had gained an average of 3.8 kg (±0.75 kg) since the completion of treatment.

Recent longitudinal data confirms that weight gain after treatment is a problem for many breast cancer survivors. Irwin and colleagues (2005) recruited 514 pre and postmenopausal women within one year of diagnosis in order to assess changes in weight and body fat after a diagnosis of stage I-III A disease. By the third year after diagnosis, 68% of the women had gained an average of 3.9 kg (±3.7 kg). Similarly, a review of consecutive patient records found
that among 185 women diagnosed with stage I-III breast cancer, 71% had gained an average of 3.7 kg one year after diagnosis (Makari-Judson et al., 2007). The mean weight change across all women was 1.5 kg at year one, 2.7 kg at year two and 2.8 kg at year three, suggesting that weight gain is progressive and persistent after diagnosis. Furthermore, only 15% of women who had gained weight at year one had lost the weight at year two and of those who did not gain weight in year one, 32% gained an average of 1.8 kg in the following year.

While post diagnosis weight gain is common, it is not universal. Limited data show that some women maintain a stable weight, while a smaller percentage of women (~10-29%) may lose weight after diagnosis (Foltz, 1985; Rock et al., 1999; Ingram & Brown, 2004; Makari-Judson et al., 2007; Tredan, Bajard, Meunier et al., 2010; Gu, Chen, Zheng et al., 2010; Nissen, Shapiro & Swenson, 2011). Among those who gain weight, the amount of weight that is gained, at different time points in the cancer trajectory, is highly variable. Moreover, it is possible that there are ethnic differences in the pattern of weight gain after a breast cancer diagnosis. A study of 260 Korean women diagnosed with early stage disease, reported a mean weight gain of 0.30 kg (p<0.5) at 3 months but no significant weight change at 6, 12 and 24 month follow-ups (Han, Lee, Kim et al, 2009). In this study, 47% of patients experienced a mean gain of 1.93 kg (±1.91 kg) at 12 months, though only 10% were reported to have gained a “significant amount of weight” (≥ 5% vs. baseline) during this time frame. The Shanghai Breast Cancer Survival Study (Gu et al., 2010), a larger prospective study of Chinese women (n=5014) however, found that 26%, 37% and 33% of women gained ≥5% of initial body weight at 6, 18 and 36 months, respectively.

Estimating average weight gain in this population is confounded by the fact that weight change has been reported using a variety of methods (absolute change, % change, “significant
In addition, some studies have reported mean weight change across all participants (e.g., including those who are weight stable or lose weight after diagnosis) and by treatment group or menopause status without providing separate data for a sizeable proportion of women who experience weight gain (Campbell et al., 2007; Freedman et al., 2004; Rock et al., 1999). While this provides an estimate of overall weight change among breast cancer survivors and is critical in comparing weight change by specific sub-categories of women, it may dilute the true magnitude of the problem for some women.

Regardless of how the data are presented, based on more than 30 years of research, it is clear that among breast cancer survivors, weight gain is a common and persistent problem. The amount of weight gain that has been reported in the months and years after diagnosis is larger than would be expected in the general population and occurs at an accelerated rate compared to age-matched healthy women (Williamson, Kahn & Byers, 1991; Guo, Zeller, Chumlea et al., 1999).

1.2.2 Patterns of Weight Gain and Body Composition Changes

Weight gain in otherwise healthy women is typically characterized by a gain in both adipose tissue and lean tissue (Demark-Wahnefried et al., 2001; Harvie, Campell, Baildam & Howell, 2004). A growing body of research however, suggests that the pattern of weight gain typical of breast cancer patients is unique in that it generally occurs in combination with no associated gains or perhaps even losses in lean tissue: changes which may lead to a body composition phenotype known as “sarcopenic obesity” (Rock & Demark-Wahnefried, 2002; Visovsky, 2006).

Using several modalities of body composition assessment, including skin-folds (Goodwin et al. 1999; Harvie et al. 2004), waist and hip circumference (Goodwin et al. 1999; Harvie et al.
dual energy x-ray absorptiometry (DXA) (Campbell et al., 2007; Demark-Wahnefried et al., 2001; Freedman et al., 2004; Kutynec et al., 1999; Irwin et al., 2005; Nissen et al., 2011; Gordon et al., 2011) and computed tomography (CT) (Cheney et al., 1997), increases in fat mass after diagnosis are well documented.

Using DXA, Demark-Wahnefried et al. (2001) reported changes in body composition in 36 premenopausal breast cancer patients (stages 0-III) during the year after diagnosis. At six and twelve months respectively, women treated with adjuvant chemotherapy had gained an average of 2.2 kg and 2.1 kg in body weight and 2.0 kg and 2.3 kg of fat mass (FM), representing a relative gain in body fat of 1.8% and 2.2%. During the same time frame, a small but non-significant decrease in fat free mass (FFM) and leg lean body mass in particular was noted. Based on a sub-sample of women from the Healthy Eating, Activity and Lifestyle Study (n=132), Irwin et al. (2005) found that 74% of early stage breast cancer survivors had gained an average of 3.6% body fat within two-three years after diagnosis.

Others have reported an increase in FM, accompanied by a significant loss (Cheney et al., 1997; Kutynec et al., 1999) or no change (Campbell et al., 2007; Freedman et al., 2004, Gordon et al., 2011) in FFM during treatment. Based on CT images, Cheney et al. (1997) found that, regardless of weight change, seven out of eight early stage breast cancer patients gained body fat and lost lean tissue over six months of adjuvant treatment. Similarly, in the absence of significant weight gain, Kutynec et al. (1999) reported a significant increase in percent body fat and a significant loss of lean body mass in 18 premenopausal women, over 12 weeks of chemotherapy or radiation. Once again, loss of lean tissue was especially pronounced in the leg region, for both chemotherapy and radiation treated women.
Using DXA at baseline (within one month of starting chemotherapy) and 12 months, Nissen et al. (2011) found that women who were normal weight at baseline (n=26) gained an average of 2.0 kg and experienced an increase in fat mass in the torso and arms. Conversely, women who were overweight or obese (n=23) lost weight (1.4 and 1.9 kg, respectively), with no increase in body fat, however greater BMI at baseline was associated with a larger decrease in lean mass in the arms. These findings suggest that, with or without weight gain, changes in body composition consistent with the development of sarcopenic obesity occur in some breast cancer survivors, during and after treatment.

1.2.3 Factors Associated with Weight Gain and Body Composition Changes

1.2.3.1 Treatment Effects

There is considerable evidence that post diagnosis weight gain among breast cancer survivors is highly correlated with the type and duration of treatment (Demark-Wahnefried et al., 1997b). Early research in this area suggested that systemic treatment (chemotherapy) produced significantly more weight gain than localized treatment (surgery and/or radiation only) and that weight gain was higher among women treated with multi-agent regimes over longer periods of time (Demark-Wahnefried et al. 1993). Findings from more recent investigations confirm an association between chemotherapy and weight gain. A summary of common chemotherapy protocols and their abbreviations (e.g. AC, CEF), used in subsequent sections of this paper, are provided in Appendix B.

A large prospective study of pre and postmenopausal women (n=535) with early stage breast cancer (Goodwin et al., 1999) demonstrated that weight gain in the first year after diagnosis was significantly greater in women treated with any form of chemotherapy (2.5 kg ± 4.45 kg) compared to those who did not receive adjuvant treatment (0.63 kg ± 3.64 kg,
Similarly in 2001, Demark-Wahnefried et al. reported a mean weight gain of 2.2 kg at six months and 2.1 kg at one year among premenopausal women treated with adjuvant chemotherapy (n=36) versus corresponding weight gains of 0.5 kg and 1.0 kg in women receiving localized treatment only (surgery, with/without radiation, n=17). Adjusting for known confounders, data from the Women’s Healthy Eating and Living (WHEL) study (n=3088), revealed that women treated with chemotherapy were 65% more likely to gain weight during treatment (OR = 1.65, CI: 1.12, 2.43) compared to women who did not receive systemic treatment (Saquib, Flatt, Natarjan et al., 2007). In this sample, the type of chemotherapy did not impact on the amount of weight that was gained.

There is some suggestion in the literature that the newer chemotherapy regimes containing anthracyclines (Doxyrubicin and Epirubicin) are associated with less weight gain (Ingram & Brown, 2004) however, this has not been a consistent finding (Costa et al., 2002; Goodwin et al., 1999; Irwin et al., 2005; Makari-Judson et al., 2007; Saquib et al., 2007; Tredan et al., 2010). Current evidence suggests that the duration of adjuvant treatment may be the more important predictive indicator. A general trend towards shorter duration treatments since the mid 1990’s may explain a reduction in the magnitude of weight gain observed in some of the subsequent research (Goodwin et al., 1999; Ingram & Brown, 2004). Furthermore, Harvie et al. (2004) reported a mean weight gain 3.3 kg (range = 1.4 – 5.3 kg) among pre and postmenopausal women (n=17) treated with six months of FEC or CMF adjuvant therapy; a finding that is consistent with studies in which patients were treated with similar protocols (Aslani, Smith, Allen et al., 1999; Del Rio et al., 2002; Lankester et al., 2002). Others have reported that, when only four cycles of AC was the dominant therapy, weight gain during treatment was minimal and in most cases not significant (Demark-Wahnefried et al., 1997a;
Freedman et al., 2004; Ingram & Brown, 2004; Kutynec et al., 1999). The use of oral agents versus intravenous administration within these and other chemotherapy regimes is associated with higher weight gain (Demark-Wahnefried et al., 1993).

Earlier suggestion that tamoxifen therapy may contribute to weight gain (Demark-Wahnefried et al., 1993) is not supported by later investigations (Goodwin et al., 1999; Kumar, Allen, Cantor et al., 1997; Lankester et al., 2002; Makari-Judson et al., 2007; Saquib et al., 2007; Gu et al., 2010). The largest of these studies (Saquib et al., 2007) found that among 3088 breast cancer survivors over a six year follow-up, tamoxifen alone was not associated with significant weight gain, nor did the addition of tamoxifen to chemotherapy treatment modify the effect of chemotherapy use on weight gain. The use of corticosteroids (Dexamethasone, Prednisone) for the treatment of nausea and vomiting associated with some chemotherapy agents and the use of Megestrol Acetate for advanced stage disease are known to produce significant weight gain during treatment (Faber-Langendoen, 1996; Goodwin, Panzarella & Boyd, 1988). The wide range of chemotherapy protocols and other medications that are currently used in breast cancer treatment may explain some of the variability in weight gain that has been observed.

1.2.3.2 Menopause Status

Studies conducted before the mid 1990’s, suggested that weight gain after diagnosis seemed to be more pronounced among premenopausal women (Demark-Wahnefried et al., 1993, 1997b): a finding that is supported by some (Caan, Edmond, Natarajan et al., 2006; Caan, Kwan, Hartzell et al., 2008; Campbell et al., 2007; Cheney et al., 1997; Freedman et al., 2004; Goodwin et al., 1999; Heideman, Russell, Gundy et al., 2009; McInnis & Knobf, 2001; Gu et
al., 2010) but not all later investigations (Aslani et al., 1999; Costa et al., 2002; Lankester et al., 2002; Kumar, Allen, Riccardi et al., 2004; Irwin et al., 2005; Tredan et al., 2010).

Heideman et al., (2009) reported a mean weight gain of 2.0 kg (±4.9 kg) and 2.4 kg (±5.6 kg), among women treated for stage 0-III disease (n=217), one year and five years after diagnosis, respectively. Stratification by menopause status however, demonstrated that weight gain in this sample was largely limited to premenopausal women who gained an average of 3.9 kg (±5.8 kg) at five years versus 1.1 kg (±5.0 kg) in postmenopausal women (p<0.05). Data from the Life After Cancer Epidemiology (LACE) and WHEL studies (Caan, et al., 2006; Caan et al., 2008), two large observational cohort studies of women previously treated for breast cancer (n=3214), revealed that women who were premenopausal at diagnosis gained significantly more weight (5.6±10.2 kg vs. 3.0±9.3 kg, p<0.001) and were significantly more likely to gain at least 5% of their body weight (47.2% vs. 30.3%, p<0.001) between pre-diagnosis (~1 year) and study entry (mean = 23 months after diagnosis) compared to women who were postmenopausal at diagnosis.

Higher weight gain in premenopausal women may correlate with treatment-induced menopause. This effect is thought to be mediated by alterations in ovarian function and sex hormone concentrations which may produce an acceleration of the normal physiological changes associated with menopause including fat accumulation, changes in fat distribution and a decrease in lean body mass (Messier, Karelis, Lavoie et al., 2009; Tremollieries, Pouilles & Ribot, 1996). Current findings however, do not support a consistent association between ovarian failure and weight gain after diagnosis. Among 535 women treated for early stage disease, Goodwin et al. (1999) found that premenopausal women who experienced treatment-induced menopause gained significantly more weight (2.65±4.75 kg) over a one year
follow-up, compared to women who remained pre or peri-menopausal (1.07±3.54 kg) or who were postmenopausal (1.05±3.58 kg, p<0.01) at diagnosis. Controlling for age, initial body weight and adjuvant treatment, a multivariate analysis revealed that onset of menopause was a significant predictor of weight gain (p<0.05) in the first year after diagnosis.

In a small sample of women with early stage disease (n=20), Freedman et al. (2004) found that while menopause status was not associated with weight gain during treatment, women who were premenopausal at diagnosis gained significantly more weight than postmenopausal women in the six month period after the completion of chemotherapy (+2.43±2.1 kg vs. -0.24±2.1 kg, p<0.01). It is noteworthy that in this study, all but one of the women became amenorrheic within 6 months of treatment. Conversely, Gordon et al. (2011) reported a median weight gain of 2.7 kg (range = -6.7 - +10.5 kg) and fat gain of 3.2 kg (range = -6.0 - +10.2 kg) in premenopausal women treated for early stage disease (n=43); changes in body weight and body fat that were not significantly different among those who developed chemotherapy induced ovarian failure, compared to those who retained ovarian function at 12 months.

Small sample size may have been a methodological barrier for some recent studies in which a relationship between menopause status and weight gain after diagnosis was not evident (Aslani et al., 1999; Campbell et al., 2007; Lankester et al., 2002). Other explanations for discordant findings include variation in timing of recruitment (Rock et al., 1999), length of follow-up (Aslani et al., 1999) and the degree of control for potential confounding variables (e.g., diet, physical activity, resting energy expenditure). Although it appears that premenopausal women may experience greater risk during and after treatment, it is important to recognize that weight gain is a persistent problem for many postmenopausal women as well.
1.2.3.3 Weight Status at Diagnosis

There is some evidence to suggest that weight gain during and after treatment may be influenced by weight status at diagnosis, however findings here are inconsistent. In a large prospective cohort study (n=5014), Gu et al. (2010) reported significantly higher weight gain over 36 months among women who had a lower BMI at diagnosis (p<0.001). The median weight gain for women who were underweight at diagnosis was 2.0, 3.0 and 3.0 kg at 6, 18 and 36 months, respectively compared to 1.0, 2.0 and 2.0 kg for those who were normal weight. No significant weight change was observed among women who were overweight. Those who were classified as obese lost a small amount of weight over 36 months (0.5 -1.0 kg). Similarly, in a smaller study (n=49), Nissen et al. (2011) found that baseline BMI (onset of chemotherapy) was inversely associated with weight gain over 12 months. Women who were normal weight at diagnosis gained an average of 2.0 kg, while those who were overweight or obese lost an average of 1.4 kg and 1.9 kg, respectively (p<0.05). Based on data from the WHEL study (n=1,116), Rock et al., (1999) reported significant weight gain, over an average of 26 months, in women who were underweight (3.6 kg), normal weight (3.1 kg) or overweight (3.3 kg) before diagnosis. It should be noted that classification of overweight in this sample was based on a BMI of 27.3-32.1 kg/m². Women with a BMI ≥32.2 kg/m² lost an average of 0.2 kg during the same time frame. These findings are consistent with Yaw, Kandiah, Shariff et al., (2010).

Despite a tendency for obese women in these studies to lose a small amount of weight on average, a wide range of weight change is reported in most studies. For example, Gu et al., (2010) reported weight change ranging from -12 kg to + 18 kg, -12.5 kg to + 20 kg and -25 kg to + 14.5 kg among women who were classified at diagnosis as normal weight (n=2709),
overweight (n=1525) or obese (n=575), respectively. This suggests that some women who are normal weight at diagnosis may move into the overweight or obese categories (Yaw et al., 2011) and some who are overweight or obese will gain additional weight after diagnosis. Furthermore, several studies have found no association between baseline BMI and weight gain after diagnosis (Goodwin et al., 1988; Costa et al., 2002; Lankester et al., 2002; Ingram & Brown, 2004; Irwin et al. 2005; Heideman et al., 2009; Tredan et al., 2010; Gordon et al., 2011), and one study (Camoriano, Loprinizi, Ingle et al., 1990) found that weight gain was significantly higher among premenopausal women who were heavier at diagnosis (8.2 kg vs. 4.9 kg, p<0.01), suggesting that further research is needed.

1.3 Health Consequences of Pre-Diagnosis Weight and Post-Diagnosis Weight Gain

The results of several studies suggest that obesity at diagnosis associates with an increase risk of disease recurrence (Chlebowski, Aiello & McTiernan, 2002; Majed, Moreau, Senouci et al., 2008), breast cancer death (Rock & Demark-Wahnefried, 2002; DalMaso, Zuccheto, Talamini, et al., 2008) and all-cause mortality (Carmichael, 2006; Dawood, Broglio, Gonzalez-Anguloro et al., 2008). This effect was evident in both pre and postmenopausal women (Chlebowski et al., 2002; Carmichael & Bates, 2004). A meta-analysis, incorporating more than 8000 women, found that obesity at diagnosis was associated with poor prognosis, with a combined effect size of 1.56 (CI: 1.22, 2.00) for all-cause mortality (Ryu et al., 2001).

More recently, Kwan, Chen, Kroenke et al, (2012) investigated associations between weight status at diagnosis and disease recurrence and survival, based on data from the After Breast Cancer Pooling Project (ABCPP). The ABCPP includes data from a large cohort of breast cancer survivors (n=14,948), pooled from three prospective studies in the US (LACE, WHEL, Nurses Health Study) and the Shanghai Breast Cancer Study (Gu et al., 2010), with a mean
follow-up period of 7.8 years. This study, the first to stratify breast cancer outcomes by degree of obesity, suggests that severe or morbid obesity at diagnosis confers the greatest risk of poor prognosis. Adjusting for several known prognostic indicators, a significant increased risk of all-cause mortality among women who were morbidly obese (BMI >40 kg/m²) at diagnosis (HR=1.81, CI:1.42, 2.32) and a small but non-significant increased risk among women who were categorized as obese or severely obese (BMI 30-34.9 and 35-39.9 kg/m², respectively) was reported. Greater risk was also seen among women who were underweight (BMI < 18.5 kg/m²) at diagnosis (HR=1.59, CI: 1.18, 2.13). Similar associations were found for breast cancer mortality and non-breast cancer mortality, however associations between weight status at diagnosis and disease recurrence were non-significant. Compared to women who were normal weight at diagnosis, overweight was not associated with increased risk of all-cause mortality, breast cancer mortality or non-breast cancer mortality. The capacity to evaluate obesity sub-categories (obese, severely obese, morbidly obese) in this large cohort of breast cancer survivors emphasizes the strong prognostic effect of morbid obesity on breast cancer outcomes and may suggest that the relationship between body weight and breast cancer prognosis is U-shaped, with normal or even high normal pre-diagnosis body weight predicting the best outcomes (Kwan et al., 2011). However, given the well established, time dependent relationships between obesity and adverse health outcomes (Abdullah, Wolfe, Stoelwinder et al., 2011), it will be important to observe if these associations modify over a longer follow-up period. Ewertz, Jensen, Gunnarsdottir et al., (2011) reported a 46% increased risk of distant metastases (HR = 1.46, CI: 1.11, 1.92) after 10 years and a 38% increased risk of breast cancer death (HR = 1.38, CI: 1.11, 1.71) after 30 years, among early stage breast cancer survivors (n=18,967) with a BMI ≥ 30 kg/m², compared to women with a BMI < 25 kg/m² at diagnosis.
Similar risk was apparent for all-cause mortality (HR = 1.31, CI: 1.05, 1.63); an effect that was evident after 10 years among women who were obese at diagnosis. Moreover, in this study, a BMI of 25-29 at diagnosis was also associated with a significantly increased risk of distant metastases (HR = 1.42, CI: 1.17, 1.73) and breast cancer death (HR = 1.26, CI: 1.09, 1.46) after 10 years. These findings are supported by Majed, Dozol, Ribassin-Majed et al., (2011) who reported a time-dependant increased risk of contralateral breast cancers (HR = 1.5, CI: 1.21, 1.86) among overweight and obese women; an association that reached statistical significance after 10 years of follow-up. It will also be important to evaluate relationships between body weight status and breast cancer specific and non breast cancer outcomes in the context of body composition, particularly in relation to lean tissue and visceral fat stores.

The relationship between obesity and prognosis is complex, seemingly influenced by several possible metabolic and hormonal pathways. Proposed mechanisms include an increase in adipose tissue derived circulating estrogens resulting from the conversion of androgens in peripheral fat stores (Stephenson & Rose, 2003). Estrogen is known to play a role in the initiation and promotion of breast cancer by stimulating cell division, increasing the potential for DNA mutations and promoting the growth of estrogen dependent tumors (Rock & Demark-Wahnefried, 2002). Body fatness also increases circulating levels of insulin, insulin-like growth factor and leptin; hormones that may exert mitogenic and angiogenic effects to promote breast cancer development (Carmichael, 2006; Stephenson & Rose, 2003) and increase the risk of disease recurrence (Goodwin, Ennis, Pritchard et al., 2002). In addition to these direct effects, insulin is known to down-regulate plasma concentrations of sex hormone binding globulin, resulting in an elevation of available bioactive estradiol and the potential for increased angiogenesis and breast epithelial cell proliferation (Stephenson & Rose, 2003).
Increased body fat may be related to physical inactivity and dietary factors, before or after diagnosis. Thus, obesity may also serve as a marker for lifestyle behaviours that contribute to poor prognosis (Carmichael, 2006). Furthermore, poor outcomes in obese women may be related to more advanced disease at diagnosis, systematic under-treatment and/or poor treatment response (Carmichael, 2006).

While the evidence for a relationship between pre-diagnosis body weight and prognosis is compelling, particularly among women who are severely or morbidly obese, it is not yet clear whether weight gain after diagnosis impacts independently on breast cancer specific outcomes.

### 1.3.1 Weight Gain and Disease Free Survival

The findings of twelve studies investigating the effects of weight gain after diagnosis on disease free survival are equivocal (Table 1.2). For the purposes of this review “disease free survival” (DFS) includes no breast cancer recurrence or breast cancer death over the follow-up period.

Five studies found a positive association between post-diagnosis weight gain and DFS (Chlebowski, Weiner, Reynolds et al., 1986; Kroenke, Chen, Rosner et al, 2005; Nichols et al., 2009; Chen, Lu, Zheng et al., 2010; Thivat et al., 2010). Chlebowski et al. (1986) reported an inverse relationship between weight gain (>10kg) and DFS, however, small sample size (n=62) and the absence of data concerning other prognostic indicators make these results difficult to interpret.

Based on a sub-sample of women with breast cancer from the Nurses Health Study (n=5204), weight gain among women who had never smoked (n=2156) was associated with poor outcomes (Kroenke et al, 2005). Compared to women who maintained a stable weight in the first 12-24 months after diagnosis, a multi-variate model revealed that women who gained
0.5 - < 2.0 BMI (kg/m²) units (median = 2.73 kg) and > 2.0 BMI units (median = 7.73 kg) were 40% and 53% more likely to experience disease recurrence over a nine year follow-up period (p<0.05). Similar findings were observed for breast cancer death and all-cause mortality. Stratification by initial body weight revealed that the relationship between weight gain and breast cancer death was significant only among women with a BMI < 25 kg/m² at diagnosis (RR = 1.63 and 1.90, p<0.01 for a median gain of 2.73 kg and 7.73 kg, respectively). Weight gain among women who were overweight or obese at diagnosis was not associated with increased risk.

Two studies reported a positive association between post diagnosis weight gain greater than 5 kg (Chen et al., 2010) or greater than 5% of initial body weight (Thivat et al., 2010) and poorer prognosis. Over a median follow-up of 46 months, Chen et al., (2010) found that among 5042 women in the Shanghai Breast Cancer Study, both modest weight gain (1-5 kg) and weight gain ≥ 5kg from one year pre-diagnosis to 18 months post diagnosis were associated with increased risk of disease recurrence (HR = 1.97, CI: 1.30, 2.97 and 1.90, CI: 1.23, 2.93, respectively) and all-cause mortality (HR = 1.89, CI: 1.27, 2.82 and 1.71, CI: 1.12, 2.60). Weight gain ≥ 5kg, restricted to the 18 month period after diagnosis, was significantly associated with all-cause mortality (HR = 1.54, CI: 1.03, 2.29). Thivat et al., (2010) reported a significantly increased risk of disease recurrence (RR = 2.28, CI: 1.29, 4.03) and all-cause mortality (RR = 2.11, CI: 1.21, 3.66) over 20.4 years, among breast cancer survivors (n=111) who gained or lost more than 5% of their initial body weight during chemotherapy treatment. This analysis makes it difficult to interpret the independent effects of weight gain after diagnosis, however, underscores the potential clinical significance of large weight variation (gain or loss) during treatment; a finding supported by those of Chen et al. (2010).
Lastly, Nichols et al. (2009) followed a large cohort of women with invasive non-metastatic breast cancer (n=3993) for an average of 6.3 years and found that weight gain >10kg was significantly associated with increased risk of all cause mortality (HR = 1.70, CI: 1.21, 2.41) and breast cancer mortality (HR = 1.78, CI: 1.01, 3.14). Among women who gained weight after diagnosis (>2kg), each 5 kg gain was associated with a 13% increase in breast cancer death (p=0.01) and a 12% increase in all-cause mortality (p<0.05). Cardiovascular disease mortality was similarly associated with weight gain (19% increase for each 5 kg weight gain, p<0.05) suggesting the possibility of a graded increase in the risk of breast cancer and non breast cancer related death and emphasizing the potential for weight maintenance to improve long-term survival (Nichols et al., 2009). It is noteworthy that 10 kg is substantially larger than the mean weight gain observed in recent studies, however represents the magnitude of weight change for some women (Gu et al., 2010, Nissen et al., 2011).

While these results are intriguing, seven additional studies, failed to identify a relationship between post-diagnosis weight gain and DFS (Heasman, Sutherland, Campbell et al., 1985; Goodwin et al., 1988; Camoriano et al., 1990; Levine, Raczynski & Carpenter, 1991; Costa et al., 2002; Caan et al., 2006; Makari-Judson et al., 2007). Camoriano et al., (1990) followed a large sample of node positive pre- and post menopausal women treated with or without chemotherapy (n=545), for more than 6 years. Controlling for age, tumor characteristics, nodal status and initial BMI, a median follow-up of 6.6 years revealed that premenopausal women who gained more than the median amount of weight (5.9 kg) were 60% more likely to die from any cause (HR = 1.62, CI: 1.01,2.62). Despite a similar trend, weight gain was not significantly associated with disease recurrence in pre or postmenopausal women.
Combined data from early stage breast cancer survivors in the LACE and WHEL studies (n=3215) found that at five and seven year follow-ups respectively, weight gain (≥5%) from one year pre-diagnosis to study entry (median = ~ 2 yrs from diagnosis) was not associated with disease recurrence (Caan et al., 2006). A second study, based on a sub-sample of LACE participants (n=1692), found that over a follow-up period of almost seven years, weight gain was not associated with DFS or overall survival (Caan et al., 2008). While obesity before diagnosis was significantly associated with all-cause mortality (HR = 1.6, CI: 1.1,2.3), with a trend toward an increased risk of breast cancer death, weight gain after diagnosis did not seem to confer additional risk of recurrence, breast cancer death or death from any cause. As is suggested by the authors, it is possible that pre-morbid body weight, which may reflect longer exposure to the effects of overweight or obesity and may correlate with other lifestyle behaviours, may be more critical in predicting breast cancer outcomes (Caan et al., 2008). Other studies are less convincing due to relatively small sample sizes, retrospective design and/or short follow-up periods (Heasman et al., 1985; Goodwin et al., 1988; Levine et al., 1991; Costa et al., 2002; Makari-Judson et al., 2007).

With conflicting results across a limited number of studies over a span of 25 years, it is clear that further research in this area is needed. Significant advances in breast cancer treatment over this time frame (e.g., shorter chemotherapy protocols) and notable differences in methodology, including variation in the timing of weight measures (Kroenke et al, 2005; Caan et al., 2006; Nichols et al., 2009; Chen et al., 2010) and the definition of recurrence endpoints, may be confounding current results (Caan et al., 2008). For example, Kroenke et al. (2005) excluded local ipsilateral or contralateral breast cancer recurrences in their definition of recurrence, while Caan et al, (2006, 2008) included all new breast cancer events. In addition,
very few studies (Caan et al., 2006, Nichols et al., 2009, Chen et al., 2010) have evaluated the possible cumulative effect of progressive weight gain after the first year, a well documented problem for many breast cancer survivors (Irwin et al., 2005; Makari Judson et al., 2007). Furthermore, all of the studies to date have investigated breast cancer and other health outcomes in relation to changes in body weight only, which may or may not adequately represent underlying changes in body composition. This is understandable, especially in the context of large population based studies, however, it is possible that some women who do not gain weight also change toward a more sarcopenic phenotype; with both fat gain and loss of lean tissue likely contributing to poorer outcomes.

1.3.2 Other Health Consequences

Excessive weight gain, especially an increase in relative adiposity, may predispose breast cancer survivors to obesity-related disorders including cardiovascular disease, diabetes, gallbladder disease and orthopedic disturbances (Brown et al., 1993; Wingo et al., 1998). This is concerning since most women diagnosed in the early stages of disease will be cured of breast cancer, but are subsequently exposed to an increased risk of chronic disease in survivorship (Demark-Wahnefried et al., 1997b; Kumar et al., 1997). Data from the Nurses Health Study and the Framingham Heart Study suggests that weight gain itself, even among women whose BMI remains within the normal range, is associated with an increased risk of morbidity and premature death (Willet, Manson, Stampfer et al., 1995; Kawachi, 1999).

Since chemotherapies are largely water soluble, distributing and metabolizing in lean body compartments, loss of lean tissue may increase the risk of treatment complications including toxicity, treatment delays and poor treatment response (Aslani, Smith, Allen et al., 2000; Prado et al., 2007; Prado, Baracos, McCargar et al., 2009). Furthermore, loss of lean tissue is
associated with decreased strength and functional impairment (Prado, Lieffers, McCargar et al., 2008) and, in conjunction with gains in adipose tissue, may lead to adverse metabolic changes including dyslipidemia, hyperinsulinemia and impaired glucose tolerance (Robinson & Graham, 2004).

Although the effect of weight gain on disease free survival is uncertain at this time, it is clear that obesity, weight gain and associated changes in body composition in the post diagnosis period have a negative effect on overall health. An extensive review of non-cancer deaths in adult cancer patients revealed an overall hazard ratio that was 1.37 times the expected age and sex-specific mortality rate for the general population (Brown et al., 1993). A greater risk of non-cancer related death was attributed to the side effects of cancer treatment and the cumulative effects of co-morbid conditions. For breast cancer survivors in particular, the relative survival rate (all-cause mortality) is known to decrease with the number of years since diagnosis declining steadily to about 70% by 20 years (Canadian Cancer Society/National Cancer Institute of Canada, 2007).

In addition, weight gain after diagnosis is distressing for many women and may contribute to poor quality of life and loss of self-esteem at a time when vulnerable patients are already under a great deal of stress (Demark-Wahnefried et al., 1997a; Lankester et al., 2002,). A recent study of weight change among African American breast cancer survivors found that weight gain was associated with psychological distress, concern about overall health and poor body image, especially among women who were not overweight before diagnosis (Halbert et al., 2008). In 1986, Knobf reported that, compared to women who lost or maintained their weight, women who gained weight during treatment were less happy, more worried and more
distressed about their appearance. Moreover, for some women, weight change after diagnosis may serve as a constant reminder of their illness and treatment (Halbert et al., 2008).

1.4 Potential Mechanisms Accounting for Energy Imbalance

Although current evidence suggests that post-diagnosis weight gain correlates most consistently with chemotherapy related factors (duration, type), some studies have reported significant, albeit smaller weight gains, among breast cancer patients who received no form of adjuvant treatment (Camoriano et al., 1990; Goodwin et al., 1988). In addition, some women who receive chemotherapy have been shown to lose or maintain a stable weight after diagnosis. These findings, coupled with data clearly showing progressive weight gain in many breast cancer survivors after initial treatment, suggest that behavioral changes affecting energy balance may play an important etiologic role (Rock et al., 1999).

Nutritional theory dictates that weight gain occurs when a state of positive energy balance follows from an increase in energy intake and/or a decrease in energy expenditure (resting metabolic rate, physical activity, thermogenesis) (Demark-Wahnefried et al., 1993; National Academy of Sciences, 2005). This section will review current evidence for the role of diet, resting energy expenditure and physical activity in the etiology of post-diagnosis weight gain. Since the contribution of diet induced thermogenesis (DIT) to total energy expenditure is relatively small (~10%) and there is no evidence at this time to suggest that a change in DIT contributes to weight gain after diagnosis, this minor component of energy expenditure will not be reviewed. It is important to recognize, at this point, that other factors including fatigue and psychosocial issues (e.g., depression, coping style) likely play a role. These factors however, are thought to be secondary, contributing to weight gain through their affect on energy intake or energy expenditure (Demark-Wahnefried et al., 1993).
1.4.1 Energy Intake – Evidence for the Role of Diet

Weight gain in breast cancer survivors has for many years been largely attributed to hyperphagia; an increase in food intake after diagnosis (Demark-Wahnefried et al., 1997b). Early support for this popular hypothesis was based on the assumption that food cravings and an increase in appetite, stress and disinhibition, depression and/or efforts to relieve treatment-related nausea may lead to overeating in the post-diagnosis period. While there is evidence that some women experience these responses to treatment (Brewin 1980; DeGeorge, Gray, Fetting & Rolls, 1990; Heasman et al., 1985; Huntington, 1985; Knobf, 1986), early studies were limited by small sample size and the absence of dietary data or statistical analysis to corroborate patient reports (Demark-Wahnefried et al., 1997b).

More recently, food frequency questionnaires (FFQ), 24-hr recalls and food records have been used to estimate changes in energy intake after diagnosis. Despite the use of more precise dietary assessment tools, recent efforts to quantify energy intake and to evaluate the relative contribution of diet in promoting weight gain have produced mixed results.

1.4.1.1 Changes in Energy Intake after Diagnosis

Four studies, in which dietary intake was assessed during treatment, found no significant change in energy intake (Del Rio et al., 2002; Harvie et al., 2004; Kumar et al., 2004; Kutynec et al., 1999). Using dietary intake before treatment as the baseline, Kutynec et al. (1999) found that mean energy intake at 12 weeks was not significantly changed from pre-treatment in pre and perimenopausal women (n=18) receiving four cycles of chemotherapy (1678±334 vs 1897±285 kcals/day) or radiation therapy (1636±376 vs 1577±375). Likewise, mean energy intake among 30 postmenopausal women (Del Rio et al., 2002) was reported to be unchanged after three months (1998±109 kcals) and six months (2042±310 kcals) of adjuvant treatment,
compared to intake before the initiation of treatment (1900±113 kcals). These findings are supported by those of Harvie et al. (2004) and Kumar et al. (2004) who found no significant change in energy intake after three months of chemotherapy compared to baseline. In the former study, participants (n=17) were followed for one year, at which time a small but non-significant reduction in mean energy intake compared to baseline was observed. All of these studies used 3-4 day food records for dietary assessment.

One study assessed energy intake pre-diagnosis, during treatment and 12 months after diagnosis and found no significant change in mean energy intake over this time period (Demark-Wahnefried et al., 2001). Using data from a 116 item FFQ, mean energy intake among 36 women receiving adjuvant chemotherapy was estimated at 1543±564 kcals/day at baseline (6 month period before diagnosis) and 1578±768 kcals/day and 1631±700 kcals/day, six and twelve months after diagnosis, respectively. In the same study, mean energy intake derived from two unannounced 24-hr recalls (monthly for six months, bimonthly 6-12 months) revealed no significant change in energy intake among women treated with chemotherapy or localized treatment only, during or after treatment.

Conversely, two studies have reported a reduction in energy intake during and after treatment (Demark-Wahnefried et al., 1997a; Goodwin et al., 1999). Demark-Wahnefried et al. (1997a) measured dietary intake one to two weeks before chemotherapy and weekly throughout treatment using 3-day diet records. Mean energy intake was significantly lower at the end of treatment in this sample of premenopausal women (n=20), compared to baseline. Mid-treatment comparisons were not reported, however energy intake over the course of treatment was reported to be highly variable and responsive to treatment day. Using data from the Block Food Frequency Questionnaire, Goodwin et al. (1999) found that among newly
diagnosed pre and postmenopausal women (n=535), energy intake decreased significantly in the first year after diagnosis compared to intake during the previous year (-88 kcals, p<0.05).

1.4.1.2 Association between Dietary Intake and Weight Gain

Efforts to establish a link between changes in energy intake and weight gain have also produced mixed results. Using a series of 24-hr diet recalls during the first and last cycles of chemotherapy, Foltz (1985) found that self-reported changes in diet were not significantly related to weight change during treatment. Women who did not gain weight (n=10) decreased their intake by an average of 193 kcals/day, while those who gained weight (n=24) reported a mean increase of 129 kcals; a difference that perhaps owing to small sample size did not reach statistical significance. Using 4-day food records before the first cycle of chemotherapy and at 6 and 12 months, Nissen et al. (2011) found that, among 49 pre and postmenopausal women, change in energy intake from baseline was not associated with weight change at 12 months.

Rock et al. (1999), however found that in a large sample of women (n=1116) recruited to a diet intervention trial (Women’s Healthy Eating and Living), current energy intake, based on four 24-hr recalls over a two week period at the time of study entry (mean=26.2 months from diagnosis), was a positive and independent predictor of weight gain after diagnosis (p=0.01). Similarly, using a 29-item FFQ, Chen, Lu, Gu et al. (2011) reported a significant positive correlation between weight gain and total dietary intake (g/day) from diagnosis to 18 months post-diagnosis (n=4561, stage 0-IV). Adjusting for age and disease stage at diagnosis, women in the highest quartile for dietary intake gained an average of 2.09±0.12 kg compared to a mean of 1.45±0.14kg among women in the lowest quartile (p<0.001). These findings were based on a limited FFQ, from which energy intake was not estimated, thus limiting ability to compare to previous studies. In the study by Goodwin et al (1999), change in energy intake
was weakly correlated with weight change but only among women who did not experience a change in menopause status during treatment (premenopausal $r=.26$, $p=0.02$, postmenopausal $r=.21$, $p=0.01$). This suggests that other mechanisms, including changes in energy expenditure (reduction in metabolic rate and/or lower levels of physical activity), may be more important than changes in diet among women who become menopausal as a result of treatment and tend to gain larger amounts of weight (Goodwin et al., 1999).

Grindel, Cahill & Walker (1989) found that energy intake among women with stage II-III breast cancer ($n=19$) was significantly higher at baseline (onset of chemotherapy) and over six months of treatment, compared to a control group of age and geographically matched healthy women. No significant differences between patients and controls were apparent on measures of education, income or body weight. These findings however, were based on a small sample of women and a limited three day, 56 item dietary diary, suggesting that they should be interpreted with caution. Energy intake did not appear to increase over the course of treatment.

Lastly, Freedman et al. (2004) found that while 25% of breast cancer patients reported an increase in appetite during treatment, no association was observed between increased appetite and weight gain. It is noteworthy, however, that no overall weight gain was observed in this small sample of breast cancer patients ($n=20$) and dietary intake was not measured.

1.4.1.3 Methodological Issues

It is clear that, at this time, there is little compelling support for the conventional belief that overeating is a primary cause of weight gain in this population. These results however, must be considered within the context of some important methodological limitations.

Most importantly, dietary assessments in this review were based on self-reported measures (FFQ, 24-hr recalls, diet records) which are subject to the well documented limitations of recall
error, inaccurate estimation of portion sizes and response bias (Hill & Davies, 2001; Kristal, Andrilla, Koepsell et al., 1998). Social expectation bias may lead to underreporting, especially of foods perceived to be unhealthy or conversely to overreporting of foods considered to be healthy and desirable (Caan, Flatt, Rock et al., 2000; Martin, Su, Jones et al., 1996; Thomson, Rock, Giuliano et al., 2005). Underreporting is known to be more prevalent among women, especially those who are overweight or obese (Hill & Davies, 2001; Trabulsi & Schoeller, 2001). In addition, the process of being closely monitored (food records, dietitian interviews) may have the effect of altering usual food intake during the recording period (Demark-Wahnefried, 1997a; Stockley, 1985; Trabulsi & Schoeller, 2001).

Data from the WHEL study suggests that underreporting may be a confounder among breast cancer survivors. Using the methods of Goldberg et al. (1991), Caan and colleagues (2000) classified 25.6% of women diagnosed with stage I-III disease as “low-energy reporters” after diagnosis and 10.8% as “very low-energy reporters”. A closer look at the data from the studies presented in this review supports the possibility of response bias in this population. Kutynek et al. (1999) for example, found that when self-reported energy intake was compared to energy expenditure, a negative energy balance was apparent despite having observed no significant change in body weight. Underreporting or an actual reduction in usual intake in response to record keeping, may explain this finding. Similarly, Harvie et al. (2004) suggested that the disparity between reported energy intake, energy expenditure and gains in body fat may have been due in part, to underreporting in this sample.

While it is recognized that self-reported measures are subject to potential bias, all are valid ($r=0.4-.06$) and reliable ($r=0.5-0.8$) dietary intake assessment tools, the precision and accuracy of which can be improved considerably by a skilled interviewer and the use of probing.
techniques (Block & Hartman, 1989; Cann et al., 2000). Most of the recent studies are based on 3-4 day food records, which eliminate the potential for recall error and with careful instructions for measuring and recording intake, provide a more accurate and sensitive measure of dietary change (Block & Hartman, 1989; Hill & Davies, 2001). Food records are generally accepted as the more precise instrument and are often used to validate other self-report measures (Demark-Wahnefried et al., 1997a). Using doubly labeled water as the standard, Prentice, Mossavar-Rahmani, Huang et al., (2011) found that 4-day food records provided a stronger estimate of energy intake (ratio of self-report to doubly labeled water = 0.80) compared to FFQ (0.72) and three 24-hr recalls (0.77). Martin et al. (1996) found that reporting accuracy, based on 7-day food records, compared to doubly labeled water, was ~80% for energy intake. There is some evidence to suggest that reporting accuracy may be improved with 3-day rather than 7-day food records (Rebro, Patterson, Kristal & Cheney, 1998); a finding that is perhaps related to the degree of burden associated with multiple days of record keeping (Caan et al., 2000). Furthermore, most studies measured intake before and after treatment, focusing on dietary change rather than precision in specific nutrient values.

It is also important to acknowledge that while some studies have reported changes in energy intake that were not statistically significant, if a true difference exists, small increases in intake after diagnosis may well be clinically relevant. Del Rio et al. (2002) observed a trend toward an increase in energy intake over six months of treatment (mean of 1900 kcals at baseline vs 1998 kcals & 2042 kcals at 3 and 6 months, respectively). An increase in energy intake of this magnitude, although not statistically significant, could translate into a 2.6 kg weight gain over six months; an estimate that is consistent with the observed weight gain in this sample group. Likewise Harvie et al. (2004) and Demark-Wahnefried et al. (2001) observed a small but non-
significant increase in mean energy intake of 96 kcals and 88 kcal/day at three months post-chemotherapy and one year, respectively; increases that might also produce clinically important weight gain over time. In addition, Foltz (1985) reported a 321 kcal/day difference in energy intake among women who gained weight compared to those who were weight stable, however small sample size, particularly in those who did not gain weight and wide variation in intake may have limited the ability of this study and others, to detect significant differences in energy intake between groups and over time.

Lastly, it must be recognized that differences in the timing of recruitment (pre-chemotherapy vs. post-treatment), treatment protocols and length of follow-up may account for some of the inconsistency in this literature. Moreover, the studies included in this review span over more than two decades, during which time chemotherapy treatments have evolved, perhaps producing differences in nutrition-related side effects and dietary change.

1.4.2 Energy Expenditure

1.4.2.1 Resting Energy Expenditure

Basal metabolic rate (BMR) is the rate at which the body expends energy to support basic physiological function (heart, lungs, temperature regulation, kidney function etc.). Basal metabolism is the largest component of energy expenditure, representing for the average person about two-thirds of daily energy needs (National Academy of Sciences, 2005). BMR varies significantly from person to person as a function of age, growth and development, body size, body composition, illness, hormone levels and environmental stresses. Evidence that cancer treatment and therapy-induced hormonal changes could reduce basal energy requirements (Arbeit, Lees, Corsey & Brennan, 1984; Demark-Wahnefried et al., 1993) suggests that changes in basal metabolism may play a role in post-diagnosis weight gain.
Research in this area however is limited and has produced inconsistent findings.

Indirect calorimetry has been used to estimate resting energy expenditure (REE) at various time points during and after treatment. Indirect calorimetry provides an estimate of resting energy expenditure derived from measured oxygen consumption and carbon dioxide production and the use of predictive equations. The accuracy and reliability of this measure is dependent on a number of factors including equipment calibration, comfortable room temperature, allowing for a stabilization period and simulating “resting conditions” as closely as possible (e.g., overnight fast, no vigorous exercise for 24-48 hrs, abstaining from smoking and caffeine for 12 hrs). Under these conditions, indirect calorimetry is reported to be accurate to within 2% of energy expenditure measured by doubly labeled water and is highly reliable (Horner, Lampe, Patterson et al., 2001; Jakicic, 2009). Although there were minor variations in the protocols, in all but one study (Foltz, 1985), these conditions were reported to have been achieved.

In seven studies in which REE was measured during treatment, two reported a decrease (Demark-Wahnefried et al., 1997a; Harvie et al., 2004), two reported an increase (Del Rio et al., 2002; Kutynec et al., 1999) and three found no significant change (Campbell et al., 2007; Demark-Wahnefried et al., 2001; Foltz, 1985). These studies are summarized in Table 1.3.

A decrease in REE was first noted among 18 premenopausal women undergoing three to six months of adjuvant chemotherapy for stage I-II disease (Demark-Wahnefried et al., 1997a). In this sample, a significant decrease in REE was seen at midtreatment (1277± 214 vs. 1354± 233 kcals/d, p< 0.01), but had returned to baseline by the end of treatment. Harvie et al. (2004) found that REE had decreased after three months of treatment (n=17, pre and postmenopausal)
and remained significantly lower than baseline, at the end of treatment (-36 kcals/day, p<0.05). Post-chemotherapy follow-up of these patients revealed that REE remained low for an additional three months (-47 kcals/day) but returned to pre-treatment levels by one year.

Two studies found that REE increased significantly after four to six cycles of chemotherapy. Kutynec et al. (1999) measured REE in pre and perimenopausal women (age 27-52 y, stage I-II) before and after four cycles of AC chemotherapy (n=8) or radiation (n=10) and found that REE expressed in kcals/kg of lean body mass (LBM) was significantly higher after treatment in both groups (39±5 vs 37±4 and 37±3 vs 35±4 respectively, p=0.01). LBM was estimated using DXA, which provides a precise measure of whole body and regional (head, trunk, limbs) bone mass and non-bone fat free soft tissue (Heymsfield, Lohman, Wang & Going, 2005). Small increases in REE in kcals/day and kcals/kg/day approached statistical significance (p=0.06). Del Rio et al. (2002) found that among 30 postmenopausal women (stage I-II), REE increased progressively over six cycles of CMF chemotherapy, reaching statistical significance at six months (p<0.05). This study further evaluated the acute effects of adjuvant chemotherapy on REE using repeat measures before and after each treatment. Among 23 patients receiving chemotherapy, a significant decrease in REE was observed during the first and sixth cycle of treatment, however, this effect was also documented in a control group of patients receiving a placebo infusion.

A recent study in which REE was measured before the initiation of treatment, once per cycle and at the end of treatment found that REE was not significantly changed at the end of treatment or at any time point across four to six cycles of chemotherapy (Campbell et al., 2007); a finding that is supported by two earlier studies (Demark-Wahnefried et al., 2001; Foltz, 1985).
Given that REE is strongly associated with lean body mass in particular (Wang, Heymsfield, Ying et al., 2010), changes in REE would be expected to correlate with changes in lean tissue, as well as changes in total body weight, however this has not been a consistent finding (Demark-Wahnefried et al., 1997a; Harvie et al. 2004). Harvie et al. (2004) for example, reported a significant reduction in REE after treatment, which was associated with a mean weight gain of 3.0 kg and no change in lean tissue. At one year, REE had increased to baseline values despite a significant loss of lean tissue, however, this finding is likely explained by progressive weight gain and a significant increase in body fat. Similarly, Demark-Wahnefried et al. (2001) suggested that a loss of lean tissue during and after chemotherapy treatment may have been offset by an increase in fat mass producing a net zero effect on basal metabolism. A significant increase in REE (kcals/kg LBM) reported by Kutynec et al. (1999) correlated, as would be expected, with a significant loss of lean tissue, however, it is not clear why a trend toward an increase in overall REE (kg/day), despite a loss of lean tissue and no change in body weight was evident at the end of 12 weeks of treatment. A second study in which an increase in REE was reported, found that REE in kcals/day increased progressively with weight gain (FM & FFM) over six months of treatment (Del Rio et al., 2002).

Collectively, these findings argue against a direct effect of chemotherapy on REE, suggesting instead that changes in REE correlate more closely with changes in body composition (Del Rio et al., 2002). Inconsistencies across a limited number of studies may have resulted from differences in the timing of measurements, chemotherapy protocols (e.g., AC, CEF, CMF, CAF) and sample characteristics (Campbell et al., 2007). Two of the current studies for example, measured REE before and after treatment (Foltz, 1985; Kutynec et al., 1999), while others (Del Rio et al., 2002; Demark-Wahnefried et al., 1997a; Demark-
Wahnefried et al., 2001) measured REE at baseline, mid-treatment and end of treatment, however mid-treatment timepoints (2 vs 3 months) varied as a function of the chemotherapy protocol that was used. Harvie et al. (2004) and Demark-Wahnefried et al., (2001) provided 12 month follow-up measurements of REE and Campbell and colleagues (2007) measured REE at each cycle. The latter study, well designed to investigate possible temporal fluctuations in REE during treatment, found no significant change in REE across four to six cycles of AC or CEF. Further research, using repeat measures of resting energy expenditure across different treatment protocols, may clarify the potential role of treatment specific changes in basal metabolism in the etiology of post-diagnosis weight gain (Campbell et al., 2007).

1.4.2.2 Physical Activity

Physical activity is the most variable component of energy expenditure, on average accounting for one-third of total energy output (National Academy of Sciences, 2005). Among sedentary adults however, physical activity may account for as little as 15-20% of energy expenditure, with low levels of physical activity strongly linked to obesity and weight gain (American College of Sports Medicine, 2009). Given that as many as 96% of patients report fatigue during treatment (Demark-Wahnefried et al., 1997b; Kumar et al., 2004), a reduction in physical activity during this time is expected. Moreover, fatigue has been shown to persist for many breast cancer survivors in the years after diagnosis (Meeske, Smith, Alfano et al., 2007); a side effect that seems to parallel progressive weight gain.

Changes in physical activity patterns after diagnosis and the degree to which these changes associate with weight gain, is an area of active research. Early studies focused largely on changes in work, home and social activities with mixed results, however, recent investigations have included more complete measures of physical activity (work related activity,
housekeeping, leisure time, structured physical activity) that can be transformed into an estimate of energy expenditure. It is important to acknowledge that all of the research to date has been based on self-report measures (diaries, questionnaires, surveys and recall interviews). Although many of these indirect measures have been validated (e.g. Standford Five-City Project Questionnaire - Sallis, Haskell, Wood et al., 1985; Modifiable Activity Questionnaire - Kriska, 1997) and offer the advantage of practicality, low cost and low response burden, all are subject to reduced precision and accuracy, recall error and response bias (Prince, Adamo, Hamel et al., 2008).

Despite these methodological challenges, several researchers have documented a significant decrease in physical activity during active treatment and in the year after diagnosis (Demark-Wahnefried et al., 1997a; Demark-Wahnefried et al., 2001; Irwin, Crumley, McTiernan et al., 2003; Irwin, McTiernan, Bernstein et al., 2004; Kumar et al., 2004). Using the Stanford Five-City Project Questionnaire, in 1997 Demark-Wahnefried et al. found a significant decrease in the daily energy cost of physical activity (-53 kcals/day, p= 0.04) over 15 weeks of adjuvant chemotherapy (n=18, stage I-II, premenopausal). Likewise, Kumar et al. (2004) reported lower levels of physical activity (work outside the home/purposeful physical activity) based on the Stanford Five-City Project Questionnaire in 56% of pre and postmenopausal women (n=198, stage I-III) during six months of treatment. Furthermore, among 53 premenopausal women treated for stage 0-III disease, a decrease in physical activity (~30-85 kcals/day) was observed in the immediate period after diagnosis compared to usual levels before diagnosis (Demark-Wahnefried et al., 2001). In the absence of a significant change in REE or energy intake, it was suggested by the authors, that reduced physical activity was the most likely contributor to positive energy balance. In this sample, a slow progressive increase in physical activity level
was observed during and after treatment, however baseline levels were still not restored in the chemotherapy treated women (n=36) at 48 weeks.

Similarly, data based on the Modifiable Activity Questionnaire from the Health, Eating, Activity and Lifestyle (HEAL) study revealed a significant decrease in physical activity among early stage breast cancer survivors (n= 812), four to twelve months after diagnosis, compared to activity in the year before diagnosis (Irwin et al., 2003). Overall, patients decreased their activity by an average of 2.0 hours per week (11%, p<0.05), with greater decreases in sports activities noted among women treated with radiation and chemotherapy (-50%) compared to those who were treated with surgery (-24%) or radiation only (-23%, p<0.05). A third study in which physical activity during and after treatment was compared to pre-diagnosis levels (n=17) found that while a trend toward a decrease in physical activity during treatment and a small increase in physical activity at one year were apparent, small sample size may have limited the ability to detect a significant difference (Harvie et al., 2004).

Not all studies have reported a reduction in physical activity during treatment. Kutynec et al. (1999) for example, measured physical activity using a structured physical activity diary and found that activity expressed in kcals/day was not significantly different before and after chemotherapy or radiation treatment (12 weeks, n=18). Consistent with the findings of Demark-Wahnefried et al. (2001), a trend toward an increase in physical activity was in fact evident over the course of 12 weeks in the chemotherapy treated women, however perhaps due to small sample size and considerable within group variability, was not statistically significant. It is noteworthy that the women in this sample did not experience significant weight gain but did show an increase in percent body fat and a significant loss of lean tissue; changes in body composition that might reasonably be attributed to a decrease in physical activity (Kutynec et
al., 1999). As is suggested by the authors, the absence of data on physical activity before diagnosis makes these findings difficult to interpret. It is possible that the use of pre-chemotherapy (after diagnosis) measures of physical activity as the baseline in this study and others (Demark-Wahnefried et al., 1997a; Kumar et al., 2004), may mask a sudden and significant reduction in physical activity that occurs at diagnosis (Demark-Wahnefried et al., 2001) and persists in some women during and after treatment (Irwin et al., 2004).

Goodwin et al. (1999) observed a significant increase in physical activity among early stage breast cancer patients (n=535) at a one year follow-up, compared to baseline measures taken before or during the first month of chemotherapy. In this study, changes in physical activity over the year did not correlate with weight change, however the absence of intermittent measures of physical activity throughout the year, may have confounded these results. As the authors suggest, lower levels of activity during treatment (not measured) among those who gained weight gain, may have prompted an increase in activity by one year. Alternatively, an increase in physical activity at one year may reflect a return to normal physical activity patterns before diagnosis. These studies highlight the utility of pre-diagnosis estimates of physical activity, as well as repeat measures during and after treatment, in order to fully capture associations between activity and weight change.

There is some evidence to suggest that lower levels of physical activity in the post-diagnosis period correlate with weight gain. Based on a sub-sample of participants from the WHEL study (n=1116), Rock et al. (1999) found that lower activity was significantly correlated with weight gain after diagnosis. The use of a non-standardized instrument to collect physical activity data and a cross-sectional design in which the analysis appears to be based on “current activity” which may not adequately reflect exercise patterns since diagnosis, suggests...
that these findings should be interpreted with caution. More recently, Nissen et al. (2011) found that a decrease in physical activity (number of blocks walked per day), based on the Paffenbarger Physical Activity Questionnaire, was significantly associated with weight gain over 12 months (p<0.05). Using the Modifiable Activity Questionnaire, Irwin and coworkers (2005) observed that weight gain and gains in percent body fat, from the first year after diagnosis to a follow-up within the third year after diagnosis, were significantly higher among women whose sports and recreational physical activity decreased over the same time frame. In addition, Goodwin, Esplen, Butler et al. (1998) found that within a multidisciplinary weight management program (psychosocial, nutrition, physical activity), aerobic exercise was the strongest predictor of success in achieving individual weight maintenance or weight loss goals in the first year after diagnosis. These associations are consistent with patient’s perceptions. In a small sample of African-American breast cancer survivors (n=34), women who reported weight gain (n=16 or 47%, mean weight gain =7.3 kg) attributed this weight gain to a decrease in physical activity after treatment (Halbert et al., 2008).

Two large cohort studies in which physical activity was measured two and three years after diagnosis, revealed that physical activity patterns among breast cancer survivors were comparable to women who are free of cancer, with only 32% meeting the minimum recommendation (150 min/week, moderate to vigorous activity) for the general adult population (Irwin et al., 2004; Caan et al., 2005). Clearly, as is the case with the majority of Canadian adults (Canadian Fitness and Lifestyle Research Institute, 2009), there is room for improvement in physical activity levels in this population and sufficient evidence to suggest that maintaining or increasing activity may assist with weight management. Furthermore, independent of weight change, physical activity has been shown to support positive changes in
body composition (Irwin, Alvarez-Reeves, Cadmus et al., 2009; Winters-Stone, Dobek, Nail et al., 2011) and improved quality of life (Courneya, 2003; Sprod, Janselsins, Palesh et al., 2012) in breast cancer survivors.

1.5 Summary of the Literature

Weight gain is a common and persistent problem for many breast cancer survivors. As many as 50-96% of women experience significant weight gain during treatment (Demark-Wahnefried et al., 1997b) and many, including some women who remain weight stable during treatment, report progressive weight gain in the months and years after diagnosis. Among those who gain weight, average increases typically range from 2.5-6.2 kg, however significantly higher gains are not uncommon. Several studies have reported unfavourable changes in body composition, with or without weight gain, in this population. Sarcopenic obesity, characterized by high body fat and a significant loss of lean tissue is prevalent. This unique pattern of weight gain and/or change in body composition is distressing for most women, poses significant risk for the development of co-morbid conditions and may impact on long term disease free survival.

Although there is an established link between adjuvant chemotherapy and weight gain, especially for women on longer duration treatments, the underlying mechanisms contributing to weight gain are not yet clearly established. It is possible that lengthy protocols, often involving the use of multi-agent therapies, simply reflect longer and harsher exposure to the conditions that affect behaviour change. Fatigue, nutrition-related side effects, psychological distress and the reality of multiple treatment days and medical consults may affect diet and physical activity patterns in ways that promote positive energy balance and weight gain.
Despite recent efforts to capture possible changes in dietary intake during and after treatment, empirical support for an increase in energy intake after diagnosis and an association between increased energy intake and post-diagnosis weight gain is lacking. The hypothesized mechanisms by which eating behaviour and energy intake might be altered after diagnosis (fatigue, stress, changes in appetite, treatment-related nausea), coupled with the known limitations of the methodology, suggests however, that the potential role of diet in post-diagnosis weight gain cannot be ruled out (Demark-Wahnefried et al., 2001).

Overall, there is little evidence at this time to suggest that a reduction in basal metabolic rate plays a significant role in post-diagnosis weight gain. In seven studies in which REE has been measured in breast cancer survivors, only two reported a significant decrease in REE during treatment: an effect that was relatively small and transient, returning to pre-treatment values within 6-12 months. Within the known limitations of the data collection methods, the bulk of the existing evidence suggests that physical inactivity is a significant contributor to energy imbalance and weight gain after diagnosis. Several studies have documented a significant reduction in physical activity during and after treatment and provide growing support for an association between lower levels of activity and weight gain.

It is important to recognize that treatment-related side effects likely play a role but are considered to be secondary, contributing to weight gain through their affect on energy intake or energy expenditure (Demark-Wahnefried et al., 1993). In addition, there is some evidence to suggest that alterations in ovarian function and sex hormone concentrations may produce an acceleration of the normal physiological changes associated with menopause (Tremollieries et al. 1996; Messier et al., 2009) promoting additional weight gain among women who experience treatment induced menopause (Goodwin et al., 1999). A conceptual framework
based on this review, showing the possible and probable pathways by which diet, physical
activity and resting energy expenditure interact with secondary factors to promote energy
imbalance and weight gain in breast cancer survivors is provided in Figure 1.1.

**Figure 1.1: Conceptual Model Showing Possible (---) and Probable (—) Factors
Promoting Energy Imbalance and Weight Gain in Breast Cancer Survivors**

1.6 Clinical Applications and Future Directions

The best clinical advice for breast cancer survivors at this time seems to be a
recommendation for regular physical activity. Post-diagnosis guidelines and interventions
should encourage and assist women to be as physically active as is possible within the context
of their treatment. Physical activity advice, including a recommendation for both
cardiovascular and resistance training, should be initiated early and delivered in conjunction with supportive programs throughout treatment. Evidence of progressive weight gain after the completion of initial treatment suggests that continued intervention and follow-up is also warranted. These recommendations are supported by the results of recent exercise interventions among breast cancer survivors, in which higher levels of physical activity, improvements in quality of life and positive changes in body composition (decreased fat mass, preservation of lean tissue and bone density) and physical function were reported (Irwin et al., 2009; Winters-Stone et al., 2011; Sprod et al., 2012; Anderson, Kimmick, McCoy et al., 2012).

Future research should use direct measures of physical activity (heart rate monitors, accelerometers, SenseWear Pro Armbands™) to confirm initial findings in relation to post-diagnosis weight change. Sensewear™ armbands, in particular, show promise as an objective measure of physical activity over longer time periods, recently providing an estimate of mean energy expenditure that was not significantly different, compared to doubly labeled water over 10 days (2237±568 vs. 2315±625 kcal/day) (Mignault, St-Onge, Karelis et al., 2005).

Despite uncertainty concerning the role of diet in post-diagnosis weight gain, current data on dietary patterns after diagnosis argue in support of dietary intervention within this population. While some women have reported positive dietary changes after diagnosis (an increase in fruits, vegetables & fibre, decrease in fat), these changes which might support weight management are reported to have been modest, especially among older women, with current intakes of fruits and vegetables in particular, still well below recommendations (Thomson, Flatt, Rock et al., 2002; Wayne, Lopez, Butler et al., 2004). At this time, there are very few studies comparing energy intake during and after treatment to usual intake before
diagnosis. Limited data in this area are largely based on semi-quantitative FFQ (before and after diagnosis) and questionnaires or interviews, in which breast cancer survivors have reported changes in dietary intake after diagnosis. While these studies have provided important insights, changes in diet after diagnosis should be further evaluated, in the context of precise measures of current dietary intake.

In addition, changes in energy and macronutrient intake relative to treatment days and treatment-related side effects have not been reported. Efforts to capture within cycle variability, in response to acute side effects of treatment, as well as possible cumulative effects of treatment over time are needed, in order to more accurately evaluate possible relationships between dietary change, energy imbalance and weight gain after diagnosis. Since not all women experience weight gain during treatment, it will also be important to investigate possible differences in diet and eating behaviour among women who gain weight versus those who remain weight stable; a level of analysis that is not reported in the current literature.

While this review has focused on energy intake, since this is central to the energy balance equation, breast cancer and its treatment may alter the quality of the diet in ways that affect overall health (Doyle et al., 2006) independent of whether or not they result in a measurable influence on energy intake and body weight. Therefore, understanding the dietary challenges that women experience during and after breast cancer treatment, including psychosocial and treatment-related factors that may interfere with healthy eating, is an important first step in designing effective nutrition intervention strategies after diagnosis.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
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<td>Reference</td>
<td>(size, key characteristics)</td>
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<tr>
<td>Aslani, Smith, Allen et al., 1999</td>
<td>n=25, age 26-70 y (mean = 47 y) Pre-Menop (60%), Post-Menop (40%), Stage I-III, CMF chemotherapy (6mos)</td>
<td>6 mos</td>
<td>measured ht &amp; wt, day 1 of cycles 2 and 6</td>
<td></td>
<td>2.35 kg</td>
<td></td>
</tr>
<tr>
<td>Basaran, Turhal, Cabuk et al., 2011</td>
<td>n=176, age 30-100 y (median = 53 y) Pre-Menop (28%), Post-Menop (72%) Stage I-III, chemotherapy (97%) with (69%) or without (28%) hormone therapy, Hormone therapy only 3%</td>
<td>1 y post treatment</td>
<td>chart review of weight at diagnosis, &lt; 1 month after chemotherapy and 1 y after chemotherapy</td>
<td>67%</td>
<td>1.7 kg (after treatment)</td>
<td>2.4 kg * (after treatment)</td>
</tr>
<tr>
<td>Campbell, Lane, Martin et al., 2007</td>
<td>n=10, mean age = 46.9 y, Pre-Menop (70%), Post-Menop (30%), Stage I-IIIA, AC or CEF chemotherapy (3-6 mos)</td>
<td>3-6 mos</td>
<td>measured ht &amp; wt before and after treatment</td>
<td>70%</td>
<td>1.98 kg</td>
<td>2.6 kg</td>
</tr>
<tr>
<td>Caan, Edmond, Natarajan et al., 2006</td>
<td>n=3215, mean age = 55.3 y Pre-Menop (26%), Post-Menop (57%), Stage I-IIIA, chemotherapy and/or radiation, (15% surgery only)</td>
<td>5-7 y</td>
<td>self-reported wt 1 yr before diagnosis and at study enrollment (~2y from diagnosis)</td>
<td>44% (&gt; 5%)</td>
<td>2.4 kg</td>
<td>5.6% * 3.0%</td>
</tr>
<tr>
<td>Cheney, Mahloch &amp; Freeny, 1997</td>
<td>n=34, age 39-73y (mean = 51-56 y) Pre-Menop (44%), Post-Menop (56%) Stage I-IIIA, current chemotherapy, or surgery and/or chemotherapy &lt; 1 y</td>
<td>6-12 mos</td>
<td>measured or chart/self-reported wt at diagnosis (&lt;6mos) and after treatment (6-12mos)</td>
<td>71%</td>
<td></td>
<td></td>
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<tr>
<td>Costa, Varella &amp; del Giglio, 2002</td>
<td>n=106, age 26-78 y (median = 49y) Pre-Menop (47%), Post-Menop (53%) Stage I-IV (23% palliative), CMF, FAC, FEC or AC chemotherapy</td>
<td>mean = 4.9 mos</td>
<td>chart review of patients with ≥ 2 weight records (≥ 1 mos apart) during chemotherapy</td>
<td>81%</td>
<td>0.91% per mos</td>
<td></td>
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<tr>
<td>Del Rio, Zironi, Valeriani et al., 2002</td>
<td>n=30, mean age = 56 y Post-Menop (100%), Stage I-II, 6 cycles of CMF chemotherapy</td>
<td>6 mos</td>
<td>measured wt before and after treatment</td>
<td>100%</td>
<td>2.8 kg</td>
<td></td>
</tr>
<tr>
<td>Demark-Wahnefried, Hars, Conway et al., 1997</td>
<td>n=20, age 27-52y (mean = 39.9 y) Pre-Menop (100%), Stage I-II, Adjuvant chemotherapy – 12-24 wks</td>
<td>12 mos</td>
<td>measured wt before and after treatment chart review at 12 mos</td>
<td></td>
<td>3.8 kg</td>
<td>No change in mean body wt during treatment</td>
</tr>
<tr>
<td>Demark-Wahnefried, Peterson, Winer et al., 2001</td>
<td>n= 53, age 27-54 y (mean = 41 y) Pre-Menop (100%), Stage I-II, Surgery with or without radiation, or adjuvant chemotherapy</td>
<td>12 mos</td>
<td>measured wt before and after treatment (6mos) and 12 mos</td>
<td>1.0 - 2.1 kg</td>
<td></td>
<td>Mean wt gain at 6 mos 0.5 - 2.2 kg</td>
</tr>
<tr>
<td>Freedman Aziz, Albanes et al., 2004</td>
<td>n=20, mean age = 48.2 y Pre-Menop (50%), Post-Menop (50%) Stage I-IIIA, Adjuvant chemotherapy</td>
<td>10.5 mos</td>
<td>measured ht &amp; wt before treatment, 2 wks after treatment and 6 mos post-treatment</td>
<td>40-60%</td>
<td>0.27 kg</td>
<td>2.43 kg * (6 mos follow-up)</td>
</tr>
</tbody>
</table>

Pre-Menop = premenopausal at diagnosis, Post-Menop = postmenopausal at diagnosis  * p<0.05 compared to postmenopausal
Table 1.1: continued

<table>
<thead>
<tr>
<th>Reference</th>
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<th>Frequency of Wt Gain</th>
<th>Mean Weight Gain</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwin, Ennis, Pritchard et al., 1999</td>
<td>n=535, mean age = 50.3 y Pre-Menop (57%), Post-Menop (38%) Stage I-III, Adjuvant chemotherapy, tamoxifen or no adjuvant treatment</td>
<td>12 mos</td>
<td>measured ht &amp; wt before or during the 1st mos of treatment and 12 mos (n=445)</td>
<td>84%</td>
<td>1.6 kg</td>
<td>1.93 kg *</td>
</tr>
<tr>
<td>Gordon, Hurwitz, Shapiro &amp; LeBoff, 2011</td>
<td>n=43, age 34-52 (median = 44) Premenopausal, Stage I-II</td>
<td>12 mos</td>
<td>measured ht &amp; wt before treatment (within 4 wks) and 12 mos</td>
<td>79%</td>
<td>median = 2.7 kg</td>
<td>Weight gain in women who developed chemotherapy induced ovarian failure N/S different vs. those who retained ovarian function</td>
</tr>
<tr>
<td>Gu, Chen, Zheng, Chen, Lu &amp; Shu, 2010</td>
<td>n=5014, mean age = 53.5 y Pre-Menop (49%), Post-Menop (51%) Stage 0-III, chemotherapy (91%), radiation (32%).</td>
<td>36 mos</td>
<td>self-reported wt at diagnosis + chart review for 95%. Measured ht &amp; wt at 6, 18 and 36 mos</td>
<td>39% ≥ 2 kg (6mos)</td>
<td>median = 1.0 kg (6mos)</td>
<td>1.5 kg *</td>
</tr>
<tr>
<td>Halbert, Weathers, Esteve et al., 2008</td>
<td>n=34, mean age = 57.4 y Completed primary treatment for early stage or locally advanced stage disease DNR mean = ~5 y</td>
<td>2 y</td>
<td>self-reported ht &amp; wt before diagnosis and at study enrollment (~ 5 y from diagnosis)</td>
<td>47%</td>
<td>79%</td>
<td>Mean gain among women who gained wt = 7.3 kg</td>
</tr>
<tr>
<td>Han, Lee, Kim et al., 2009</td>
<td>n=260, mean age = 47 y Pre-Menop (61%), Post-Menop (38%) Stage I-III, Adjuvant chemotherapy and/or hormonal therapy</td>
<td>2 y</td>
<td>chart review of ht &amp; wt before and after (3, 6, 12, 24 months) treatment</td>
<td>47% (12 mos)</td>
<td>0.30 kg</td>
<td>Mean gain among women who gained wt at 12 mos = 1.93 kg</td>
</tr>
<tr>
<td>Harvie, Campbell, Baildam &amp; Howell, 2004</td>
<td>n=17, mean age = 46 y Pre-Menop (76%), Post-Menop (24%) Early stage, Adjuvant chemotherapy</td>
<td>12 mos</td>
<td>measured ht &amp; wt before, mid (3rd cycle) and after treatment (1 month and 9,12 months from diagnosis)</td>
<td>55%</td>
<td>2.4 kg</td>
<td>3.9 kg *</td>
</tr>
<tr>
<td>Heideman, Russell, Gundy et al., 2009</td>
<td>n=271, mean age = 54 y Pre-Menop (47%), Post-Menop (53%) Stage I-III, 71% chemotherapy and/or hormone therapy, 29% no systemic treatment median = 3.1 y</td>
<td>median = 3.1 y</td>
<td>chart review of ht &amp; wt at diagnosis, 1 y after diagnosis and -5 y after diagnosis</td>
<td>55%</td>
<td>2.4 kg</td>
<td>3.9 kg *</td>
</tr>
<tr>
<td>Ingram and Brown 2004</td>
<td>n=76, age 26-54 y (mean = 44 y) Pre-Menop (100%) Stage I-II, Adjuvant chemotherapy</td>
<td>6 mos</td>
<td>measured ht &amp; wt before, every other cycle, after treatment</td>
<td>34% (≥ 2.5 kg)</td>
<td>1.4 kg</td>
<td>Mean gain among women who gained wt = 5.0 kg</td>
</tr>
</tbody>
</table>

Pre-Menop = premenopausal at diagnosis, Post-Menop = postmenopausal at diagnosis   * p<0.05 compared to postmenopausal
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</tr>
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<tbody>
<tr>
<td>Irwin, McTiernan, Baumgartner et al., 2005</td>
<td>n=514, mean age = 56 y Pre-Menop (31%), Post-Menop (69%) Stage 0-III A, surgery only (30%), surgery and radiation (42%), chemotherapy (27%)</td>
<td>3 y</td>
<td>measured ht &amp; wt within first year of diagnosis (~ 6 mos) and 2 years after baseline (within third year of diagnosis)</td>
<td>68%</td>
<td>1.7 kg</td>
<td>Mean gain among women who gained wt = 3.9 kg 18% gained ≥ 5 kg</td>
</tr>
<tr>
<td>Kumar, Allen, Cantor et al., 1997</td>
<td>n=200, mean age = 56-62 y Pre-Menop (11-26%), Post-Menop (74-89%), Stage I-II Surgery only or surgery plus tamoxifen and/or radiation</td>
<td>chart review of ht &amp; wt at diagnosis, after treatment (mean = 34 mos for tamoxifen) and final follow-up</td>
<td></td>
<td>1.2 kg</td>
<td>No systemic chemotherapy treatment</td>
<td></td>
</tr>
<tr>
<td>Kumar, Allen, Riccardi et al., 2004</td>
<td>n=198, mean age = 49 y Pre-Menop (47%), Post-Menop (53%) Stage I-IIIB, Adjuvant chemotherapy with or without radiation</td>
<td>measured ht &amp; wt before and after treatment - self-reported 6 mos post-treatment</td>
<td></td>
<td>3.1 kg (6 mos follow-up)</td>
<td>Mean wt gain during treatment N/S 22% gained ≥ 2.3kg Wt gain in pre-menop vs. post-menop – N/S</td>
<td></td>
</tr>
<tr>
<td>Kutynec, McCargar, Barr &amp; Hislop, 1999</td>
<td>n=18, mean age = 42-44 y Pre or perimenopausal (100%) Stage I-II, AC chemotherapy (44%) or radiation only (56%)</td>
<td>measured ht &amp; wt before and after treatment</td>
<td></td>
<td>0.0 -1.0 kg</td>
<td>Follow-up (66-103wks) for 13 of 18 women revealed wt gain in 57-66% of women (mean = 4.1-4.7kg)</td>
<td></td>
</tr>
<tr>
<td>Lankester, Phillips &amp; Lawton, 2002</td>
<td>n=100, age 29-73 y (mean = 50 y) Pre-Menop (69%), Post-Menop (31%) Stage I-III, 6 cycles of FEC or CMF chemotherapy</td>
<td>chart review of ht &amp; wt before and after treatment</td>
<td>64% (&gt; 2 kg) 27% (&gt; 5 kg)</td>
<td>3.68 kg</td>
<td>Wt gain in pre-menop vs. post-menop – N/S</td>
<td></td>
</tr>
<tr>
<td>Makari-Judson, Judson &amp; Mertens, 2007</td>
<td>n=185, age 20-91 y (mean = 51 y) Pre-Menop (50%), Post-Menop (50%) Stage I-IIIB, Adjuvant chemotherapy and/or hormonal therapy, 4% no systemic treatment</td>
<td>chart review of ht &amp; wt at diagnosis and 1, 2, 3 y after diagnosis</td>
<td>71% (1y) 70% (2y) 70% (3y)</td>
<td>1.5 kg (1y) 2.7 kg (2y) 2.8 (3y)</td>
<td>Mean gain among women who gained wt (1 y) = 3.7 kg Among women who were weight stable in year 1, 32% gained weight in year 2</td>
<td></td>
</tr>
<tr>
<td>Mclarnes &amp; Knobf, 2001</td>
<td>n=44, age 29-75 y (mean = 50 y) Pre-Menop (57%), Post-Menop (43%) Stage I-II, Adjuvant chemotherapy with or without radiation</td>
<td>chart review of ht &amp; wt at diagnosis and 1, 2, 3 y after diagnosis</td>
<td>78% (1y) 82% (2y) 71% (3y)</td>
<td>4.1 kg (1y) 4.0 kg (2y) 4.9 kg (3y)</td>
<td>Mean gain among women who gained significant wt (≥ 2.3 kg) = 4.7 kg (1 y) Frequency of weight gain &gt; 2.3 kg = 63%, 68% and 40% at 1, 2 and 3 y</td>
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</tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Nissen, Shapiro &amp; Swenson, 2011</td>
<td>n=49, age 40-54 y (mean = 47 y) Pre-Menop (71%), Peri/Post Menop (29%). Stage I-III, Adjuvant or neoadjuvant chemotherapy randomized to physical activity or bisphosphonate intervention</td>
<td>12 mos</td>
<td>measured ht &amp; wt at baseline (within one month of starting chemotherapy) and 12 mos</td>
<td>27% (&gt;5%)</td>
<td>Baseline BMI was inversely associated with weight gain at 12 mos (mean wt change: normal weight + 2.0 kg, overweight - 1.4 kg obese - 1.9 kg, p=0.01) Age – N/S</td>
<td></td>
</tr>
<tr>
<td>Rock, Flatt, Newman et al., 1999</td>
<td>n=1116, age 26 – 70 y (mean = 51 y) Pre-Menop at study entry (mean = 26 mos from diagnosis) (21%), Post-menop at study entry (79%) stage I-IIIA, Adjuvant chemotherapy (completed) and/or anti-estrogen treatment</td>
<td>mean = 26 mos</td>
<td>self reported ht &amp; wt 1 y before diagnosis and study entry + measured ht &amp; wt at study entry</td>
<td>60%</td>
<td>2.7 kg</td>
<td>Postmenopausal women &lt; 50 y were likely premenopausal at diagnosis</td>
</tr>
<tr>
<td>Tredan, Bajard, Meunier et al., 2010</td>
<td>n=272, age 25-73 y (median = 52 y) Pre-menop (45%), Post-Menop (55%) Non metastatic breast cancer. Adjuvant chemotherapy</td>
<td>15mos</td>
<td>measured ht &amp; wt at baseline (before treatment), 9 and 15 months * 6 and 12 mos post chemotherapy</td>
<td>52% (9 mos) 60% (15 mos)</td>
<td>0.7 kg (9 mos) 1.5 kg (15 mos)</td>
<td>Mean gain among women who gained = 3.2 kg at 9 mos and 3.9 kg at 15 mos</td>
</tr>
<tr>
<td>Thivat, Therondel, Lapirot et al., 2010</td>
<td>n=111, age 32-55 y (median = 54) Pre-Menop (45%), Post-Menop (55%) Stage I-III, Anthracycline- based chemotherapy</td>
<td>Median = 20.4 y</td>
<td>measured ht and wt beginning of treatment and in the last chemotherapy cycle</td>
<td>14% (&gt;5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yaw, Kandiah, Shariff et al., 2010</td>
<td>n=368, mean age = 54 y Pre-Menop (20%), PostMenop (80%) Stage I-III, completed chemotherapy</td>
<td>mean = 4.9 y</td>
<td>self reported wt at diagnosis. Measured ht &amp; wt at study entry (mean = 4.9 y post treatment)</td>
<td>49.5%</td>
<td>3.47 kg</td>
<td></td>
</tr>
</tbody>
</table>

Pre-Menop = premenopausal at diagnosis, Post-Menop = postmenopausal at diagnosis * p<0.05 compared to postmenopausal ¶ p<0.05 compared to premenopausal & postmenopausal > 50 y
Table 1.2: Studies Investigating Weight Gain after Breast Cancer Diagnosis and Disease Free Survival (DFS)
(References for studies in which a positive association between weight gain and DFS are bolded)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample (size, key characteristics)</th>
<th>Follow-up</th>
<th>Weight Measures</th>
<th>Weight Gain</th>
<th>Relationship between Weight Gain &amp; OS/DFS</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Camoriano et al., 1990</td>
<td>n=646, age 20-75 y Node positive disease treated with or without adjuvant chemotherapy</td>
<td>median = 6.6 y</td>
<td>Body weight at randomization (within 8 wks of surgery) and after treatment (60 wks)</td>
<td>Median weight gain: Premenopausal = 5.9 kg Postmenopausal treated = 3.6 kg Postmenopausal non-treated = 1.8 kg</td>
<td>Premenopausal women who gained &gt; median weight had higher risk of death (RR=1.6, p&lt;0.05). Trend toward increased risk of recurrence but N/S (RR=1.5, p=0.17)</td>
<td>Controlled for multiple known prognostic indicators Postmenopausal women – weight gain N/S</td>
</tr>
<tr>
<td>Caan et al., 2006</td>
<td>n=3250, age 18-70 y (mean age at diagnosis = 55.3 y) Stage 1-111A</td>
<td>median = 5 y (LACE) 7 y (WHEL)</td>
<td>Body weight 1 y before diagnosis and at enrollment (mean = 23 mos from diagnosis)</td>
<td>Mean weight gain = 2.4 kg Weight gain was progressive after diagnosis in both groups, stabilizing at ~ 3 yrs</td>
<td>No association between weight gain and risk of breast cancer recurrence No association between weight gain and DFS or all-cause mortality (LACE only ~ 7 y)</td>
<td>Controlled for multiple known prognostic indicators</td>
</tr>
<tr>
<td>Chen et al., 2010</td>
<td>n=5042, age 20-75 y (mean = 53.5) Non metastatic disease treated with chemotherapy (93%) and/or radiation (32%)</td>
<td>median = 46 mos</td>
<td>Body weight 1 y before diagnosis, at diagnosis, 6 and 18 mos after diagnosis</td>
<td>Mean weight gain = 1.0 kg at 6 mos and 1.7 kg at 18 mos Weight gain 1-5 kg (37%) Weight gain &gt;5kg (24%)</td>
<td>Weight gain 1-5 kg and &gt;5kg from one year pre-diagnosis to 18 mos associated with an increased risk of recurrence (HR=1.97 and 1.90, p&lt;0.05) and all-cause mortality (HR=1.89 and 1.71, p&lt;0.05) Weight loss &gt;1.0 kg also associated with increased risk of disease recurrence and all-cause mortality. Controlled for multiple known prognostic indicators</td>
<td></td>
</tr>
<tr>
<td>Chlebowski et al., 1986</td>
<td>n= 62, ≥ 4 positive nodes Adjuvant chemotherapy</td>
<td>median = 112 mos (range 104-128)</td>
<td>Body weight before and after treatment (12 mos)</td>
<td>91% of CMF treated women gained weight Mean = 3.7 kg 74% of 5FU treated women gained weight Mean = 2.0 kg</td>
<td>Weight gain &gt; 10 kg assoc with poor prognosis - all 5 women who gained &gt; 10 kg had not survived at follow-up vs. 48% survival in women who gained &lt; 10 kg</td>
<td>All patients at high risk for recurrence, based on inclusion criteria</td>
</tr>
<tr>
<td>Costa et al., 2002</td>
<td>n=106, age 26-78 y, (median = 49 y) Adjuvant, neoadjuvant and palliative chemotherapy</td>
<td>median follow-up not given ~ 54 mos</td>
<td>Body weight before and after one or more cycles of chemotherapy (mean=4.9 mos)</td>
<td>81% of women receiving adjuvant or neoadjuvant treatment gained weight Mean = 0.91 ± 1.19 % / mos</td>
<td>Trend toward decreased DFS for women who gained weight but N/S (p = 0.08)</td>
<td></td>
</tr>
<tr>
<td>Goodwin et al., 1988</td>
<td>n=637, mean age across groups = 42.2-56.5 y Localized disease treated with or without adjuvant chemotherapy</td>
<td>median follow-up not given Recruitment 1960-1984</td>
<td>Body weight at diagnosis and 1 year after diagnosis</td>
<td>Mean weight gain = 1.21 – 5.55 kg across 5 treatment groups</td>
<td>No association between weight gain (quartiles) and DFS or overall survival</td>
<td>Controlled for multiple known prognostic indicators Weight missing in up to 22% for some groups</td>
</tr>
<tr>
<td>Reference</td>
<td>Sample (size, key characteristics)</td>
<td>Follow-up</td>
<td>Weight Measures</td>
<td>Weight Gain</td>
<td>Relationship between Weight Gain &amp; OS/DFS</td>
<td>Comments</td>
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<tr>
<td>Heasman et al., 1985</td>
<td>n=237, age 25-70 y (mean = 47.5 y) Stage 11 Adjuvant chemotherapy</td>
<td>≥ 2 y</td>
<td>Body weight before and after treatment (12 mos)</td>
<td>96% of patients gained weight during treatment Mean = 4.3 kg</td>
<td>No association between weight gain (quartiles) and DFS or overall survival</td>
<td>Controlled for lymph node status, menopause status and type of treatment</td>
</tr>
<tr>
<td>Kroenke et al., 2005</td>
<td>n=5204, age 30-55 y Invasive non-metastatic disease Sub-sample from the Nurses Health Study US</td>
<td>median = 9 y (range 2-26 y) Pre-diagnosis BMI and post-diagnosis BMI (most recent measure ≥ 12 mos)</td>
<td>32% of patients gained 0.5-&lt;2.0 kg/m² Median = 2.73 kg 14% of patients gained ≥ 2.0 kg/m² Median = 7.73 kg</td>
<td>Among never smokers weight gain associated with increased risk of recurrence Wt gain 0.5-&lt;2.0 kg/m² RR = 1.40, p&lt;0.05 Wt gain ≥ 2.0 kg/m² RR = 1.53, p&lt;0.05</td>
<td>Controlled for multiple known prognostic indicators Similar findings for breast cancer death and all-cause mortality</td>
<td></td>
</tr>
<tr>
<td>Levine et al., 1991</td>
<td>n=32, age 26-68 y (mean = 46 y) 27/32 lymph node involvement Adjuvant chemotherapy</td>
<td>~ 2 y</td>
<td>Body weight before and after treatment (3 mos) and 2 y follow-up</td>
<td>69% of patients gained weight during treatment Mean = 1.8 kg 84% of patients gained wt at 2y Mean = 4.18 kg</td>
<td>Women who had gained weight at 2 y had a 36% higher risk of recurrence but this effect was N/S (p&gt;0.05)</td>
<td>Stratification by menopause status did not effect relationship between weight gain and DFS</td>
</tr>
<tr>
<td>Makari-Judson et al., 2007</td>
<td>n=185, age 20-91 y (mean = 50.8 y) Stage 1-111 Adjuvant chemotherapy and/or hormonal therapy</td>
<td>3 y</td>
<td>Body weight at diagnosis and 1,2,3 years after diagnosis</td>
<td>71% of patients gained weight in the first year- Mean = 1.5 kg Mean wt gain at 2 y = 2.7 kg Mean wt gain at 3 y = 2.8 kg</td>
<td>Weight gain (&gt;2.5 kg) at 1 y was not associated with DFS (any breast cancer event including new primary), relapse-free survival (recurrence) or overall survival</td>
<td></td>
</tr>
<tr>
<td>Nichols et al., 2009</td>
<td>n=3993, age 25-87 (mean = 59 y) Invasive non-metastatic disease</td>
<td>6.3 y</td>
<td>Body weight 1-5 y before diagnosis and at study enrollment (mean = 5.8 y from diagnosis)</td>
<td>56% of patients gained &gt; 2.0 kg 14% of patients gained &gt; 10kg</td>
<td>Weight gain &gt;10 kg - 70% &amp; 78% increase in all-cause and breast cancer mortality. Among women who gained weight, each 5 kg gain was associated with increased risk of all-cause mortality (RR = 1.12, p&lt;0.05) and breast cancer death (RR =1.13, &lt;0.05)</td>
<td>Controlled for multiple known prognostic indicators</td>
</tr>
<tr>
<td>Thivat, Therondel, Lapriot et al., 2010</td>
<td>n=111, age 32-55 y (median = 54) Pre-Menop (45%), Post-Menop (55%) Stage I-III, Anthracycline-based chemotherapy</td>
<td>median = 20.4 y</td>
<td>measured ht and wt beginning of treatment and in the last chemotherapy cycle</td>
<td>14% of patient gained &gt; 5% of initial body weight</td>
<td>Weight variation - gain or loss &gt;5% of initial body weight was associated with an increased risk of disease recurrence (RR 2.28, p&lt;0.05 and death (RR 2.21, p&lt;0.05)</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Sample size, key characteristics</td>
<td>REE Measure</td>
<td>Timing of REE Measures</td>
<td>Key Findings/Comments</td>
<td></td>
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<tr>
<td>Campbell et al., 2007</td>
<td>n=8, mean age = 46.9 pre and postmenopausal, stage 1-111A</td>
<td>Indirect calorimetry using formula provided by manufacturer (K4 b² metabolic cart) in the patient’s home Fasted for 12 hrs</td>
<td>Before chemotherapy, once per cycle (within 7 days of last dose, every 3-4 weeks) and after chemotherapy (4-6 months)</td>
<td>No significant change in REE from baseline to after treatment (1190±80.27 vs. 1206±56.71 kcal/day, p=0.74) or across 4 cycles of chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Del Rio et al., 2002</td>
<td>n=30, mean age 56 y, postmenopausal, stage 1 or 11</td>
<td>Indirect calorimetry using the abbreviated Weir formula Fasted for 12 hrs</td>
<td>First day of the 1ˢᵗ, 3ʳᵈ and 6ᵗʰ cycles of chemotherapy (6 months)</td>
<td>Significant increase in REE at 6 months (p&lt;0.05) correlating with weight gain (mean = 2.8 kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demark-Wahnefried et al., 1997</td>
<td>n=18, age 27-52 y, premenopausal, stage 1 or 11</td>
<td>Indirect calorimetry using the Weir formula Fasted and no physical activity for 12 hrs</td>
<td>Before chemotherapy, midtreatment and after chemotherapy (3-6 months)</td>
<td>Significant decrease in REE at midtreatment (1277kcal/d ±214 vs. 1354± 233 kcal, p&lt;0.01), but had returned to baseline by the end of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demark-Wahnefried et al., 2001</td>
<td>n=53, mean age 41 y premenopausal, stage 0-111A</td>
<td>Indirect calorimetry using the Weir formula Fasted and no physical activity for 12 hrs</td>
<td>Before chemotherapy, 2 months, 6 months and 1 year</td>
<td>No significant change in REE over time in women treated with chemotherapy or localized treatment only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foltz, 1985</td>
<td>n=34, mean age 50 y, stage 11</td>
<td>Indirect calorimetry Not fasted Resting state not achieved</td>
<td>Before and after 6 cycles of chemotherapy (6 months)</td>
<td>Change in REE N/S different between women who gained weight and those who were weight stable. Significance of change over time – not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harvie et al., 2004</td>
<td>n=17, mean age = 46.1 y pre and postmenopausal, invasive disease</td>
<td>Indirect calorimetry using the Weir formula Fasted for 12 hrs, no caffeine or smoking for 12 hrs, no vigorous exercise for 24 hrs</td>
<td>Before chemotherapy, midtreatment, after chemotherapy, 3 months post-chemotherapy and 1 year</td>
<td>REE appeared to be lower midtreatment (-93 kcal/day) (statistical analysis not undertaken at this time point). Significant decrease in REE at the end of chemotherapy (-36 kcal/day, p&lt;0.05). REE lower (-47 kcal/day) at 3 months post chemotherapy but had returned to baseline at 1 year (p=0.94). REE in kcal/kg FFM appeared to be lower midtreatment but was not significantly changed at the end of chemotherapy or 1 year follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kutyne et al., 1999</td>
<td>n=18, mean age 42-46 y pre and perimenopausal, stage 1 or 11</td>
<td>Indirect calorimetry using the Weir formula Fasted for 12 hrs and no physical activity for 48 hrs</td>
<td>Before and after 4 cycles of chemotherapy</td>
<td>REE in kcal/kg LBM/day increased significantly from before treatment to after treatment (p&lt;0.01) in chemotherapy and radiation treated women – correlating with significant loss of lean tissue. Small increases in REE in kcal/day and kcal/kg/day approached significance (p=0.06)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER 2: METHODS

2.1 Sample Recruitment and Selection Criteria

Participants were recruited from the Waterloo, Guelph, Hamilton and London, Ontario Regions to participate in a single qualitative interview, complete validated questionnaires (physical and psychological distress), identify changes in diet since diagnosis and provide 3-day food records. The catchment area was initially limited to the Waterloo and Guelph regions, in an effort to increase the homogeneity of the sample (e.g., increase likelihood that participants were treated with similar chemotherapy protocols, at the same regional cancer centre). Recruitment was expanded to include the Hamilton and London regions after eight months, in response to slower than anticipated accrual rates.

Recruitment took place over a 14 month period and was conducted using several strategies. First, through collaboration with the Canadian Breast Cancer Foundation, a recruitment letter (Appendix C) was placed in the “run kits” for the Guelph location of the CIBC Run for the Cure on October 3, 2010. On the same day, the recruitment letter was available in the survivor tent in the Waterloo location, with the researcher present before and after the run to respond to questions. Also in October 2010, the recruitment letter was posted in the Well-Fit Centre at the University of Waterloo and with prior consent, four eligible women who had participated in our pilot study were re-contacted and invited to participate.

In December 2010 the recruitment letter was posted on the Canadian Breast Cancer Network (CBCN) online Bulletin Board, with a follow-up research summary posted in the CBCN “Outreach” online newsletter in June 2011. Local support groups and programs (identified through the CBCN website) were contacted in December 2010, leading to an opportunity to provide a brief presentation to breast cancer survivors in Guelph in January
2011 and an offer to circulate the recruitment letter at the Annual General Meeting of the Guelph Dragonboat Team later in the month. In addition, advertisements were placed in several local, community newspapers early in January 2011 and again in June, July and August 2011. (Appendix D).

In February 2011, the recruitment letter was posted in the HopeSpring Cancer Support Centre in Waterloo and forwarded to all group leaders in the main centre and satellite location in Cambridge. The recruitment letter was also posted in the Nu Me Boutique in Kitchener, a boutique catering to post surgical breast form, compression garments and lingerie needs for women having undergone mastectomy, with additional copies made available to interested customers. Later in the month, a display booth was set up at the Total Woman Show in Kitchener, with the recruitment letter and researcher present over a two day period.

With assistance from the Applied Health Sciences Communications Manager, a news release providing an overview of the research and contact information was posted in the University of Waterloo Daily Bulletin on March 7, 2011 (Appendix E). Also in March 2011, contact was made with the Clinical Trials Manager at the Grand River Regional Cancer Centre in Kitchener, leading to an invitation to present to the Scientific Review Committee in May 2011 and subsequent approval (August 2011) to post the recruitment letter in key areas of patient care (chemotherapy clinic, supportive care) within the centre.

In June 2011, the recruitment letter was circulated via Dietitians of Canada to the Waterloo Region Registered Dietitians network, prompting further interest from HopeSpring and a research summary posting on the homepage of their website. Finally, attempts to contact additional programs for breast cancer survivors (YMCA Encore, Juravinski Cancer Centre: Wellness Program, Canadian Cancer Society: Living Well Beyond Cancer Program) were
made in May, June and September 2011 and the recruitment letter was posted on Kijiji online, an advertising/sales network, in the Waterloo and London areas. Recruitment and accrual results summarized in table 2.1.

Table 2.1: Recruitment Procedures and Accrual Results

<table>
<thead>
<tr>
<th>Organization</th>
<th>Procedure</th>
<th>Accrual Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Waterloo</td>
<td>Recruitment letter posted in Well-Fit, Oct/10 (group exercise program for cancer patients)</td>
<td>5</td>
</tr>
<tr>
<td>University of Waterloo</td>
<td>Contacted eligible participants from our pilot study (n=4). Interest in pilot study but not eligible (n=1), Oct/10</td>
<td>5</td>
</tr>
<tr>
<td>Canadian Breast Cancer Network</td>
<td>Recruitment letter posted - online “Bulletin Board”, Dec/10 Research summary posted in “Outreach” online newsletter, June/11</td>
<td>0</td>
</tr>
<tr>
<td>Women’s Breast Cancer Support</td>
<td>Email to Kitchener/Waterloo Support Group, Dec/10</td>
<td>0</td>
</tr>
<tr>
<td>Guelph &amp; Wellington Breast Cancer Support Group</td>
<td>Research overview - presentation to breast cancer survivors, Jan/11 support group meeting</td>
<td>1</td>
</tr>
<tr>
<td>Guelph DragonBoat Team</td>
<td>Recruitment letter circulated - Annual General Meeting, Jan/11</td>
<td>0</td>
</tr>
<tr>
<td>Your Classifieds</td>
<td>Cambridge Times, Kitchener Record, Guelph Mercury, Jan/11</td>
<td>0</td>
</tr>
<tr>
<td>HopeSpring Cancer Support Centre</td>
<td>Recruitment letter posted in centre and forwarded to all group leaders, Feb/11. Research overview posted online, June/11</td>
<td>2</td>
</tr>
<tr>
<td>Nu Me Boutique</td>
<td>Mastectomy Specialist Recruitment flyer posted in store, Feb/11</td>
<td>0</td>
</tr>
<tr>
<td>Total Woman Show</td>
<td>Display booth, recruitment letter and researcher present, Feb/11</td>
<td>0</td>
</tr>
<tr>
<td>University of Waterloo</td>
<td>UW Daily Bulletin - Research overview, March/10</td>
<td>2</td>
</tr>
<tr>
<td>Grand River Regional Cancer Centre</td>
<td>Contacts/Meetings Clinical Trials Manager, March-April/11 Presentation to Scientific Review Committee, May/11 Recruitment letter posted in patient areas including chemotherapy clinic and supportive care, Aug/11</td>
<td>1</td>
</tr>
<tr>
<td>Juravinski Cancer Center</td>
<td>Email to supportive care services - Wellness Program, May/11</td>
<td>0</td>
</tr>
<tr>
<td>YWCA Encore</td>
<td>Email to Encore (exercise program for cancer survivors), June/11</td>
<td>0</td>
</tr>
<tr>
<td>Dietitians of Canada</td>
<td>Recruitment letter circulated to Waterloo Region – Registered Dietitians network, June/11</td>
<td>0</td>
</tr>
<tr>
<td>Your Classifieds</td>
<td>Cambridge Times, Kitchener Record, Guelph Mercury, June/11</td>
<td>2</td>
</tr>
<tr>
<td>Kijiji</td>
<td>Recruitment letter posted online Waterloo, London, July-Sept/11</td>
<td>0</td>
</tr>
<tr>
<td>Canadian Cancer Society</td>
<td>Email to “Living Well Beyond Cancer Program”, Sept/11</td>
<td>0</td>
</tr>
<tr>
<td>Friends/Business Associates</td>
<td>“word of mouth” – exposure from previous participants</td>
<td>3</td>
</tr>
</tbody>
</table>
Those who were interested in the study, based on these initiatives, were asked to call a local telephone number or to contact the researcher by email for further information. Once initial contact was made, potential participants were screened for eligibility (telephone or email) and provided with a detailed information letter (Appendix F). A second telephone call or email contact was made within one week, to determine if they were still interested in participating in the study, to review study details and respond to any questions. At this point, 100% of eligible participants chose to proceed and interviews were scheduled within one-two weeks. All women provided written consent before participating (Appendix G).

**Eligibility Criteria**

1. Female breast cancer survivors > 18 years of age
2. Within 12 months of completing chemotherapy
3. Clinical stage I-IIIA
4. Able to communicate freely in English (oral and written)
5. Sufficient cognitive ability to provide informed consent and participate in the study.

Eligibility was initially based on clinical stage I-II but was expanded to include stage I-III A after 3 months, in the interest of being more inclusive and to expand recruitment potential. This modification prompted a decision to include women who had received both adjuvant and neoadjuvant chemotherapy. Two women who were just beyond the 12 month eligibility criteria (13 months) but were highly motivated to participate were included early in the research. Two women who were five year survivors and one who was pregnant during treatment were excluded.

Theoretical sampling; a process in which decisions are made as the research unfolds where to look for data to best develop an emerging theory (Daly, 2007), was used in the final month of recruitment to screen for additional women who had gained weight after diagnosis. At this time, it was felt that theoretical saturation had been reached among women who had not gained weight, but that further data would be useful in evaluating factors related to weight gain during
or after treatment. Based on this sampling technique, one potential participant was excluded and one was added; this shift in recruitment emphasis thus having minimal impact on the final sample.

2.2 Data Collection Procedures & Instruments

2.2.1 Study 1

The purpose of study 1 was to describe the unique challenges associated with chemotherapy in relation to diet and weight management and to explore possible relationships among psychosocial and treatment-related factors, dietary intake and weight gain during treatment.

2.2.1.1 Demographic/Medical Questionnaire

All participants completed a demographic/medical questionnaire with the researcher before the interview, to collect background data on age, marital status, education and employment status, medical and treatment information and weight history (Appendix H). Where there were uncertainties (e.g., names of chemotherapy agents or other medications, clinical stage) participants referred to official medical documents in their possession or consulted with their medical oncologist. Current weight was measured on the same portable scale (Tanita, BF680, Arlington Heights, Illinois), calibrated against a standard platform balance scale, with participants wearing one light layer of clothing and no shoes. Participants were also asked to self-report their weight at diagnosis, end of treatment and current weight and to recall their weight history in the year before diagnosis (stable vs. gain or loss > 2.3 kg/5lbs).

2.2.1.2 Qualitative Interview

A semi-structured qualitative interview explored individual experiences of chemotherapy in relation to food intake, eating patterns and factors which may have influenced changes in diet during treatment (see Interview Script, Appendix I). All interviews were conducted by the
researcher and audio recorded, with the written and verbal consent of participants, for subsequent analysis. Interviews were scheduled in the participant’s home (n=18) or at the University of Waterloo (n=9) based on participant preference. In one case, at the request of the participant, the interview was conducted at a local library in close proximity to her home. The average interview length was 90 minutes.

**Qualitative Approach**

Interview questions were largely open-ended with *a priori* “probes” (based on the current literature) in place, to encourage elaboration and richer description. Probes addressed each of the following: changes in appetite, food cravings, changes in eating patterns, treatment-related side effects, fatigue, emotional distress/mood, family/social support and burden of treatment. In many cases, probes were introduced to support elaboration on spontaneously generated concerns. Where these factors did not arise spontaneously, they were specifically probed for.

For example, probes were expressed in either of the following ways, “*You mentioned that taste changes were a problem for you during treatment, can you tell me a little more about that and talk about how it may have impacted on your food intake?*” or “*Some women have spoken about changes in smell during treatment, was this something that you experienced?*”.

In addition closed-ended questions asked the participants to identify changes in the quantity of food intake and physical activity during treatment, compared to their normal diet and activity level (before diagnosis). For example: “*During treatment, compared to your normal diet before diagnosis, do you feel you ate the same amount as you would usually eat, more than you would usually eat, or less than you would usually eat?*”. These questions were followed by probes for changes in food intake and physical activity relative to treatment days, the duration of acute treatment effects on diet and physical activity and whether there were consistent diet
and physical activity patterns within cycles or across treatment. Lastly, participants were asked to discuss their previous knowledge and level of concern about weight control during treatment, including their experience of weight change, their reaction to weight gain or loss and whether they were engaged in any weight management efforts during treatment.

This approach is consistent with the key tenets of grounded theory methodology; “systematic yet flexible guidelines for collecting and analyzing qualitative data to construct theories ‘grounded’ in the data”, that start with an emergent, open-ended design (Charmaz, 2006; Daly, 2007). As outlined in the introduction of this thesis, the qualitative approach was designed to circumvent some of the research gaps and methodological challenges associated with collecting dietary data during treatment and to go beyond food intake to understand the reasons behind dietary choices that women make. Grounded theory methodology provided a framework in which to explore the rich detail of the “lived experience” (Charmaz, 2006) that would not be captured by food records alone. Using this approach, recalled food intake and dietary patterns were placed within the context of the psychosocial and treatment-related challenges that women face as they undergo chemotherapy treatment for breast cancer.

Grounded theory methods lend well to this exploratory area of research, since there is a good fit between the outcomes of grounded theory research and clinical practice (Daly, 2007). Aspects of the emergent theory can highlight potential barriers to healthy eating and weight management during treatment and suggest possible intervention strategies that are “rooted in the lived experience of the participants”. As such, a grounded theory approach may expedite the link between research and practice (Daly, 2007) by guiding the development of dietetic counseling and nutrition interventions.
It is important to recognize that the kinds of explanations presented in a grounded theory are generative rather than definitive, meaning they are offered as a framework that can be further tested and are subject to change, as the conditions and experiences of participant’s lives change (Daly, 2007). This is a critical concept in the research area under study, since cancer treatments are evolving rapidly and the experiences of patients receiving chemotherapy are likely to change over time.

In keeping with the principles of grounded theory, interviews proceeded according to the interview script, which provided structure, consistency and focus (Daly, 2007), but were permitted to vary in response to participant issues or concerns. In other words, interviews were semi-structured but flexible, with an openness and appreciation for any concerns that arose. When necessary, the researcher asked for clarification, invited additional comments, paraphrased and summarized responses, in order to ensure that the interview accurately reflected each woman’s experience. Informal pre-testing of interview questions was conducted with a breast cancer survivor who was ineligible for the current study, to ensure that questions were understandable and appropriate (e.g., allowing for open discussion focused on participant concerns).

*Statement of Disclosure*

The current study was designed around a constructivist theoretical position to gather and analyze the data. This contemporary approach differs from traditional objectivist grounded theory by the belief that theory is not “discovered” based on an objective external reality, but instead is co-constructed between the researcher and research participants (Charmaz, 2006). This viewpoint suggests that while there is one reality to be understood and represented, there
are many perspectives on the same reality and meaning is attached through social interaction (Charmaz, 2006, Daly, 2007).

Based on this assumption, rather than “assuming the pretense of a blank slate”, the researcher approaches the investigation with an understanding that qualitative research is influenced by the researcher’s guiding interests, previous knowledge and experience (Daly, 2007). Sensitizing concepts provide initial ideas or questions that serve as “points of departure” but should be held lightly, as participants offer clues about the importance of key issues (Charmaz, 2006, Daly, 2007). In this study, sensitizing concepts originated from my understanding of the current literature and our pilot work, which informed potential and presumably relevant lines of inquiry. For example, a priori probes for changes in food intake relative to treatment day were based on preliminary findings from our pilot study suggesting that energy intake was highly responsive to time from treatment.

It is important to acknowledge that, while I adopted a constructivist approach in conducting the interviews, some of the methods that were employed reflect an objectivist position. For example, the semi-structured format and probes that were used across all interviews, allowed for frequency counts to support qualitative findings and to assist in establishing the salience of emerging themes (Daly, 2007). This is not uncommon in grounded theory research, since variations in grounded theory share many of the same methodological practices (Daly, 2007).

It is also important to disclose that my interest in pursuing this area of research was shaped by my personal experiences with close friends and family members who have undergone chemotherapy treatment for breast cancer. Lastly, several women articulated their comfort in sharing their personal information with a health professional, suggesting that my experience and training as a Registered Nurse may have influenced the tone and depth of the interviews.
2.2.2 Study 2.

The purpose of study 2 was to investigate relationships among physical and psychological distress, current dietary intake, changes in diet and weight gain since the completion of chemotherapy treatment. The data for study 2, with the exception of current dietary intake, were collected in conjunction with the qualitative interview for study 1.

2.2.2.1 The Rotterdam Symptom Checklist (RSCL)

Symptoms of physical and psychological distress were assessed using the Rotterdam Symptom Checklist (Appendix J). This self-report instrument was designed to measure quality of life (QOL) in cancer patients and has been used and validated \( r = 0.52 - 0.84 \) for anxiety, physical function and depression) in patients with disease at different sites, including breast cancer (deHaes, van Knippenberg & Neijt, 1990; Hopwood, Howell & Maguire, 1991; Ibbotson, Maguire, Selby, et al., 1994; deHaes, Olschewski, Fayers et al., 1996; Hall, A’Hern & Fallowfield, 1999). In breast cancer patients \( n = 478 \), internal consistency based on Cronbach’s alpha \( r = 0.8 - 0.9 \) suggests that the Rotterdam Symptom Checklist (RSCL) is highly reliable in this population (deHaes et al., 1996).

The RSCL is a multidimensional tool, providing sub-scales for physical distress (23 items), psychological distress (7 items) and global QOL (1 item), which is easily administered and takes approximately 8 minutes to complete. This instrument has been used with early and late stage patients undergoing different treatments (surgery, chemotherapy, radiation), proving to be easily understandable in a variety of settings (de Haes et al., 1996). A standardized method of scoring and extensive normative data, allowed for comparisons of the level of impairment across scales and to outcomes from earlier studies (de Haes et al., 1996).
Using this instrument, participants were asked to indicate the extent to which they have been bothered by a series of common symptoms (e.g., lack of appetite, tiredness, worrying, depressed mood) in the past week. Symptoms of physical and psychological distress were interspersed, with responses ranging from 1 (not at all) to 4 (very much). A single global QOL item asked the participants to respond to the question “all things considered, how would you describe your quality of life during the past week?” This item was scored on a 7 point scale ranging from 1 (excellent) to 7 (extremely poor). The sum of physical (range = 23-92) and psychological (range = 7-28) symptom scores were calculated to provide a summary estimate (composite score) of overall physical and psychological distress, respectively.

All raw scores (physical distress, psychological distress, global QOL) were transformed ([raw score – minimum raw score / maximum – minimum score] X 100) to provide a standardized score on a 100 point scale for each domain (see sample raw score transformation, pg. 2 of Rotterdam Symptom Checklist). This transformation adjusts for differences in the number of items for each sub-scale and allows for comparisons of the level of impairment across domains (deHaes et al., 1996). Lower scores imply better functioning or well-being.

2.2.2.2 Distress Thermometer (DT)

The distress thermometer (DT) is a simple, self-report measure in which participants were asked to circle the number (0-10) on a visual scale that best describes the amount of distress they have been experiencing in the past week (pg. 2 of Rotterdam Symptom Checklist, Appendix I). The DT was developed for the evaluation of distress in cancer patients (National Comprehensive Cancer Network, 2012) and has been used and validated in breast cancer patients (Jacobsen, Donovan, Trask et al., 2005; Hegel, Moore, Collins et al., 2006; Dabrowski, Boucher, Ward et al., 2007; Hegel, Collins, Kearing et al., 2008; Yong, Zubaidah,
Saidi et al., 2012). Recent studies have indicated good overall accuracy of this single item to identify clinically significant distress in breast cancer patients, relative to the 14-item Hospital Anxiety and Depression Scale (0.80-0.95), the 18-item version of the Brief Symptom Inventory (0.78) and the Patient Health Questionnaire 9-item Depression Module (0.87) (Jacobsen et al., 2005; Hegel et al., 2008; Yong et al., 2012). The DT has been reported in the cancer survivorship literature and was included to allow for comparisons of findings.

2.2.2.3 Fatigue Symptom Inventory (FSI)

The Fatigue Symptom Inventory (Appendix K) was used to conduct a more comprehensive assessment of current fatigue. The Fatigue Symptom Inventory (FSI) is designed to measure the intensity and duration of fatigue and the extent to which fatigue impacts on quality of life (Hann, Jacobsen, Azzarello et al., 1998). This symptom was of particular interest at the time of interview, since it is the most commonly reported symptom among breast cancer survivors and has been reported to persist for several months (Meeske et al., 2007). This 13 item questionnaire has been used with breast cancer patients (Hann et al., 1998; Kumar et al., 2004) and has proven to be moderately to highly valid (r=0.57-0.86) among breast cancer survivors, both during and after treatment (Hann et al., 1998). Internal consistency based on Cronbach’s alpha (r=0.93-0.95) suggest that the FSI is a highly reliable scale (Hann et al., 1998).

The FSI consists of 4 items related to intensity, in which participants were asked to rate their level of fatigue at its most, least and “on average” in the last week, as well as current fatigue, on an 11 point rating scale ranging from 0 (not at all) to 10 (extreme fatigue). Participants were also asked to rate how much, in the last week, fatigue had interfered with daily living (e.g., general activity, work activity, concentration, relationships) in a 7-item subscale with responses ranging from 0 (no interference) to 10 (extreme interference). Two
final items related to duration evaluated how many days in the past week participants were fatigued for any part of the day (range = 0-7) and how much of the day “on average” they felt fatigued in the past week (range = 0 - none of the day to 10 – the entire day). Single scores were reported for most, least, mean and current fatigue (intensity), number of days and amount of time (duration), with a composite score (mean of 7 items) calculated for “interference”.

Based on extensive use and strong psychometric properties of the RSCL, DT and FSI in breast cancer survivors and evidence that they are easily administered and understood in multiple settings, it was determined that further pilot testing of these instruments for the current study was not required.

2.2.2.4 Changes in Food Intake and Physical Activity since the Completion of Treatment

Changes in diet since the completion of treatment were assessed using a closed-ended question asking participants to identify changes in the quantity of food intake since the completion of treatment, compared to their normal diet (before diagnosis) and an initial “filter” question asking “since your diagnosis have you made any changes to the kinds of foods you eat?” Women who indicated that they had made changes to their diet were asked to elaborate about specific changes in food groups/dietary components (Qualitative Interview pg 3, Appendix I). Nine items, used in previous research with breast cancer survivors and grounded in current dietary recommendations for healthy eating (Maunsell, Drolet, Brisson et al., 2002, Health Canada, 2007), were evaluated including fruits and vegetables, legumes, meat, fish, dairy products, breads/cereals, desserts, alcohol and supplements. Participants were asked to indicate whether they had “introduced”, “increased”, “decreased” or “eliminated” these items from their diet since the completion of treatment. In addition, 4 items were further explored to determine if there had been a “change in type” including meat, dairy products, breads/cereals
and supplements. Based on the work of Maunsell et al. (2002), changes were categorized as positive if intake of fruits and vegetables, legumes and fish were reported as increased (or introduced) and if intake of meat, desserts and alcohol were reported as decreased (or eliminated). Changes in dairy products and breads/cereals were considered positive if women report consuming products with a lower fat content or higher fibre content, respectively. Added to this study was one additional positive change, based a “change in type” for meat intake (lower fat content). Changes in dietary supplement use were of interest, however, in the absence of clear evidence (Greenlee, Hershman & Jacobson, 2009) were not classified as positive or negative (Maunsell et al., 2002).

Although a comprehensive assessment of current physical activity was not included in this study, a single closed-ended question asked participants to identify changes in the quantity of physical activity since the completion of treatment, compared to their normal activity level before diagnosis. This question was followed by probes for changes in work, leisure and structure exercise, changes in activity since the completion of treatment compared to activity levels during treatment and current level of exercise (type, frequency and duration) over the past week. These data were used to provide context for dietary data and energy balance and to estimate current physical activity level (sedentary, lightly active, etc) for the purposes of calculating estimated energy requirements.

2.2.2.5 Perceptions of Weight Change, Dietary Supports and Patient Care

Lastly, participants were asked to discuss any concerns they may have regarding weight management since the completion of treatment, including their experience of weight change, their reaction to weight gain or loss and whether they have been engaged in any weight management efforts. Participants were also asked to reflect on their experience of
chemotherapy treatment, to discuss their knowledge and use of dietary support services and if they felt there were additional supports and services that might have been helpful in promoting healthy eating and weight management after diagnosis (Appendix I). Probes for the type of services, specific guidelines and whether, from the participant’s perspective, there is an optimal time in the cancer trajectory to intervene, were designed to inform future research and the development of guidelines (with appropriate supports) for healthy eating and weight management after diagnosis.

2.2.2.6 3-Day Food Record

Current dietary intake was assessed using a 3-day food record (Appendix L). The 3-day food record was provided at the time of interview, for completion in the following week. Dietary records were chosen as the method of assessment since, compared to other self-report measures (FFQ, 24 hr recalls), they do not rely on recall and may provide a more precise measure of dietary intake (Block & Hartman, 1989) (see methodological limitations, pg 36). Two weekdays and one weekend day were included in each 3-day record, to control for possible day-of-the-week effects (Trabulsi & Schoeller, 2001).

Participants were asked to record everything they eat or drink over a 3-day period. Detailed written instructions for recording daily food intake and a “sample day” were provided. Each day was broken down into separate pages for morning meal, mid-morning snack, mid-day meal, mid-afternoon snack, evening meal and evening snack, with columns on each page to provide a description (brand, flavour, method of cooking), unit of measure (teaspoon, cups ounce, piece) and the number of units for each food item. The time and location of each meal and snack was recorded, as well as intake of vitamin/mineral and herbal supplements over the 3-day period. In addition, participants were asked to identify for each day if, compared to their
normal diet (over the last couple of weeks), they felt they had eaten the same amount, more or less than they usually eat. In other words, did this day of recording accurately reflect habitual intake?

The diet record was reviewed with each participant at the time of interview, to clarify instructions and answer any questions. Participants were encouraged to provide as much detail as possible and to use household measures (teaspoons/measuring cups/scales) and food labels to estimate serving sizes. The goal of capturing usual eating habits (e.g., importance of eating as they would normally eat on that day), in as accurate and honest a record as possible, was emphasized. During the recording period, participants were contacted by the researcher, by telephone or email to see if they had any questions or concerns. Arrangements were made, at this time, to pick up the completed diet record at the participant’s home or to coordinate pick up at another location that was convenient for the participant (local library, workplace, HopeSpring, Well-Fit). Each completed record was reviewed with the participant, for clarification and completeness.

2.3 Data Analysis and Statistics

2.3.1 Study 1

Descriptive statistics were used to characterize the sample in terms of age, marital status, education and employment status, medical and treatment background and weight history. Self-reported weight at diagnosis and end of treatment, and measured weight at the time of interview were used to categorize participants by weight change (weight gain, weight loss, weight stable) during (diagnosis to end of treatment) and after treatment (end of treatment to the time of interview). Weight gain or loss was defined in this study as a change in body weight greater than 2.0 kg. Some studies have used a cut-off of 2.5 kg (Ingram & Brown,
2004) or more recently, a change from baseline weight greater than 5% (Thivat et al., 2010; Nissen et al., 2011) to define weight change, while others have elected to use the 2.0 kg criterion used in the present study (Lankester et al., 2002; Nichols et al., 2009; Gu et al., 2010). This definition was chosen since normal short-term fluctuations in body weight (changes in water balance, glycogen stores, dietary intake, illness) may be as high as 2.0 kg in some adults (Groff & Gropper, 2000). Recognizing that this level of flux may be transient, several longer term studies suggest that weight gain in breast cancer survivors is progressive and durable, with a very small percentage of women returning to their pre-diagnosis weight within three years of treatment (Irwin et al., 2005, Makari-Judson et al., 2007, Gu et al., 2010). Furthermore weight gain itself, regardless of baseline BMI, is associated adverse health consequences (Kawachi, 1999; Willet et al., 1995) and may be more distressing among women who were not overweight before diagnosis (Halbert et al., 2008). Therefore it was decided that a weight gain greater than 2.0 kg in the first year after diagnosis, which is likely to endure, may have important clinical relevance. Body mass index (BMI) at diagnosis, end of treatment and time of interview were calculated as weight (kg) divided by height (m²). Weight status at each of these time points were categorized, according to the World Health Organization classification system (WHO, 2011b), as underweight (BMI<18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25-29.9 kg/m²) or obese (BMI ≥30 kg/m²).

The use of self-reported weight is a potential limitation, however several studies have reported excellent correlation (r=0.92-0.99, p<0.01) between self-reported weight and measured weight in this population (Rock et al, 1999; Herman, Ganz, Petersen et al. 2005; Caan et al, 2006; Gu et al., 2010). In this study, the intra-class correlation coefficient for
self-reported weight versus measured weight at the time of interview was 0.99 (p<0.01), suggesting that self-reported weight is reliable in this sample.

Audio recordings were transcribed verbatim by a professional transcriber and imported into N-Vivo 9 (QSR International, Cambridge MA) data management software, for organization and coding. Qualitative analysis was based on a grounded theory approach (Charmaz, 2006), in which key themes and sub-themes around food intake and eating patterns (objective 1) and common psychosocial and treatment-related factors associated with changes in food intake (objective 2) were coded. The constant comparative method (Charmaz, 2006) was used to compare emerging themes across participants and among women who gained weight versus women who did not gain weight during treatment (objective 3). These data were used to develop a theoretical model (objective 4) to identify possible relationships between psychosocial and treatment-related factors, food intake and eating patterns and weight gain during treatment.

In order to complete this process, coding progressed through three distinct phases. Initial coding was based on a line by line review of the transcripts to describe the data and identify preliminary codes for subsequent analysis. A list of recurring themes (preliminary codes) was established and through a process of focused coding, those most salient were retained and combined into related categories, while less frequently occurring themes were excluded from the present analysis. Sub-themes within each category were then identified, and compared across women who gained weight, lost weight or were weight stable during treatment. Theoretical coding was employed in the final stage of analysis, to identify possible relationships between categories, to explain how psychosocial and treatment-related factors might influence food intake in ways that promote weight gain. Memo writing (summary notes)
was employed throughout data collection and analysis in order to preserve context and support the development of key themes and categories (Charmaz, 2006).

Samples of transcripts were reviewed by a second researcher trained in qualitative analysis, to establish inter-rater reliability for emerging themes and sub-themes. Inter-rater reliability checks were designed to minimize researcher bias and “generate confidence in the interpretation of the data” by determining the extent to which similar conclusions were drawn (Daly, 2007). During this phase, samples of initial line by line coding of broad themes (n=21), as well as detailed summary notes and frequency counts were reviewed.

Finally, Spearman’s nonparametric correlation coefficient was used to assess relationships between self-reported changes in the quantity of food intake or physical activity and weight gain during treatment. Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS version 20 IBM, Armonk, New York). Significance was set at p< 0.05.

2.3.2 Study 2

Objective 1: Descriptive statistics (mean, SD, range) were used to present self-reported symptoms of physical and psychological distress (past week), global quality of life and distress thermometer scores. These findings are presented in the context of previously reported data in early stage breast cancer survivors and random samples of cancer-free adults from the general population (deHaes et al., 1996; Hegel et al., 2006; Yong et al., 2011).

Objective 2: Descriptive statistics (mean, SD, range) were used to present the intensity (4 items) and duration (2 items) of fatigue and the level of interference (1 item) of fatigue on daily activities. A composite score for “interference” was calculated based on the mean values across 7-items. These findings are presented in the context of previously reported data in early stage breast cancer survivors and a comparison group of healthy women (Hann et al., 1998).
Objective 3: Descriptive statistics were used to identify the nature (positive/negative) and extent (percentage of women reporting changes, mean number of changes) of self-reported changes in diet (quantity, specific foods groups/dietary components) since the completion of treatment.

Objective 4: Current intake (mean, SD, range) of energy (kcal), carbohydrates (g, % energy), protein (g, % energy), fat (g, % energy), fibre (g), calcium (mg) and vitamin D (ug/IU) are presented and compared to current dietary recommendations (percentage of women above, within, below the DRI Acceptable Macronutrient Distribution Ranges, percentage of women below the EAR cut-point). Servings of vegetables & fruit (total, dark green and orange) and milk & alternatives were hand calculated based on the 3-day food record. Intake of these food groups (mean, SD, range) are presented and compared to Eating Well with Canada’s Food Guide (percentage of women above and below age and gender specific recommendations). Mean intakes (energy, % energy from macronutrients, fibre, food groups, calcium and vitamin D) are also described relative to national data from the Canadian Community Health Survey, Cycle 2.2, Nutrition (2004) (Health Canada, 2009).

Objective 5: Pearson’s correlations were used to investigate relationships between weight gain (kg) since the completion of treatment (dependant variable) and composite scores for symptoms of physical and psychological distress, intensity of fatigue, duration of fatigue, level of interference associated with fatigue, current dietary intake (energy, carbohydrate, protein and fat intake) and self-reported changes in diet (number of positive changes) after diagnosis. In order to identify women more likely to gain weight since the completion of treatment, crude odds ratios comparing women who gain weight to those who do not gain weight (stable/loss), on the basis of physical and psychological distress, intensity of fatigue, duration of fatigue,
level of interference associated with fatigue, current dietary intake (energy, carbohydrate, protein and fat intake) and self-reported changes in diet (number of positive changes) were calculated. (Cohen, Cohen, West et al., 2003; Maunsell et al., 2002). Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS version 20 IBM, Armonk, New York). Statistical significance was set at p< 0.05.

2.3.3 Sample Size Considerations

The projected sample size (n=30) was based on the expected number of participants required to reach saturation of qualitative data (Halbert et al., 2008) and to provide novel description of physical and psychological distress after treatment, changes in diet and current dietary intake. Based on a medium to large effect size and a desired power level of 0.8, a sample size of 28-85 is required to detect significant correlations at $\alpha = 0.05$ (Cohen, 1992). It was acknowledged in the design stage that a sample size of 30 may limit statistical power to detect significant correlations between survey and diet variables, however we anticipated that this research would serve to generate hypotheses and power calculations for future studies.

2.4 Ethics Approvals

This research project was reviewed and received ethics clearance through the Office of Research Ethics at the University of Waterloo on September 20, 2010 (Appendix M). Ethics modifications were approved on January 14, 2011 to expand the inclusion criteria to clinical stage IIIA, add the distress thermometer to the study instruments and to include advertising in local newspapers in the recruitment process. Additions to the participant recruitment procedures (minor modifications to recruitment letter, permission to include collaboration with the Grand River Regional Cancer Centre and expanding the recruitment region to include the Hamilton and London, Ontario regions) were submitted and approved on July 5, 2011.
2.5 Remuneration/Participant Feedback

Participants received an honorarium of $30 and a breast cancer bracelet at the time of interview, in appreciation for their time. In addition, all participants were provided with a participant feedback letter (Appendix N) and personalized nutritional assessment (Appendix O), based on their 3-day food record, and a summary of the research findings upon study completion.
CHAPTER 3: FOREWARD

Chapters 3 presents the qualitative findings from study 1 and is focused on food intake and eating patterns, factors associated with changes in food intake, and weight change during treatment. The data for study 1 are based on the recalled experiences of 28 early stage breast cancer survivors who were within 12 months of completing chemotherapy treatment.
 CHAPTER 3: The Voice of Experience: A Qualitative Analysis of Food Intake, Psychosocial and Treatment-related Factors and Weight Change in Women Treated with Chemotherapy for Early Stage Breast Cancer.

The work presented in this chapter will be submitted to the Journal of the Academy of Nutrition and Dietetics as:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. The voice of experience: a qualitative analysis of psychosocial and treatment-related factors, food intake and weight change in women treated with chemotherapy for early stage breast cancer.

3.1 Overview

Objectives: Weight gain is a common and persistent problem for many breast cancer survivors, however relationships between acute and chronic effects of treatment, dietary change and weight gain after diagnosis are poorly understood. The purpose of this study was to gain an appreciation of the experience of food intake and weight change during treatment, as recalled by women who have received chemotherapy for breast cancer.

Methods: Comprehensive qualitative interviews were conducted with 28 breast cancer survivors, within 12 months of completing treatment, to explore individual experiences of chemotherapy in relation to food intake and eating patterns and factors which may have influenced changes in diet during treatment. Demographic, medical, treatment and weight history were collected via questionnaire.

Results: Food intake during treatment appears to be highly responsive to treatment day, with most women reporting smaller, irregular meals and snacks as tolerated and lower food intake for the first few days after receiving chemotherapy. In most women, acute side effects of treatment began to recede toward the end of the first week, leading to gradual increase in food intake and more structured eating in the second and third weeks of the cycle. Women who lost weight during treatment (n=6) tended to report more severe and persistent side effects of treatment, leading to a more prolonged reduction of food intake after each cycle. Increased appetite, food cravings and intake of energy dense comfort foods seemed to be more common among women who gained weight during treatment (n=11). In these women, changes in taste, nausea and emotional distress were central in promoting these dietary responses. Most women reported a reduction in physical activity during treatment.

Conclusions: While the etiology of weight gain in this population is complex, findings from this study suggest that food intake and dietary patterns during treatment may play an important role for some women. A theoretical model based on these findings may serve to guide future research and the development of nutrition intervention strategies.
3.2 Introduction

In 2011, it was estimated that 23,400 Canadian women and 230,480 American women would be diagnosed with breast cancer (Canadian Cancer Statistics, 2011; National Cancer Institute, 2011). Increased screening and advances in treatment have lead to significant improvements in survival rates over the last 25 years, however a growing number of women, currently estimated to include more than 2.7 million Canadian and American women, are living with a diagnosis of breast cancer (Canadian Breast Cancer Foundation, 2011; National Cancer Institute, 2011).

While most women, particularly those diagnosed in the early stages of disease, will be cured of breast cancer, many will gain weight, increase body fat and lose lean tissue after diagnosis (Vance et al., 2011). These unfavourable changes in body composition are distressing for many women (Halbert et al., 2008; Knobf, 1986) and may increase the risk of co-morbid conditions (Brown et al., 1993; Wingo et al., 1998; Robinson & Graham, 2004), treatment complications and poor clinical outcomes (Carmichael, 2006; Prado et al., 2007). Identifying and addressing modifiable risk factors that will promote overall health, disease remission and long-term survivorship is an important health care concern.

There are several hypothesized mechanisms by which breast cancer and its treatment might influence diet and eating behaviours in ways that promote positive energy balance, but little empirical evidence at this time. Although nutrition-related side effects are well documented, relationships between acute and chronic effects of treatment, dietary change and weight gain after diagnosis are poorly understood. Previous research however, is limited by imprecise dietary assessment methods, small sample size and limited dietary data over the treatment trajectory. Given the stresses of a cancer diagnosis and the known gastrointestinal side effects
of treatment, food intake and eating patterns would be expected to be highly variable across
treatment and within treatment cycles. Dietary intake relative to treatment days and treatment-
related side effects however, has not been reported. This research was designed to explore
these gaps in the literature; to gain an appreciation of the experience of food intake and body
weight during treatment, from the perspective of women who have received chemotherapy for
breast cancer. These findings will help to identify women who may be most at risk of weight
gain and may assist in the development of nutrition guidelines and appropriate targeted weight
management interventions after diagnosis.

Specific objectives were (1) to describe food intake and eating patterns in relation to the
experience of chemotherapy, (2) to identify common psychosocial and treatment-related
factors associated with changes in food intake and eating patterns during treatment, (3) to
describe similarities and differences in food intake and eating patterns, among women who
gained weight during treatment, compared to women who did not gain weight and (4) to
develop a theoretical model based on the experiences of breast cancer survivors, to explain
how psychosocial factors and treatment-related side effects might influence diet and eating
patterns in ways that promote weight gain during treatment.

3.3 Participants and Methods

3.3.1 Study Sample

Female breast cancer survivors were recruited from the Waterloo, Guelph, Hamilton and
London, Ontario regions to participate in a semi-structured qualitative interview. To be eligible
for this study, women had to be >18 y, clinical stage I-IIIA, within 12 months of completing
chemotherapy treatment, able to communicate freely in English (oral and written) and capable
of providing informed consent.
3.3.2 Procedures

Participants were made aware of the study by a recruitment letter that was posted through professional organizations/events (Canadian Breast Cancer Foundation Run for the Cure, Canadian Breast Cancer Network online Bulletin Board/Newsletter, Waterloo Region Registered Dietitians network), local businesses and community support groups. Advertisements were also placed in several local newspapers and a recruitment letter was posted in the University of Waterloo’s Well-Fit Centre (group exercise program for cancer patients) and the Grand River Regional Cancer Centre, Kitchener, Ontario. Interested participants were asked to call a local telephone number or to contact the researcher via email, at which time they were screened for eligibility and provided with a detailed information letter. A second telephone call or email contact was made within one week, to review study details and respond to questions. Interviews were scheduled within one-two weeks in the participant’s home or at the University of Waterloo, based on participant preference. This research project received ethics clearance through the Office of Research Ethics at the University of Waterloo. All women provided written consent before participating.

Before the interview proceeded, participants completed a demographic and medical questionnaire with the researcher, to collect background data on age, marital status, education and employment status, medical and treatment information and weight history. Participants were asked to self-report their weight at diagnosis and end of treatment and to recall their weight history in the year before diagnosis (stable versus gain or loss > ~2.3 kg/5 lbs). In the event of uncertainty regarding medical or treatment information, participants referred to official medical documents in their possession or consulted with their medical oncologist.
The qualitative interview explored individual experiences of chemotherapy in relation to food intake, eating patterns and factors which may have influenced changes in diet during treatment. Interview questions were largely open-ended with a priori “probes” (based on the current literature) in place, to encourage elaboration and richer description. Probes addressed each of the following: changes in appetite, food cravings, changes in eating patterns, treatment-related side effects, fatigue, emotional distress/mood, family/social support and burden of treatment, and were used consistently across interviews.

Closed-ended questions asked the participants to identify changes in the quantity of food intake and physical activity during treatment, compared to their normal diet and activity level (before diagnosis). These questions were followed by probes for changes in food intake and physical activity relative to treatment days, the duration of acute treatment effects and patterns of diet and physical activity within cycles or across treatment. Interviews were conducted by the same researcher and audio recorded for subsequent analysis. The average interview length was 90 minutes. Participants received a $30 honorarium and a breast cancer bracelet at the time of interview and a summary of the research findings at the completion of the study.

### 3.3.3 Data Analysis

Descriptive statistics were used to characterize the sample in terms of age, marital status, education and employment status, medical and treatment background and weight history. Weight at diagnosis and end of treatment was used to categorize participants by weight change (weight gain, weight loss, weight stable) during treatment. Given that normal short-term fluctuations in body weight may be as high as 2.0 kg in some adults (Groff & Gropper, 2000), weight gain or loss was defined in this study as a change in body weight greater than 2.0 kg. Body mass index (BMI) at diagnosis, and end of treatment were calculated as weight (kg)/height (m)².
Weight status was categorized according to the World Health Organization classification system (WHO, 2011), as underweight (BMI<18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25-29.9 kg/m²) or obese (BMI ≥30 kg/m²).

Qualitative analysis was based on a grounded theory approach, in which key themes and sub-themes around food intake and eating patterns and common psychosocial and treatment-related factors associated with changes in food intake were coded. The constant comparative method (Charmaz, 2006) was used to compare emerging themes across participants and among women who gained weight versus women who did not gain weight during treatment. Samples of transcripts (n=21) were reviewed by a second researcher trained in qualitative analysis, with good consensus for themes and sub-themes between both researchers (Daly, 2007). The sample size was based on data saturation, however a target of 30 women was anticipated based on similar research (Halbert et al., 2008). Spearman’s nonparametric correlation coefficient was used to assess relationships between self-reported changes in the quantity of food intake and physical activity, and weight gain during treatment. Data management and analysis were conducted using N-Vivo 9, (QSR International, Cambridge, MA) and SPSS version 20 (IBM, Armonk, New York). Statistical significance was set at p< 0.05.

3.4 Results

3.4.1 Sample Characteristics

A total of 28 women were recruited over a 14 month period between Oct, 2010 and Nov, 2011. The mean age was 49.8±8.5 y (range = 33-69). Eighteen of the participants (64%) were married and most (n=22, 79%) had a college or university education. At the time of interview, 10 women (36%) were working outside the home, 7 (25%) were on an extended leave of absence and 11 (39%) were unemployed or retired. Most of the women (n=25, 89%) were diagnosed at clinical stage II or IIIA and 19 (68%) were premenopausal at diagnosis.
Twenty-five women (89%) had undergone lumpectomy or mastectomy. Most of the sample group (n=21, 82%) had received or were scheduled to receive radiation therapy. Participants received an average of 5.9±1.9 chemotherapy treatments, over a period of 15±4 weeks. The mean length of time from completing chemotherapy treatment was 6.4±4.4 months. Twenty-two women (79%) were receiving hormone therapy at the time of interview. Sample characteristics are summarized in Table 3.1.

**Table 3.1: Demographic, Clinical and Treatment Characteristics of the Participants**

<table>
<thead>
<tr>
<th>Characteristic (n=28)</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>n (%)</th>
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</thead>
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<td>Age (yrs)</td>
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<tr>
<td>Ethnicity</td>
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<tr>
<td>White</td>
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<td></td>
<td>25 (89%)</td>
</tr>
<tr>
<td>Black, Asian, West Asian</td>
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<td></td>
<td>3 (11%)</td>
</tr>
<tr>
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<td>18 (64%)</td>
</tr>
<tr>
<td>Married</td>
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<td>14 (52%)</td>
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<tr>
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<td>6 (22%)</td>
</tr>
<tr>
<td>Education Completed</td>
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<td>College</td>
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<td></td>
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</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
<td>15 (54%)</td>
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<td>Unemployed/Retired</td>
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<td>II</td>
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<td>IIIA</td>
<td></td>
<td></td>
<td>10 (36%)</td>
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<tr>
<td>Menopause Status (at diagnosis)</td>
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<td>19 (68%)</td>
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<td>Premenopausal</td>
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<tr>
<td><strong>Treatment History</strong></td>
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<tr>
<td>Surgery Type</td>
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<td></td>
<td>15 (54%)</td>
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<tr>
<td>Lumpectomy</td>
<td></td>
<td></td>
<td>13 (35%)</td>
</tr>
<tr>
<td>Mastectomy</td>
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<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Planned (Mastectomy)</td>
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<td></td>
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<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td>5.9 (1.9)</td>
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<tr>
<td>Number of Cycles</td>
<td>15 (4.0)</td>
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<td>Duration of Treatment (weeks)</td>
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<td>Treatment Type</td>
<td>7 (25%)</td>
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<td></td>
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<tr>
<td>AC + T *</td>
<td>6 (21%)</td>
<td>2 (7%)</td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>2 (7%)</td>
<td>0.5-13</td>
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<tr>
<td>FEC + T</td>
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<td></td>
</tr>
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</tr>
<tr>
<td>Time from Treatment (months)</td>
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<td></td>
</tr>
<tr>
<td>Radiation Therapy</td>
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</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Planned</td>
<td></td>
<td></td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td></td>
<td></td>
<td>17 (61%)</td>
</tr>
<tr>
<td>Tamoxifen</td>
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<td></td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Aromatase Inhibitor</td>
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<td></td>
<td>6 (21%)</td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td>6 (21%)</td>
</tr>
</tbody>
</table>

* A = Adriamycin, C = Cyclophosphomide, T = Paclitaxel or Docetaxel, F =5-Flourouracil, E = Epirubicin
**Weight History**

The mean BMI at diagnosis was 25.9±5.7 kg/m², with 14 women (50%) in the normal weight category and 13 (46.4%) classified as overweight or obese. The mean weight change during treatment for all participants was +0.8± 4.6 kg (range = -12.3 - +9.1). Among women who gained >2.0 kg (n=11), the mean weight gain was 5.1±2.8 kg. Six participants lost an average of 5.2±3.7 kg during treatment. At the end of treatment, the mean BMI was 26.2±5.5 kg/m², with 11 women (39.3%) in the normal weight category and 16 (57.1%) classified as overweight or obese. Over the treatment period, three women moved from normal weight status to the overweight category, while one woman who was overweight at diagnosis was classified as obese at the end of treatment. The majority of women (n=19, 68%) reported that their weight had been stable in the year preceding their breast cancer diagnosis. Weight history is summarized in Table 3.2.

**Table 3.2: Weight History**

<table>
<thead>
<tr>
<th>Weight History (n=28)</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight Status (at diagnosis)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Body Weight (kg)</td>
<td>72.1 (15.2)</td>
<td>50.9-104.5</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9 (5.7)</td>
<td>18.1-38.6</td>
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<tr>
<td><strong>Body Weight Classification</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (BMI &lt; 18.5)</td>
<td>1 (3.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Weight (BMI 18.5-24.9)</td>
<td>14 (50.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI 25-29.9)</td>
<td>7 (25.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese (BMI ≥30)</td>
<td>6 (21.4%)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Weight Change During Treatment</strong></td>
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<td></td>
</tr>
<tr>
<td>All participants (kg)</td>
<td>+ 0.8 (4.6)</td>
<td>-12.3 - +9.1</td>
<td>11 (39.3%)</td>
</tr>
<tr>
<td>Women Who Gained Weight (kg)</td>
<td>+ 5.1 (2.8)</td>
<td>+ 2.3 - +9.1</td>
<td>6 (21.4%)</td>
</tr>
<tr>
<td>Women Who Lost Weight (kg)</td>
<td>- 5.2 (3.7)</td>
<td>-2.3 - -12.3</td>
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<tr>
<td><strong>Weight Status (end of treatment)</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>72.9 (14.6)</td>
<td>48.2-101.8</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 (5.5)</td>
<td>17.1-36.7</td>
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<tr>
<td><strong>Body Weight Classification</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (BMI &lt; 18.5)</td>
<td>1 (3.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Weight (BMI 18.5-24.9)</td>
<td>11 (39.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI 25-29.9)</td>
<td>9 (32.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese (BMI ≥30)</td>
<td>7 (25.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight Change - Year Preceding Diagnosis</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Weight Stable</td>
<td></td>
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<td>19 (68%)</td>
</tr>
<tr>
<td>Weight Gain</td>
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<td></td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Weight Loss</td>
<td></td>
<td></td>
<td>4 (14%)</td>
</tr>
</tbody>
</table>
3.4.2 Food Intake and Eating Patterns during Treatment

Changes in food intake and eating patterns were universal during chemotherapy treatment, with several recurring themes emerging from the data. Most salient among them were changes in food intake relative to treatment day, changes in appetite and “food appeal”, including food cravings, comfort foods and food aversions. Each of these key themes arose frequently and spontaneously in response to an open-ended question inviting women to “discuss their experience of chemotherapy from the perspective of food intake and eating patterns”, with sub-themes and patterns identified through the use of probes and follow-up questions.

Changes in Food Intake Relative to Treatment Day

Most women reported considerable disruption to their normal eating patterns, relative to the day of their chemotherapy treatments. Changes in eating patterns were predominant in the first week after treatment, during which time a general trend toward lower food intake was reported. Mealtimes tended to be less regular during the first week, with most women reporting smaller more frequent meals and snacks, as tolerated. Post-treatment recovery led to a gradual increase in food intake and enjoyment in eating in the second and third weeks of the cycle. More structure to meals and a return to regular eating patterns were apparent in week three, among women who received chemotherapy on a three week treatment cycle (n=19, 68%).

* Janelle: So right after the chemo [first day] it was, yeah I wanted to sleep. I didn’t want to eat, I just wanted to sleep. By the weekend [3-4 days] it was getting better.

Connie: By the weekend before my next treatment I was starting to feel a little more energy, a little stronger, wanted to eat a little bit more.....

Bridget: Back to normal was I’d say, that last 7 days..... because my mouth felt better and so on, I made an effort to say you know, I’m eating this for breakfast, this for lunch.....

* Note: all names presented in this paper have been changed and bear no resemblance to the names of women who participated in this study.
While most women found that eating was disrupted from the day of treatment, two women reported three or four “good” days, during which they could eat relatively normally, in terms of both type and amount of food, before treatment effects presented fully. One of these women however, reported fewer good post-chemotherapy days as treatment progressed, while several other women found that the “acute” effects of treatment lasted longer with each cycle; both patterns suggesting cumulative effects across treatment.

*Lana: Initially, I’d say four or five days and then I found as you go, you get more chemo, it knocks you back even more so. It would take longer to do the recovery.*

For some women (n=7, 25%), side effects of treatment persisted into the second and third weeks, allowing for a very short window of time in which they felt they could eat normally before the next cycle. Three other women reported gradual improvements in eating in the second or third week but felt that they had not fully recovered before it was time for the next treatment.

*Heather: …..then I’d have about three days I’d feel really good. Not really good, but just felt like you were kind of getting better and then it would be time for another one.*

*Gail: You know I never actually got back to normal with the taste, with regards to the food. But it would have been a lot better compared to the first week.*

**Changes in Appetite**

Many women reported varying degrees of reduced appetite during treatment (n=17, 61%). Since the terms appetite and hunger are often used interchangeably, for the purposes of this paper, appetite refers to the “desire to eat”, based on the sight, smell, taste and thought of food (Sizer, Whitney & Piche, 2012). Consistent with eating patterns relative to treatment day, low appetite was most commonly reported in the first few days after treatment, generally improving by the second and third weeks within two-three week cycles. Many foods were reported to be unappealing during the first week, producing low motivation to eat and difficulty in selecting
foods that would be well tolerated. Most women reported lower food intake in response to low
appetite, including irregular meals and smaller portion sizes.

_Quin:_ I just didn’t have enough energy to grasp any appetite really, nothing was
appealing.

_Faye:_ For the first three days after treatment, I only ate the bare minimum, wasn’t
hungry, I had no interest in doing anything and then my appetite increased a little…

Some women reported an increase in appetite during the treatment cycle (n=8, 29%).
Among these women, appetite was low for the first couple of days after treatment but spiked
quickly thereafter. Two women found that their appetite was elevated for 2-3 days only, while
others felt their appetite was higher through the remainder of each cycle.

_Bridget:_ That was during the AC [Adriamycin, Cyclophosphomide] that I would get those
hunger spikes right at the end of that first week and I would eat, that whole weekend.

Seven out of eight of these women felt that increased appetite had led to increased food intake;
either eating more frequently or an increase in portion sizes at regular meals.

_Odette:_ …I would eat three servings of lasagna. All of my family noticed... ”mom
you’re finishing that?” Yeah, I ate like a horse and I was hungry.

_Nina:_ …..yeah, I took in a bigger amount of food, that’s for sure.

**Food Appeal - Food Cravings, Comfort Foods and Food Aversions**

Many women in this sample reported food cravings during treatment (n=21, 75%). Most
common were cravings for starchy carbohydrates (potatoes, pasta, bread/crackers), salt or sour
(potato chips, citrus fruits) and sweet foods (ice cream, chocolate milk). Food cravings were
often very specific, in some cases for foods or food combinations not typically consumed. A
few women reported a craving for high protein foods (fish, eggs) or high fat foods including
deli meats, bacon, hamburgers and cheese. Most women accommodated their food cravings
during treatment.

_Odette:_ …things that I wouldn’t normally eat, like deli stuff, so maybe salami and cheese.
Bridget: …and it would have to be a specific food, so I would make pasta or with fish in it or something bizarre because I wanted to eat that much protein or fat or something.

Heather: …every once in a while I’d get a craving and it would be something that I wouldn’t even really eat. I wanted macaroni and cheese out of the box. Now it’s not something I grew up with, but I said “oh today I really want macaroni and cheese”.

With or without specific cravings, some foods and food groups were reported to be especially comforting and well-tolerated during treatment. The most frequently reported “comfort foods” during chemotherapy included starchy carbohydrates, bananas, applesauce, puddings, yogurt, ice-cream, soups and chocolate milk. With considerable overlap in the characteristics of these foods, the common underlying traits were a preference for bland, easily digested foods and soft texture or cool temperature, in response to treatment-related gastrointestinal disturbance.

Karen: I pretty much went to a BRATT diet [banana, rice, applesauce, tea and toast]. So it worked. I had crackers - you know little crackers and munchies like that.

Bridget: Well I made a lot of soup in the first half. I would make squash and then I would mix it with kale and broccoli and beans and I’d make myself a real kind of heavy vegetable soup. I’d mash it up and I’d put spice in it like ginger, cinnamon ….it would make me feel better.

Roberta: I ate an awful lot of applesauce….. it was good, yes the coolness, the texture. I put in some extra cinnamon and that was good, applesauce was really, really good.

Less commonly reported comfort foods included eggs, ginger ale, sweet foods (cookies, syrup) and citrus fruits. While most comfort foods were described in terms of providing physical comfort, some women (n=7, 25%) reported that occasional “treats”, typically sweet foods or starchy carbohydrates, also provided some emotional comfort during treatment.

Food aversions were equally common during treatment (n=21, 75%). Among the most commonly reported aversions were meats (red meat in particular), raw vegetables and sweet foods. Citrus fruits and juices were poorly tolerated by a few women (n=3, 11%) and were eliminated entirely during treatment. Four women (14%) reported food aversions directly
related to what they had eaten on or around the day of treatment; a negative association that persisted for two of the women beyond treatment.

*Bridget*: So I used to be a big fan of Tim Hortons™ coffee, and I can’t drink it anymore. Since then, because there’s something just reminds me of doing chemo and just that taste in my mouth and I’ll never touch it again.

While there were some common themes around food cravings and food aversions in this sample group, a preference or distaste for certain foods seemed to be highly individual and variable across treatment. Some women for example, reported a craving for sweet foods or citrus fruits, while others identified the same foods as extremely unappealing and poorly tolerated during treatment.

Key themes emerging from the data on food intake and eating patterns during treatment are summarized in Figure 3.1.

**Figure 3.1: Key Themes for Food Intake and Eating Patterns during Treatment**

- **(1) Changes in Food Intake Relative to Treatment Day**
  - irregular meals and snacks and lower food intake in week 1
  - gradual increase in food intake and meal structure in weeks 2-3

- **(2) Changes in Appetite**
  - decreased appetite
  - increased appetite

- **(3) Food Appeal**
  - food cravings
  - comfort foods
  - food aversions

### 3.4.3 Treatment-Related and Psychosocial Factors Affecting Food Intake

Most women appeared to have excellent recall of their chemotherapy experience at the time of interview, and identified several common psychosocial and treatment-related factors associated with changes in food intake during treatment. Key themes including fatigue, changes in taste and nausea, emerged frequently and spontaneously in response to an open-
ended question asking “can you talk about how you were you feeling during treatment and what factors you think may have influenced your food intake and eating patterns during this time”. Follow up questions and probes for other common gastro-intestinal disturbances, emotional distress, family/social support and burden of treatment served to identify psychosocial factors, sub-themes and patterns within categories.

3.4.3.1 Treatment-Related Side Effects

Most treatment-related side effects presented within one to two days of treatment, with the full impact of chemotherapy and associated medications experienced by most women by day three or four. Most women found that side effects began to recede by the end of the first week, reporting gradual improvements across most symptoms in the second and third weeks after treatment. Women on an accelerated dosing schedule (chemotherapy every two weeks, n= 9, 32%), tended to report fewer days in which they felt well before the next cycle.

Karen: Well the timing of the chemo, like I got to experience that within about four days. The full impact of the chemo would be there and that affected taste and energy and you know, just the desire to eat or cook.

Fatigue

Fatigue was a pervasive and progressive side effect of chemotherapy, reported in 100% of women in this sample. Fatigue was described as more acute in the first week after treatment, improving gradually for most women in the second and third weeks of the cycle. In addition, most women reported a cumulative effect across treatment, with reduced energy and longer recovery periods as treatment progressed. For one participant, fatigue was an overwhelming side effect that did not relent until the completion of treatment.

Faye: ......the actual three to five days [after] in all the treatments were extreme fatigue. I didn’t go anywhere. And then after that I would gradually start feeling stronger and stronger. But with each treatment I had more fatigue. By the fourth one I had no strength left it felt like...each time I was knocked back a little bit more...
Valerie: It was very severe in the first week and then by the third week you’d feel ok.

Elise: I could feel myself starting to feel a bit more run down towards the end, so I was glad I was only doing four [cycles] and then it was going to be done, because I was just feeling more tired.

Quin: The day after I might be fine. Maybe even into the second day. And then after that it started going downhill. I got more tired, more tired, more weak, more weak. By the time we hit the fourth chemo, I got pretty weak.

The impact of fatigue was far reaching, with most women reporting very little activity in the first week after treatment. Low energy interfered with activities of daily living during this phase, including cooking, housecleaning, socializing and structured exercise. The typical response to treatment induced fatigue was to rest and recover at home until the acute phase passed; afternoon naps and/or resting for much of the day were common. Most women appeared to adapt to low energy by doing what they could in small increments and accepting that other things could wait until their energy level improved.

Lana: I was definitely sleeping, napping through the day. Or just flaked out on the couch. I watched more TV than I’ve ever watched in my life.

Maureen: Quite tired, certainly there were a couple of days I just spent on the sofa, rather than doing anything at all.

Fatigue was associated with lower food intake in some women (n=9, 32%), particularly in the first few days after treatment. This group of women described that they were “too tired to eat”, “couldn’t be bothered” or didn’t have the energy to prepare food, especially if they were living alone.

Gail: Sometimes, as I said, it’s really the whole thought of food, to make yourself start cooking and that can be pretty difficult.

**Changes in Taste**

Taste changes were reported in all but one woman in this sample and appeared to have a significant impact on food intake during treatment. Most women reported a metallic or
chemical taste in their mouth, presenting within one to three days of receiving chemotherapy and persisting well into the second week after treatment. During this time, there was a general sense that their taste buds were “off”; that many foods and beverages tasted bad (n=18, 64%) or had no taste at all (n=9, 32%), a loss of taste sensation known as hypogeusia.

Taste changes were frequently described in relation to specific foods (e.g., milk, meat, fruits, vegetables, coffee) and produced a wide range of dietary responses including food cravings, food aversions and lower appetite. Cravings for salt, sour and sweet foods, for example were often explained in this context.

Odette: … I felt a need for salt and just something sort of vinegary…..something that I could taste I think was the reason, because other things were just so bland.

Maureen: The first few days, really the only thing that tasted half way decent was sweets, sweet foods, so I was eating more of that. It was pretty much the flavour, everything else did not taste good at all. I didn’t even want it. Not interested.

Others found that taste changes promoted food aversions; the metallic or chemical taste in their mouth exacerbated by certain foods.

Heather: Toast tasted like metal, so I just, I wouldn’t even eat it. Peanut butter and jam on it, eww no. So I’d make myself eat an egg. Something like that...eggs were ok for me.

Roberta: I never drank milk, I hardly remember eating any salads or fruits, I didn’t eat a whole lot, bananas were horrible, peanut butter was horrible, all those things. Everything tasted horrible.

For some women, lack of taste led to low interest in food and poor appetite.

Lana: There’s just no taste and so it just became kind of a chore to think about eating.

Roberta: …..the worse thing for me with chemo was the taste in my mouth and nobody told you about that. I didn’t want to eat anything, nothing. Like nothing tasted good. The things that I loved, I don’t know what I survived on really for the first two weeks.

A common strategy for coping with taste changes was to add salt or lemon to foods and beverages in an effort to enhance flavour or to mask unpleasant tastes. Most women found that by the third week after treatment, their taste buds were returning to normal and they were able
to resume their regular pattern of eating. For some women (n=5, 18%), severe and persistent changes in taste during treatment produced lower than normal food intake and decreased enjoyment in eating throughout treatment.

**Gastrointestinal Disturbance**

Common chemotherapy protocols for non-metastatic breast cancer include 3-4 cycles of combined chemotherapy including Adriamycin and Cyclophosphamide (AC) or 5-Florouracil, Epirubicin and Cyclophosphamide (FEC), followed by 3-4 cycles of Paclitaxel or Docetaxel (T) alone. Among women receiving one or the other of these treatment combinations (n=19, 68%), many expressed having had more difficulty with gastrointestinal disturbance during the AC or FEC cycles. Gastrointestinal symptoms seemed to be less severe while receiving Paclitaxel or Docetaxel and most women reported an increase in appetite and food intake during this phase of treatment. Paclitaxel or Docetaxel were more commonly associated with muscle and joint pain.

*Connie: The Taxol was different because I didn’t really not want to eat. I didn’t have any nausea. It’s just after three to four days, maybe two days, by the Saturday I had the aches and pains.*

*Amy: The Taxol was much better than the AC in terms of diet and that nauseous feeling. The Taxol I had more leg and joint pain and numbness.*

**Nausea and Vomiting**

Some degree of nausea was reported by most women (n=23, 82%) during treatment. Based on their recall of the severity and duration of symptoms, nausea was generally mild to moderate, frequently described as an unpleasant, flu-like feeling for 3-4 days after treatment.

*Yvonne: Almost like you’re getting the flu kind of thing, just down more than all out nausea.*

*Roberta: I felt nauseated. I didn’t throw up….but if just felt like my stomach was queasy all the time.*
Nausea occurred without vomiting in most cases, however a small group of women (n=8, 29%) reported single episodes of vomiting or more prolonged periods of vomiting in one or two cycles of their treatment. During this period, dietary responses varied across women. Some women reported a decrease in appetite and lower than normal food intake, while others found that eating more frequently, starchy carbohydrates in particular, helped to relieve nausea for the first few days after treatment.

Donna: You want something that’s going to satisfy you and you just keep your stomach full because you’re always hungry and you always want something in your mouth…. I was nauseous and I just wanted to always have something to eat.

Zoe: Well I also felt like if I didn’t eat, I’d feel more nauseous. So I did try to eat, you know small meals and snacks.

Overall it appears that for most women, routine use of anti-nausea medications (reported in 100% of participants) provided reasonably good control of this common side effect of chemotherapy treatment. Persistent nausea or extended periods of vomiting however, were reported by five women (18%), leading to longer periods of reduced food intake. For most women, symptoms tended to be more acute in the first cycle, improving based on increased awareness of treatment effects and better anti-nausea medication management in subsequent cycles.

Maureen: .....and then I went back to oncology [second cycle] and she changed up all my anti-nausea drugs. So the next time was much easier. Still felt kind of icky, but not too bad. By the third time I was eating dinner when I got home from chemo.

Other strategies to help manage nausea included drinking club soda, snacking on soda crackers and being outdoors/exercise.

Alison: .....even if I was nauseous, six whole wheat crackers would calm it down.
**Constipation and Diarrhea**

Constipation and diarrhea were common concerns during treatment, reported in 21 (75%) and 11 (39%) women, respectively. Constipation typically occurred within the first day or two after chemotherapy, lasting for two to five days and followed in some cases by diarrhea. Most women reported some degree of bloating and abdominal discomfort during this time and ate smaller portions until the problem had resolved. Diarrhea seems to have been a relatively minor gastro-intestinal side effect of treatment that did not interfere with food intake for most women. Diarrhea was generally described as mild and of short duration, however four women experienced intermittent episodes throughout treatment. Medications to prevent constipation are commonly recommended during treatment such that, with routine use from the onset of chemotherapy, some women were able to minimize or avoid this well established side effect. For others, the addition of stool softeners (e.g., Colace, Dulcolax) and fibre laxatives after the first cycle helped to relieve symptoms. In addition, many women managed this potential side effect using dietary strategies including increased fruit and vegetable intake, high fibre cereals and plenty of fluids.

**Heartburn**

Heartburn was an issue for 16 women (57%) during treatment, five of whom had a history of acid reflux before diagnosis. The majority of women described their experience of heartburn as mild, occasional and/or of short duration, however some reported more severe or persistent symptoms across treatment. For these women, the discomfort associated with heartburn lead to sleep disturbance and lower food intake.

*Irene: All the time. I ate Tums like there was no tomorrow. I’d wake up in the middle of the night with it. Oh, it doesn’t matter what you eat and there was no rhyme or reason to it. You’d get heartburn and ok I’ll stay away from that food. Try another one, poof, there it goes again.*
Some women reported the routine use of prescription medications or over-the-counter antacids to manage symptoms. Others found that heartburn resolved within a few days, without the need for medical intervention.

**Mouth Sores**

Mouth sores are a common side effect of chemotherapy, however they were reported in this sample in only 9 women (32%). In addition, a few women (n=4, 14%) reported tender gums or sore throat that did not develop into open mouth sores. Symptoms were typically mild, with minimal sores occurring in a single cycle for most women. The majority of women managed this side effect through careful oral hygiene and regular use of mouthwash or salt water rinses. One woman experienced more severe symptoms in the first four cycles. Her symptoms were relieved somewhat by initiating routine use of mouthwash in the second half of treatment; stressing the importance of prophylactic management early in treatment.

*Tory: Once I sort of figured it out, like just used it [mouthwash] as much as possible, it really helped. I think mine got really bad because I didn’t start using it right away. And then I learned that right after chemo, there are certain days that they would just flare up.*

Overall mouth sores did not seem to have a significant influence on food intake during treatment. Some women however, mentioned that soft or cool “comfort foods” were especially well tolerated when mouth sores were present.

### 3.4.3.2 Psychosocial Influences on Food Intake

**Family Influences and Social Support**

Twenty of the women in this sample group (71%) were married or living with a partner or parent during the treatment period. Most reported that their husband, partner or parent had done much or all of the food shopping and cooking while they were in treatment and that they were able to eat with their family on most days. In some cases, special foods that were better tolerated were prepared, in addition to the family meal, particularly in the first few days after
treatment. Living with a spouse, partner or parent appeared to have a significant impact on food intake for these women, with many suggesting that having someone else do the cooking contributed to both the quantity and quality of meals and snacks throughout treatment. A few women (n=5, 18%) found that they were able to do most of the cooking, with some help from family and friends. Two of these women reported that they preferred to do the cooking and were focused on preparing healthy meals for themselves and their families.

Seventeen women (61%) had children living at home while they were receiving treatment. Having children at home did not seem to influence food intake for most women, however some expressed that maintaining family meals was part of an effort to create a sense of “normalcy”, especially for younger children.

Extended family and friends prepared and delivered food for most of the women during treatment, however very few women felt that this impacted significantly on their overall food intake. Some women reported that meals and snacks from family and friends were well tolerated and alleviated worry about food preparation after treatments.

Paula: People were bringing in food and things like that, which was really nice. Then I thought to myself I don’t have to worry about eating today.

Others found that enjoyment of outside foods was challenged by taste changes that were not well understood by those bearing food. Although meals and snacks provided by family and friends were sometimes poorly tolerated by the women themselves, many expressed appreciation for the practical assistance this provided, since these foods were frequently enjoyed by their husbands and children. Moreover, many women commented that regardless of their food tolerances, the show of support and social visits around food provision were comforting. Many women also emphasized that practical assistance (parents caring for young children, friends and family accompanying them to appointments and treatments), as well as
other expressions of support (phone calls, cards, flowers) provided much comfort during treatment. In most cases there was a strong sense of having been “well cared for”, which seems to have played a significant role in emotional well-being.

*Gail: I was extremely lucky and I think I had a very, very good support system and everybody wanted to do something whenever they could, you know. That was great.*

*Heather: Yeah a lot of good people and cards came every day. I got 150 cards. And some people, one friend, she was working all the time but she wrote me every week.*

*Tory: My parents live [close by], so yeah they’ve been good through all this, and my dad… he used to come with me for my oncology checkups and he always wanted to….. yeah they were excellent.*

**Emotional Impact**

Many of the women in this sample expressed that “all things considered” they felt “reasonably good” emotionally and that the emotional impact of cancer and its treatment was not a determinant of food intake during treatment. Others (n=13, 46%) however, expressed some degree of anxiety, largely centered on anticipated or unknown side effects of treatment.

*Karen: Like the first time, you didn’t know what to expect. I mean people tell you all this stuff, but your experience is your own…..bit of anxiety with that you know.*

Most of these women felt that stress may have contributed to nausea and fatigue, leading to lower food intake (n=6, 21%) or an increase in intake of energy dense, comfort foods (n=5, 18%) for at least a portion of the treatment period.

*Connie: Well I think the first time for sure there’s a little bit of stress and fear and that would have contributed to some of that [nausea].*

*Janelle: I think I probably eat less when I’m stressed. Yeah, I know some people love to eat when they’re stressed, other people don’t.*

*Yvonne: If I have a lot of emotions, I tend to overeat. So if anything it would have caused me to eat the high calorie stuff….frozen yogurt with sauce or something like that.*

*Fran: Well I’m an emotional eater so yeah, if I’m feeling down I would eat more.*
For most women however, anxiety was mild and transient, dissipating somewhat as treatment progressed. A small group of women (n=4, 14%) appeared to have a more pronounced emotional response to their breast cancer diagnosis that persisted throughout treatment. These women expressed anxiety about survival, low mood or concern for being dependent on others. Two of these women reported that during treatment they had eaten more than they would usually eat compared to their normal diet before diagnosis. The other two women reported that they had eaten less than they would usually eat, suggesting that food responses to stress are highly variable.

**Treatment Burden**

It was expected that the burden of multiple appointments, medical tests and treatments may contribute to fatigue and changes in food intake during treatment. Although most women acknowledged that treatment for breast cancer was a “full time job”, only two reported interference with food intake associated with the burden of treatment. For one woman, lower food intake on treatment day was associated with anxiety and longer waiting periods, while the other felt that she had relied more on convenience foods after treatments.

*Sadie: The first time I went [for chemotherapy], I sat there for a very long time and that got me you know, very anxious and all there was was those cookies there.*

*Wendy: …..if you’re mentally tired, you don’t have the energy then to make the food. You know, you look at the fridge or the freezer and you think “ugh”. There was a time when all I was doing was buying Lean Cuisines™ and eating those basically.*

Most women found that their appointments and treatments were predictable and were thus able to plan accordingly. Depending on the time of day, many women took snacks with them on treatment days, especially when lengthy intravenous chemotherapy was anticipated.

*Elise: My appointments were pretty well scheduled…..When you first decide you’re going to do chemotherapy, there’s a great flurry of appointments and then I find it kind of leveled off and it was pretty predictable, so easy to work around.*
Three women who lived a further distance from the cancer centre, were accommodated with appointments and treatments scheduled on the same day and likewise reported no difficulties or interference with food intake. Although there was no direct link between treatment burden and changes in food intake for most women, many felt that keeping pace with the need for multiple appointments, contributed to fatigue during treatment.

Key themes emerging from the data on treatment-related side effects and psychosocial factors associated with food intake and eating patterns during treatment are summarized in Figure 3.2.

**Figure 3.2: Key Themes for Treatment-Related Side Effects and Psychosocial Factors Associated with Food Intake and Eating Patterns during Treatment**

**Treatment-Related Side Effects**

1. Fatigue
   - acute effects within cycles
   - cumulative effects across treatment

2. Changes in Taste
   - foods taste bad/metallic
   - hypogeusia (loss of taste sensation)

3. Gastrointestinal Disturbance
   - nausea
   - constipation
   - heartburn

**Psychosocial Factors**

1. Family Influences & Social Support
   - cooking support
   - emotional wellness

2. Emotional Impact
   - lower food intake
   - comfort eating

While common underlying themes were apparent across the sample group, individual dietary responses to psychosocial and treatment-related side effects varied considerably. Taste changes, for example, were associated with both food cravings and food aversions and
responses to nausea ranged from decreased appetite and lower food intake to reports of increased appetite and eating more frequently throughout the day, in an effort to relieve symptoms. Likewise, the emotional impact of cancer and its treatment was associated with increased intake of energy dense comfort foods in some women but not others. With these key themes in mind, the constant comparative method was used to identify similarities and difference in food intake and eating patterns among women who gained weight versus women who did not gain weight during treatment.

3.4.4 Food Intake and Eating Patterns in Women who Gained Weight Compared to Women who Did Not Gain Weight During Treatment.

The qualitative design of this study precludes statistical comparisons, however, some patterns emerged from the analysis suggesting possible group differences among women who gained, maintained or lost weight during treatment. Among women who gained weight, acute disruption in eating patterns (lower food intake after treatment) appeared to be shorter in duration, with most experiencing a return to normal eating patterns within one week of treatment. Those who were weight stable during treatment reported disruptions in eating generally ranging from 7-14 days. Women in either category generally reported more regular meals or smaller, more frequent meals/snacks across treatment compared to women who lost weight. Conversely, most of the women who lost weight during treatment reported a more prolonged reduction in food intake or irregular eating patterns throughout treatment. These women were more likely to report pronounced day to day variability in food tolerance and more difficulty in selecting foods that were appealing and enjoyable compared to women who gained weight or were weight stable during treatment.

Increased appetite appeared to be more commonly experienced by women who gained weight during treatment. In this sample, 55% of the women who gained weight during
treatment reported an increase in appetite, compared to 12% among those who lost weight or were weight stable during treatment. Although many of the women who gained weight reported an increase in appetite, others felt that their appetite was lower during treatment. Some of these women however, were conscious of eating regular meals, despite poor appetite, over concern for maintaining adequate nutrition and avoiding treatment delays.

Paula: I had to force myself to eat because I know that if I didn’t, if the blood result were not good, they weren’t going to give me my treatment. So I tried to eat nutritious meals.

Heather: I wasn’t really interested in food during all of chemotherapy. I made myself get up and eat breakfast. I told myself I was going to make sure I got up every day and I ate every day.

For some women who gained weight, low appetite and low food intake alternated with food cravings and increased intake of energy dense comfort foods.

Faye: There again it’s up and down. I wouldn’t want any food. I could go days without eating food and then I would want comfort food, and then I’d eat too much.

Heightened awareness of eating enough food and periods of comfort eating in this sub-group of women may account in part, for positive energy balance during treatment. Others may have compensated or over-compensated for lower energy intake in the first few days, as acute side effects receded and regular eating patterns resumed in the second week after treatment. Furthermore for two of these women, appetite improved after the first cycle of treatment, with the introduction of a new medication and better control of treatment-related nausea.

Food cravings also seemed to be more commonly described by women who gained weight (82%), compared to those who were weight stable (72%) or lost weight during treatment (66%). Overall, the types of food cravings across weight change categories were quite similar, however women who lost weight or were weight stable described their cravings as occasional and of short duration, while those who gained weight tended to report food cravings that were
more enduring across treatment. The nature of food aversions or comfort foods did not appear to vary between women who gained weight and those who did not gain weight during treatment.

There were some apparent differences in the experience of chemotherapy, across weight change categories, that may explain some of the variability in food intake and dietary patterns that were reported. First, although fatigue was a universal side effect of treatment, six women (21%) felt that extreme fatigue had led to a more prolonged reduction in food intake. Four of these women lost weight during treatment. Persistent, overwhelming fatigue was reported in one woman who lost more than 12 kg over 18 weeks. Two women felt that they had eaten more in response to fatigue, in an effort to increase energy. Both of these women gained more than 2.0 kg during treatment. Similarly, taste changes were reported across all weight change categories, however, a search for foods that would taste good or a “need to eat” in order to mask bad taste was a response described only by women who gained weight or were weight stable during treatment.

Sadie: They put all this stuff in your body and then it just comes out. Like I could taste the poison in my mouth. And then at the same time like you know, you want to eat because you want to get rid of that taste.

Persistent nausea or extended periods of vomiting were reported in only a small number of women, most of whom lost weight during treatment. One woman who was weight stable, despite persistent nausea, received two cycles of chemotherapy and refused further treatment and one who gained weight reported several episodes of vomiting in one cycle only. The latter participant and others (n=4) found that eating more frequently and having starchy carbohydrate rich foods in the stomach helped to relieve treatment-related nausea. All of these women gained weight during treatment.
Constipation seemed to be reported more frequently among women who lost weight during treatment (100%) compared to those who gained weight (64%) or were weight stable (73%), producing abdominal discomfort and reports of decreased food intake in many of these women, for longer periods of time between cycles. Heartburn concerns were equally dispersed across weight change categories, although seemed to be more severe among women who lost weight during treatment, producing sleep disturbance and decreased food intake. The timing of heartburn symptoms was highly variably across women and within cycles, such that no consistent patterns were evident.

Severe muscle and joint pain was reported only in women who gained weight or were weight stable suggesting that this side effect of treatment and the associated reduction in physical activity may play a role in promoting energy imbalance during treatment.

Living arrangements may also be associated with weight change during treatment. Forty-five percent of women who were married or living with a partner or parent during treatment gained weight and 20% lost weight, compared to 25% and 33% respectively, among women who lived alone. This finding likely reflects the level of cooking support available to women after treatment, since those who had a significant other in the home, expressed that their husband, partner or parent had assumed most of the responsibility for food preparation. Some women who lived alone found that fatigue interfered with their ability or motivation to prepare meals.

While dietary responses to stress seem to be highly variable, weight gain was reported in four out of five of the women who felt that anxiety and stress had lead to periods of overeating during treatment; suggesting that the emotional impact of breast cancer and its treatment may play a role in weight gain for some women.
In response to the standardized question “during treatment, compared to your normal diet before diagnosis, do you feel you ate the same amount as you would usually eat, more than you would usually eat or less than you would usually eat?”, 18 women (64%) reported that they had eaten less and 9 (32%) reported that they had eaten more. Seventy-three percent (n=8) of women who gained weight during treatment reported an increase in food intake. Most of these women felt that they had increased their portion sizes and/or increased their consumption of energy dense foods including fast foods, high fat and high sugar snacks.

Fran: …I was craving certain things probably more than I used to….hamburgers, fries and anything really. I don’t eat that kind of stuff ever…..maybe bread, sugar, stuff with sugar in it.

All of the women who were weight stable and 83% of women who lost weight, reported a decrease in food intake during treatment. Self-reported increase in food intake was significantly correlated with weight gain during treatment (r=0.55, p<.01).

3.4.5 Diet, Physical Activity and Weight Gain during Treatment.

These findings provide support for an association between diet and weight gain, however in order to characterize energy imbalance during treatment, changes in food intake must be considered within the context of changes in physical activity during the same time frame. In response to the standardized question, “during treatment, compared to your normal physical activity level before diagnosis, do you feel were as active as usual, less active or more active?”, 22 women (79%) reported that they were less active during treatment, 3 (10.5%) felt that they were as active as usual and 3 (10.5%) felt they were more active.

Lower levels of activity were attributed to treatment-related side effects (fatigue, nausea, muscle/joint pain), as well as a reduction in work-related activity. Physical activity was generally lowest in the first week after treatment, during which time most women reported a
reduction in both structured exercise and activities of daily living. Most women reported a gradual increase in activity in the second or third weeks, with many able to resume their normal day to day activities (shopping, housecleaning, socializing) and some structured but lower intensity exercise by week three.

Gail: The first week I literally wouldn’t or couldn’t do a whole lot. And then by the second and third week I would feel like doing some exercise, you know, trying to move and do things.

Faye: Initially... probably the first 10 days, I didn’t feel like doing much activity at all. I didn’t have the strength. ...as the weeks got up, into the second week after treatment, I would start feeling a little better and feel like getting up and doing more.

For some women (n= 6, 21%) the effects of fatigue in particular were persistent and cumulative across cycles, leading to reports of very low levels of activity throughout treatment.

Quin: I was watching a lot of television, not much desire to do anything.....no, go for a walk, are you kidding? No way, no energy for that kind of thing.

Among those who felt they were as active as usual or more active during treatment (n=6, 21%), there was an underlying theme of having “pushed themselves” to keep going. These women were able to maintain their regular walking or running routines throughout treatment or to resume their structured exercise within a few days of receiving chemotherapy.

Roberta: Everyday, I’d get up in the morning and I would get up and get out there [walking]. So I kept going and I just thought “just do it”.

Bridget: By that third week it was always my goal on that Friday of the third week, before that weekend, I’d say “those are my 15 km days.... just go and don’t think about it, just go”.

Sadie: I really pushed myself to still walk the dogs.

Social support played a role in maintaining physical activity for some women who found that family and friends were helpful in motivating them to exercise, as tolerated, during treatment.

Most of the women who gained weight during treatment reported a decrease in physical activity during treatment (82%). Many of the women who lost weight or were stable however,
also felt they had been less active during treatment. Among those reporting an increase or no change in activity during treatment (n=6), two gained weight, one lost weight and three were weight stable. Self-reported change in physical activity did not correlate with weight change during treatment (r=0.08, p=.69). Collectively, these findings suggest that while lower levels of physical activity likely play a role, physical inactivity is clearly not the only factor contributing to energy imbalance. Based on the current data, it appears that dietary factors also play a role in promoting weight gain during treatment.

A theoretical model to explain how psychosocial factors and treatment-related side effects may influence diet and eating patterns in ways that promote energy imbalance and weight gain during treatment is presented in Figure 3.3. In light of emerging evidence to suggest that weight loss is also associated with adverse health effects (Chen et al., 2010; Thivat et al., 2010) the model is expanded in Figure 3.4, to include factors associated with weight loss during treatment.
Figure 3.3: Relationships between Psychosocial & Treatment-related Factors, Food Intake and Weight Gain in Breast Cancer Survivors during Treatment.
Figure 3.4: Relationships between Psychosocial & Treatment-related Factors, Food Intake and Weight Change in Breast Cancer Survivors during Treatment.
3.5 Discussion

This study provides a unique description of recalled food intake and eating patterns, psychosocial and treatment-related factors and weight change during chemotherapy treatment, among early stage breast cancer survivors. Twenty-eight women were interviewed, within 12 months of competing treatment, in order to gain an appreciation of food intake and weight change during treatment and to investigate possible differences in diet and eating patterns among women who gained weight compared to those who were weight stable or lost weight during treatment.

Overall, food intake during treatment appears to be highly responsive to treatment day, with most women reporting smaller, irregular meals and snacks as tolerated and lower food intake for the first few days after receiving chemotherapy. Fatigue, taste changes, nausea and constipation were key factors contributing to changes in food intake during this time. In most women, acute side effects of treatment began to recede toward the end of the first week, leading to gradual increase in food intake and more structured eating in the second and third weeks of the cycle. While there were underlying themes across the sample group, treatment-related side effects and psychosocial factors produced a wide range of dietary responses including changes in appetite, food cravings, food aversions and comfort eating that varied across women. The constant comparative method was used to look for patterns in women who gained weight versus women who were weight stable or who lost weight during treatment. Some notable differences in food intake and eating patterns were evident.

It appears that women who gain weight, may experience a shorter acute treatment response (fatigue, gastrointestinal disturbance), in which food intake is generally lower after each cycle. Women who lost weight tended to report more severe and persistent side effects of treatment,
leading to a more prolonged reduction of food intake after treatment. Increased appetite, food cravings and intake of energy dense comfort foods seemed to be more prevalent and persistent among women who gained weight during treatment. Based on women’s perceptions, changes in taste, nausea and emotional distress were central in promoting these dietary responses. Given that fatigue is a pervasive side effect of treatment affecting activities of daily living, weight gain and weight loss may also be influenced by living arrangements and the level of cooking support that is available in the home. In this sample, weight loss appeared to be more common among women who lived alone.

Most studies to date support physical inactivity, in response to treatment-related fatigue, as the dominant factor contributing to energy imbalance and weight gain after diagnosis (Demark-Wahnefried et al., 1997a; Demark-Wahnefried et al., 2001; Kumar et al., 2004). The majority of women in our study also reported a decrease in physical activity during treatment, compared to their usual activity before diagnosis. Lower activity however, was reported in both women who gained weight and those who lost weight and some women who gained weight reported an increase in physical activity, suggesting that other components of energy balance contribute to weight change during treatment. It has been suggested that changes in basal metabolism may play a role in post-diagnosis weight gain (Foltz, 1985; Demark-Wahnefried et al., 1997a), however research in this area is limited and has produced inconsistent findings. In addition, there is some evidence to suggest that alterations in ovarian function may promote additional weight gain among women who experience treatment-induced menopause (Goodwin et al., 1999). In the current sample, the prevalence of treatment-induced menopause could not be determined, since the length of time from treatment was less than 12 months. However, it is possible that alterations in ovarian function contributed to weight gain in this sample, given
that 19 women (68%) were premenopausal at diagnosis and only one reported a return of menses at the time of interview. While the etiology of weight gain in this population is complex, based on several possible inter-related pathways, our findings suggest that food intake and dietary patterns may play an important role for some women.

Despite recent efforts to capture possible changes in food intake during and after treatment, empirical support for an increase in energy intake after diagnosis and an association between increased energy intake and post-diagnosis weight gain is lacking. Using 4-day weighed food records, Harvie et al. (2004) found that, in 17 pre and postmenopausal women, mean energy intake did not change significantly over six cycles of chemotherapy; a finding that is supported by three other investigations (Kutynec et al., 1999; Del Rio et al., 2002; Kumar et al., 2004). Based on 24-hr recalls (Foltz et al., 1985) and 4-day food records (Nissen et al., 2011) changes in energy intake from the first cycle to the last cycle of chemotherapy were not significantly related to weight change during treatment. Most of these studies, however, are limited by small sample size and the absence of dietary data over the treatment trajectory. Many studies, for example, have used pre and post chemotherapy measures only, which will not detect fluctuations in intake over the course of treatment or within treatment cycles (Kutynec et al., 1999; Kumar et al., 2004; Nissen et al., 2011). This limitation likely reflects the elevated level of burden that multiple days of record keeping would place on patients during active treatment. Demark-Wahnefried et al., (1997a) measured food intake one-two weeks before the initiation of chemotherapy and weekly throughout treatment using 3-day diet records and found that energy intake over the course of treatment was highly variable and responsive to treatment day. Mean energy intake was significantly lower at the end of treatment in this sample, compared to baseline, however it was suggested that participants may have reduced their food intake in
response to intense monitoring. Alternatively, it is possible that intense record keeping may have lead to underreporting. There is some evidence to suggest that reporting accuracy may be improved with 3-day rather than 7-day food records (Rebro et al., 1998); a finding that is perhaps related to the degree of burden associated with multiple days of record keeping (Caan et al., 2000).

In an effort to circumvent some of these research gaps and methodological challenges, we chose to investigate food intake and eating patterns during treatment using a qualitative design. Grounded theory methodology provided a framework in which to explore the rich detail of the “lived experience” (Charmaz, 2006) that was designed to go beyond food intake to understand the reasons behind dietary choices that women make. Using this approach, recalled food intake and dietary patterns were placed within the context of the psychosocial and treatment-related challenges that women face as they undergo chemotherapy treatment for breast cancer.

The decision to interview women after treatment was based on our pilot work with patients in active treatment, which suggested post-treatment interviews would be less invasive and may allow for a larger, more representative sample. Furthermore, follow-up consultations revealed that most women had vivid recall of their chemotherapy experience and could provide important insights that had not been explored. To the author’s knowledge, this study is the first to relate changes in food intake and dietary patterns to treatment days and treatment-related side effects and to describe changes in food intake and dietary patterns in women who gained weight compared to those who did not gain weight during treatment.

Our findings support earlier studies, in which it was hypothesized that food cravings, increased appetite, nausea and emotional distress may lead to overeating in the post-diagnosis period (Brewin 1980; Heasman et al., 1985; Huntington, 1985; Knobf, 1986; DeGeorge et al.,
1990). Our findings are also consistent with those of Demark-Wahnefried and colleagues (1997a), suggesting that food intake is highly variable across treatment and within treatment cycles. Moreover, variation in individual responses that were described, underscore the difficulty in choosing the optimal days and weeks for dietary assessment during active treatment. Together, these findings suggest that efforts to capture fluctuations in intake via food records or 24-hr recalls would clearly be challenging, especially in light of the extreme fatigue that seems to be associated with the days of most disturbed intake.

Most notable among our findings were some apparent differences in the experience of chemotherapy and associated dietary responses among women who gained weight compared to those who did not gain weight during treatment. In this sample, nausea, taste changes and emotional distress were associated with food cravings, increased appetite and increased intake of energy dense comfort foods in women who gained weight during treatment; qualitative findings which are supported by a significant correlation between perceived changes in the quantity of food intake and weight gain during treatment. While this single self-reported measure is a crude assessment of dietary change, these findings add to the limited data in this area and are further supported by the subjective impressions of women in this sample group, who felt that both increased food intake and lower levels of physical activity had contributed to weight gain during treatment.

Since not all women gain weight during treatment, possible differences in treatment-related effects, food intake and eating patterns among those who gain weight versus those who do not gain weight is an important question that is not addressed in the current literature. One early study in this area (Foltz, 1985), presented change in energy intake between the first and last cycles of chemotherapy, for women who gained weight compared to those who were weight
stable during this timeframe. In this study, women who did not gain weight decreased their intake by an average of 193 kcals/day, while those who gained weight reported a mean increase of 129 kcals; a difference that perhaps owing to small sample size did not reach statistical significance. It is noteworthy that other studies have also reported small increases in mean energy intake (88 - 142 kcals) over the course of treatment, that were not statistically significant (Demark-Wahnefried et al., 2001; DelRio et al., 2002; Harvie et al., 2004). If a true difference exists, increases in energy intake of this magnitude may lead to clinically important weight gain over time.

Grounded theory methods lend well to this exploratory area of research, since there is a good fit between the outcomes of grounded theory research and clinical practice (Daly, 2007). Data on food intake and associated psychosocial and treatment factors, that are “rooted in the lived experience of the participants”, highlight the challenges that women face while receiving chemotherapy and may inform the development of tailored dietary intervention strategies, within this context. For example, dietitians should be alerted to the potential role of nausea in promoting weight change (both gain and loss) during treatment and draw on the experiences of breast cancer survivors to develop dietary management strategies that support energy balance. It is important to recognize that the kinds of explanations presented in a grounded theory are generative rather than definitive, meaning they are offered as a framework that can be further tested and are subject to change, as the conditions and experiences of participant’s lives change (Daly, 2007). This is a critical concept in the research area under study, since cancer treatments are evolving rapidly and the experiences of patients receiving chemotherapy are likely to change over time.
The current study is not without limitations. The use of self-reported weight is a potential limitation, however several studies have reported excellent correlation ($r=0.92-0.99$, $p<0.01$) between self-reported weight and measured weight in this population (Rock et al., 1999; Herman et al. 2005; Caan et al., 2006; Gu et al., 2010). In the current study, the intra-class correlation coefficient for self-reported weight versus measured weight at the time of interview was 0.99 ($p<0.01$), suggesting that self-reported weight is reliable in this sample. The magnitude of weight gain reported in our sample is lower than some studies (Lankester et al., 2002; Del Rio et al., 2002) but comparable to others, in which the mean weight change across all participants during treatment was not significant (Demark-Wahnefried et al., 1997a; Kutynece et al., 1999; Freedman Aziz et al., 2004). Almost 40% of women in our study however, gained a mean of 5.1 kg; a finding that is consistent with other investigations (Lankester et al., 2002; Ingram & Brown, 2004; Gu et al., 2010).

A cut-off of 2.0 kg was used to define weight change in our sample, a criterion that has been used in previous studies with breast cancer survivors (Lankester et al., 2002; Nichols et al.2009; Gu et al., 2010). Others have used a cut-off of 2.5 kg (Ingram & Brown, 2004) or more recently, a change from baseline weight greater than 5% (Thivat et al., 2010; Nissen et al., 2011) to define weight change. Recognizing that weight flux as high as 2.0 kg may be transient in some adults (Groff & Gropper, 2000), several long-term studies suggest that weight gain in breast cancer survivors is progressive and durable, with a very small percentage of women returning to their pre-diagnosis weight within three years of treatment (Irwin et al., 2005, Makari-Judson et al., 2007, Gu et al., 2010). Moreover weight gain itself, regardless of baseline BMI, is associated with adverse health consequences (Kawachi, 1999; Willet et al., 1995) and may be more distressing among women who were not overweight before diagnosis.
Therefore it was decided that a weight gain greater than 2.0 kg during treatment, which was expected in some women over 4-6 cycles of chemotherapy (Lankester et al., 2002, Ingram & Brown, 2004) and is likely to endure, may have important clinical relevance.

Data on body composition were not available for our sample, therefore we cannot ascertain if weight changes reflect changes in body composition as well. Furthermore, previous studies suggest that unfavourable changes in body composition may occur with or without weight gain (Demark-Wahnefried et al. 2001; Kutynec et al., 1999). Absence of weight change in some participants, may have masked increases in body fat and loss of lean tissue; both of which are associated with adverse health consequences. Lastly our study was based on a convenience sample of self-selected women, who may not be representative of the population of breast cancer survivors. However this was an exploratory study, designed to be hypothesis generating and to provide novel description of food intake and dietary patterns during treatment.

In summary, the experience of chemotherapy, from the perspective of breast cancer survivors, supports several pathways by which psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight gain. In depth, qualitative interviews with women who have completed chemotherapy provided the opportunity to explore factors associated with changes in food intake during treatment; a critical first step in understanding the dietary challenges experienced by women after diagnosis. Our theoretical model is presented as a preliminary framework that may serve to guide the development of nutrition intervention and future research in this area.
CHAPTER 4: FOREWARD

Chapter 4 presents the findings from study 2 (objectives 3 and 4). The data for this chapter are based on self-reported changes in diet after diagnosis and current dietary intake estimated from 3-day food records, at the time of interview. Study 2 was a follow-up to study 1, within the same study population.
CHAPTER 4: Dietary Changes and Food Intake after a Breast Cancer Diagnosis.

The work presented in this chapter will be presented to the Canadian Journal of Dietetic Research and Practice as:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. Dietary Changes and Food Intake after a Breast Cancer Diagnosis

4.1 Overview

Objectives: For the growing population of women who have undergone treatment for breast cancer, healthy eating and weight management are important to support optimal health in survivorship. Understanding dietary habits of women after diagnosis is an important first step in developing nutrition guidelines and effective intervention strategies. The objective of this study was to describe self-reported changes in diet among breast cancer survivors in the first year after treatment, and to evaluate these changes in the context of current dietary intake.

Methods: Changes in diet were assessed in 28 early stage breast cancer survivors, using a self-reported survey in which women identified if they had introduced, increased, decreased or eliminated several foods since their diagnosis. Current dietary intake was estimated from 3-day food records and described relative to age and gender specific recommendations and data from the 2004 Canadian Community Health Survey, for women in corresponding age ranges.

Results: Participants in this study were a mean of 6.4±4.4 months from completing chemotherapy treatment. The mean energy intake for the sample was 1883±359 kcals, with protein, carbohydrate and fat providing 17.9%, 52.2% and 28.5% of energy, respectively. Mean intakes for macronutrients fell within the AMDR and saturated fat intake (8.9±2.8%) was, on average, below the current American Dietetic Association and Dietitians of Canada recommendation. Compared to women from the general population, women in this sample appeared, on average, to have lower fat intake, higher fibre intake and higher mean vegetable and fruit servings. The majority of women reported positive changes in diet after diagnosis. Dietary changes were largely consistent with current recommendations for cancer prevention, however some women were still above the guidelines for total (11%) and saturated fat (39%), and many were below Canada’s Food Guide’s minimum recommendation for vegetables/fruit (61%), and milk/alternatives (≤50y-65%, >50y-91%). Based on the EAR cut-point method, the group prevalence of inadequate calcium and vitamin D intakes from foods was high (47-96%) in this sample and even when supplements were included, intakes below the EAR for calcium and vitamin D were found in 18% and 36% of women, respectively. Many women reported that they had initiated dietary changes while they were in active treatment, while others had waited until the post-treatment period.

Conclusions: Our findings add to a limited number of studies in which dietary changes among breast cancer survivors have been reported. Evidence that some women are willing and able to initiate positive changes in diet early in the treatment trajectory suggests that early intervention may be effective in promoting dietary habits that will assist with weight management and overall health. Data on current dietary habits highlights several possible targets for intervention in this population.
4.2 Introduction

The population of breast cancer survivors in Canada and the U.S. is growing substantially, with more than 250,000 new cases expected each year and significant improvements in survival rates since the mid 1980’s (Canadian Cancer Statistics, 2011; National Cancer Institute, 2011). Many of these women gain weight, both during and after treatment (Vance et al., 2011). Furthermore, with or without weight gain, gains in body fat and loss of lean tissue are prevalent in this population (Rock & Demark-Wahnefried, 2002; Visovsky, 2006). These unfavourable changes in body composition are distressing for many women (Knobf, 1986; Halbert et al., 2008) and may lead to metabolic disturbance (Robinson & Graham, 2004), increased risk of obesity-related disorders (Brown et al., 1993; Wingo et al., 1998) and poorer prognosis (Nichols, 2009; Chen et al., 2010; Thivat et al., 2010). As prevalence increases, the need for dietary counseling and nutrition intervention after diagnosis is expected to grow.

The optimal diet for breast cancer survivors is uncertain at this time, however current evidence suggests that a diet aimed at primary prevention may also improve long-term disease free (World Cancer Research Fund/American Institute for Cancer Research, 2007) and overall survival (Kroenke, Fung, Hu et al., 2005, Kwan, Weltzien, Kushi et al., 2009). Thus a diet that supports a healthy body weight, is low in fat and rich in a variety of fruits and vegetables is currently recommended for women who have undergone treatment for breast cancer (Hauner, Janni, Rack et al., 2011). With these guidelines in mind, understanding dietary habits of women after diagnosis is an important first step in developing intervention strategies. At this time there are very limited data concerning dietary changes made by women after a breast cancer diagnosis, when these changes are initiated and how nutrient intakes in this population compare to current recommendations. The objective of this study was to describe self-reported
changes in diet among breast cancer survivors in the first year after completing chemotherapy treatment, and to evaluate these changes in the context of current dietary intake. These findings may help to identify factors associated with energy imbalance after primary treatment and will provide a preliminary basis on which to develop nutrition guidelines that may guide dietetic counseling and nutrition intervention.

4.3 Participants and Methods

4.3.1 Study Sample

Data for this analysis were collected as part of a more extensive study in which breast cancer survivors participated in qualitative interviews to explore individual experiences of food intake and weight change during chemotherapy. Participants were recruited from the Waterloo, Guelph, Hamilton and London, Ontario regions. Eligibility requirements included female breast cancer survivors >18 y, clinical stage I-IIIA, within 12 months of completing chemotherapy treatment, able to communicate freely in English (oral and written) and capable of providing informed consent.

4.3.2 Procedures

Participants were made aware of the study via a recruitment letter posted at local events (e.g., Canadian Breast Cancer Run for the Cure), businesses and community support programs, as well as online through the Canadian Breast Cancer Network (Bulletin Board/Newsletter) and Dietitians of Canada (Waterloo Region Registered Dietitian’s network). The recruitment letter was also posted in the University of Waterloo’s Well-Fit Centre (group exercise program for cancer patients) and the Grand River Regional Cancer Centre, Kitchener, Ontario and advertisements were placed in several local, community newspapers. Women who were interested in participating were asked to call a local telephone number or to contact the
researcher via email. At this time, they were screened for eligibility and provided with a detailed information letter. Potential participants were contacted by the researcher by telephone or email within one week of initial contact, to review study details and respond to questions. Interviews were scheduled within one-two weeks in the participant’s home or at the University of Waterloo, based on participant preference. Background data were collected via a demographic and medical questionnaire. This research project received ethics clearance through the Office of Research Ethics at the University of Waterloo. All women provided written consent before participating.

**Dietary Changes after Diagnosis**

Changes in diet after diagnosis were assessed using a closed-ended question asking participants to identify changes in the quantity of food intake since the completion of treatment, compared to their normal diet (before diagnosis) and an initial “filter” question asking “since your diagnosis have you made any changes to the kinds of foods you eat?” Women who indicated that they had made changes to their diet were asked to elaborate about specific changes in food groups/dietary components. Nine diet categories, adapted from previous research with breast cancer survivors and grounded in current dietary recommendations for healthy eating (Maunsell et al., 2002; Health Canada, 2007), were evaluated including vegetables and fruit, legumes, meat, fish, dairy products, breads/cereals, desserts, alcohol and supplements. Participants were asked to indicate whether they had “introduced”, “increased”, “decreased” or “eliminated” these items from their diet since their diagnosis. In addition, four items were further explored to determine if there had been a “change in type” including meat, dairy products, breads/cereals and supplements. Based on the work of Maunsell et al. (2002), changes were categorized as positive if intake of vegetables
and fruit, legumes and fish were reported as increased (or introduced) and if intake of meat, desserts and alcohol were reported as decreased (or eliminated). Changes in dairy products and breads/cereals were considered positive if women reported consuming products with a lower fat content or higher fibre content, respectively. Added to this study was one additional positive change, based a “change in type” for meat intake (lower fat content). Changes in dietary supplement use were of interest, however, in the absence of clear evidence (Greenlee, Hershman & Jacobson, 2009) were not classified as positive or negative (Maunsell et al., 2002).

3-Day Food Records

Current dietary intake was assessed using a 3-day food record. Dietary records were chosen as the method of assessment since they do not rely on recall and, compared to other self-report measures (FFQ, 24 hr recalls), they may provide a more precise measure of dietary intake (Block & Hartman, 1989). Two weekdays and one weekend day were included, to control for possible day-of-the-week effects (Trabulsi & Schoeller, 2001). Detailed verbal and written instructions for recording daily food intake and a “sample day” were provided. Participants were encouraged to provide as much detail as possible and to use household measures (teaspoons, measuring cups, scales) and food labels to estimate serving sizes. During the recording period, participants were contacted by telephone or email to see if they had any questions or concerns. Completed records were reviewed with participants, for clarification and completeness.

4.3.3 Data Analysis

Nutrient analysis was conducted using The Food Processor SQL version 10.5.2 (Esha Research, Salem, Oregon), including the current Canadian Nutrient File Database (Health
Servings of vegetables and fruit (total, dark green/orange vegetables) and milk and alternatives were hand calculated, based on servings sizes from Eating Well with Canada’s Food Guide (2007).

Descriptive statistics were used to characterize the sample group and to identify the nature and extent of self-reported changes in diet since diagnosis. Current dietary intakes are presented as means, standard deviations and ranges, and described relative to age and gender specific recommendations (Dietary Reference Intakes, National Academy of Sciences, 2005; Eating Well with Canada’s Food Guide, Health Canada, 2007) and data from the Canadian Community Health Survey (Cycle 2.2, 2004). The Canadian Community Health Survey (CCHS) data are based on multiple pass 24-hr recalls and represent the weighted averages for reported intakes among women in the 31-50 y (n=2686) and 51-70 y (n=3200) age groups. Milk and alternatives, fibre and calcium intakes are presented separately for women ≤ 50 y (n=17) and > 50 y (n=11), to reflect differences in the current dietary recommendations for these age groups. Distributions of nutrient intakes across the sample are provided, including the percentage of women whose intake fell below, within and above current guidelines.

4.4 Results

4.4.1 Sample Characteristics

A total of 28 women were recruited over a 14 month period between Oct, 2010 and Nov, 2011. Mean age was 49.8±8.5 y. Sixty-four percent of participants were married and 79% had a college or university education. Most of the women were diagnosed at clinical stage II or IIIA and 68% were premenopausal at diagnosis. Participants received an average of 5.9±1.9 chemotherapy treatments, over a period of 15±4 weeks. The mean time from the completion of treatment was 6.4±4.4 months. Sample characteristics are summarized in Table 4.1.
Table 4.1: Demographic, Clinical and Treatment Characteristics of the Participants

<table>
<thead>
<tr>
<th>Characteristic (n=28)</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>49.8±8.5</td>
<td>33-69</td>
<td>25 (89%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td>25 (89%)</td>
</tr>
<tr>
<td>Black, Asian, West Asian</td>
<td></td>
<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td>18 (64%)</td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
<td>4 (14%)</td>
</tr>
<tr>
<td>Single</td>
<td></td>
<td></td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Divorced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Completed</td>
<td></td>
<td></td>
<td>6 (21%)</td>
</tr>
<tr>
<td>High School</td>
<td></td>
<td></td>
<td>7 (25%)</td>
</tr>
<tr>
<td>College</td>
<td></td>
<td></td>
<td>15 (54%)</td>
</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment Status</td>
<td></td>
<td></td>
<td>10 (36%)</td>
</tr>
<tr>
<td>Employed</td>
<td></td>
<td></td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Leave of Absence</td>
<td></td>
<td></td>
<td>11 (39%)</td>
</tr>
<tr>
<td>Unemployed/Retired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
<td>15 (53%)</td>
</tr>
<tr>
<td>IIIA</td>
<td></td>
<td></td>
<td>10 (36%)</td>
</tr>
<tr>
<td>Menopause Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td></td>
<td></td>
<td>19 (68%)</td>
</tr>
<tr>
<td>(at diagnosis)</td>
<td></td>
<td></td>
<td>9 (32%)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumpectomy</td>
<td></td>
<td></td>
<td>15 (54%)</td>
</tr>
<tr>
<td>Mastectomy</td>
<td></td>
<td></td>
<td>13 (46%)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Cycles</td>
<td>5.9 (1.9)</td>
<td>2-8</td>
<td></td>
</tr>
<tr>
<td>Duration of Treatment (weeks)</td>
<td>15 (4.0)</td>
<td>4-24</td>
<td></td>
</tr>
<tr>
<td>* Time from Treatment (months)</td>
<td>6.4 (4.4)</td>
<td>0.5-13</td>
<td></td>
</tr>
<tr>
<td>Radiation Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
<td>16 (57%)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>5 (18%)</td>
</tr>
<tr>
<td>Planned</td>
<td></td>
<td></td>
<td>7 (25%)</td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>17 (61%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aromatase Inhibitor</td>
<td>5 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6 (21%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* completed

4.4.2 Dietary Changes after Diagnosis

Twenty-four women (86%) reported that they had made changes to their diet since diagnosis, the majority of which were categorized as positive. The most common change was an increase in vegetables and fruit (75%), followed by a decrease in overall meat consumption or a change to lower fat options (decreased red meat, increased chicken, 57.1%), increased intake of fish (46.4%) and reduced alcohol intake (39.3%). Reports of negative dietary changes were minimal in this sample, most common among them being an increase in desserts (14.3%).
Among women reporting any dietary change, the mean number of positive changes was 3.88±1.4 (range = 0-6).

Many women reported that they had initiated these changes while they were in active treatment (n=10, 36%), while others (n=14, 50%) had waited until the post-treatment period. Among the latter group, most women reported that trying to make changes in their diet earlier in the treatment trajectory was challenged by the stress of their cancer diagnosis and the side effects of treatment.

Supplement changes were reported by 61% of women. Most common was the addition of calcium and/or vitamin D (32%) and removal of multi-vitamins or single antioxidant nutrients (18%). Dietary changes after diagnosis are summarized in Table 4.2.

Table 4.2: Self-reported Changes in Diet after a Diagnosis of Breast Cancer.

<table>
<thead>
<tr>
<th>Change Type</th>
<th>n=28</th>
<th>Yes</th>
<th>No</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported any Dietary Change</td>
<td>28</td>
<td>24 (85.7)</td>
<td>4 (14.3)</td>
<td>21 (75.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vegetables &amp; Fruit</td>
<td>28</td>
<td>21 (75.0)</td>
<td>7 (25.0)</td>
<td>21 (75.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Legumes</td>
<td>28</td>
<td>7 (25.0)</td>
<td>21 (75.0)</td>
<td>7 (25.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Meat</td>
<td>28</td>
<td>17 (60.7)</td>
<td>11 (39.3)</td>
<td>16 (57.1)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Fish</td>
<td>28</td>
<td>13 (46.4)</td>
<td>15 (53.6)</td>
<td>13 (46.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dairy</td>
<td>28</td>
<td>8 (28.6)</td>
<td>20 (71.4)</td>
<td>7 (25)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Breads/Cereals</td>
<td>28</td>
<td>10 (35.7)</td>
<td>18 (64.3)</td>
<td>9 (32.1)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Desserts</td>
<td>28</td>
<td>13 (46.4)</td>
<td>15 (53.6)</td>
<td>9 (32.1)</td>
<td>4 (14.3)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>28</td>
<td>11 (39.3)</td>
<td>17 (60.7)</td>
<td>11 (39.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Supplements</td>
<td>28</td>
<td>17 (60.7)</td>
<td>11 (39.3)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

In response to the standardized question “since the completion of treatment, compared to your normal diet before diagnosis, do you feel you have been eating: the same amount as you would usually eat, more than you would usually eat or less than you would usually eat?”, 53% of women (n=15) reported that they had been eating less, while 36% (n=10) and 11% (n=3) felt they had eaten the same amount or more than they would usually eat, respectively. For many women, food intake at the time of interview (mean = 6.4±4.4 months from the completion of
treatment) reflected a receding of symptoms and a return to normal eating patterns, in terms of
the overall quantity. Two of the women who reported that they were eating more felt that they
had been eating lighter and healthier immediately after treatment but as time passed they were
eating more and had become less diligent about making healthy choices. Eating less was
related to one of two underlying themes. About half of the women who felt they were eating
less (n=7), reported that their appetite had not yet returned to normal and they were still
experiencing early satiety with small portions of food. Others (n=8) were actively engaged in
weight management and were consciously reducing food intake in an effort to lose weight after
treatment. Self-reported change in quantity of food intake was not associated with weight
change since the completion of treatment.

4.4.3 Current Dietary Intake

Current dietary intake based on the mean daily values from 3-day food records are
summarized in Table 4.3, relative to national data from the CCHS (Cycle 2.2, 2004) and age
and gender specific recommended intakes.

The mean energy intake for the sample was 1883±359 kcals, with protein, carbohydrates
and fat providing 17.9%, 52.2% and 28.5% of energy, respectively. Mean intakes for
macronutrients fell within the Acceptable Macronutrient Distribution Ranges (AMDR) and
saturated fat intake (8.9±2.8%) was, on average, below the current recommendation (<10%)
(American Dietetic Association / Dietitians of Canada, 2007). Mean fibre intake was above the
adequate intake (AI) for women ≤ 50 y (25.6±12.3 vs. 25 g) and > 50 y (28.4±8.9 vs. 21 g).

Vegetable and fruit servings (6.0±3.1) were below the minimum recommendation (7/day),
based on Canada’s Food Guide to Healthy Eating (2007). The mean intake of milk and
alternatives (servings/day) for women ≤ 50 y (1.4±0.9) and > 50 y (1.9±0.8) were below
recommendations for both age groups. Mean calcium intakes from foods among women ≤ 50 y (813±299 mg) and >50y (1032±294 mg) were also below current recommendations (1000 mg and 1200 mg, respectively). Mean vitamin D intake from foods was 4.7±3.0 ug (185±121 IU) across all participants; well below the recommendation for women in this age group (15ug).

Calcium and vitamin D supplement use was common in this sample of breast cancer survivors (n=15, 54%). When supplement use was considered in the calculation of total intake of these nutrients, mean calcium intakes from food and supplements among women ≤ 50 y (1224±476.7 mg) and >50y (1613±586 mg) were above the current recommendation for both age groups. Similarly, mean vitamin D intake from food and supplements combined (18.7 ug) exceeded the recommended intake for adult women.

Statistical comparisons are not possible, however compared to women of similar age from the general population (CCHS, 2004), it appears that the mean energy intake in this sample may be a little higher (1883 vs. 1767 kcals), while the percent energy derived from total fat (28.5 vs. 31.7%) and saturated fat (8.9 vs. 10.2%) may be slightly lower. Vegetable and fruit intake in this sample (6.0 servings/day) was, on average, a little higher than vegetable and fruit intake reported in the CCHS (5.1 servings/day). Mean fibre intake appears to be higher in the current study (26.7 vs. 16.7 g).

Average intake of milk and alternatives was consistent with the CCHS data for women ≤ 50 y (1.4 vs. 1.5 servings/day), however women > 50y reported a mean of 1.9 servings compared to 1.3 servings in the CCHS. This apparent difference is reflected in the mean calcium intake from foods, which appears to be higher among women >50 y in this sample (1032 mg), compared to women in the same age range from the CCHS (740 mg). The mean vitamin D intake from foods in the current sample (4.7 ug) was similar to the mean intake
among women in the CCHS (5.1 ug). Current dietary intakes relative to the CCHS data and age and gender specific recommended intakes are summarized in table 4.3.

Table 4.3: Current Dietary Intake Relative to the CCHS (2004) and Age/Gender Specific Recommended Intakes

<table>
<thead>
<tr>
<th>Dietary Intake *</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>CCHS Mean</th>
<th>Recommended Intakes a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcals)</td>
<td>1883 (359)</td>
<td>933-2553</td>
<td>1767</td>
<td>1677-2674 b</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>85.9 (18.7)</td>
<td>30.6-137.8</td>
<td>73.8</td>
<td>10-35</td>
</tr>
<tr>
<td>% energy</td>
<td>17.9 (3.4)</td>
<td>12.1-28.3</td>
<td>16.8</td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>251.6 (64.4)</td>
<td>148.1-422.9</td>
<td>217.4</td>
<td>45-65</td>
</tr>
<tr>
<td>% energy</td>
<td>52.2 (7.7)</td>
<td>36.7-68.8</td>
<td>49.1</td>
<td></td>
</tr>
<tr>
<td>Total Fat (g)</td>
<td>61.3 (16.2)</td>
<td>19.4-91.6</td>
<td>65.2</td>
<td>20-35</td>
</tr>
<tr>
<td>% energy</td>
<td>28.5 (5.6)</td>
<td>18.4-40.8</td>
<td>31.7</td>
<td></td>
</tr>
<tr>
<td>Saturated fat (% energy)</td>
<td>8.9 (2.8)</td>
<td>3.7-13.6</td>
<td>10.2</td>
<td>&lt;10 c</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>26.7 (10.9)</td>
<td>7.4-46.6</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td>≤50 y **</td>
<td>25.6 (12.3)</td>
<td>7.4-46.6</td>
<td>15.7</td>
<td>25</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td>28.4 (8.9)</td>
<td>13.6-42.1</td>
<td>16.6</td>
<td>21</td>
</tr>
<tr>
<td>Vegetables</td>
<td>3.3 (2.3)</td>
<td>0.2-9.5</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td>(servings/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dark Green</td>
<td>1.1 (0.87)</td>
<td>0.0-3.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orange</td>
<td>0.6 (0.6)</td>
<td>0.0-2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>2.7 (1.5)</td>
<td>0.8-6.6</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td>(servings/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables &amp; Fruit</td>
<td>6.0 (3.1)</td>
<td>1.2-15.0</td>
<td>5.1</td>
<td>7-8</td>
</tr>
<tr>
<td>(servings/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk/Alt.</td>
<td>1.6 (0.9)</td>
<td>0.0-2.9</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>(servings/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>1.4 (0.9)</td>
<td>0.0-2.8</td>
<td>1.5</td>
<td>2</td>
</tr>
<tr>
<td>≤50 y</td>
<td>1.9 (0.8)</td>
<td>0.7-2.9</td>
<td>1.3</td>
<td>3</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foods</td>
<td>899 (311)</td>
<td>264-1577</td>
<td>780</td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>813 (299)</td>
<td>264-1577</td>
<td>827</td>
<td>1000</td>
</tr>
<tr>
<td>≤50 y</td>
<td>1032 (294)</td>
<td>520-1437</td>
<td>740</td>
<td>1200</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foods + Supplements</td>
<td>1350 (537)</td>
<td>(496-2270)</td>
<td>1000</td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>1224 (477)</td>
<td>(496-2144)</td>
<td></td>
<td>1200</td>
</tr>
<tr>
<td>≤50 y</td>
<td>1614 (587)</td>
<td>(878-2270)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D (ug / IU)</td>
<td>5 (3) / 185 (121)</td>
<td>1-12 / 40-492</td>
<td>5 / 185</td>
<td>15 / 600</td>
</tr>
<tr>
<td>Foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foods + Supplements</td>
<td>19 (16) / 745 (620)</td>
<td>1-62 / 40-2492</td>
<td>5 / 185</td>
<td>15 / 600</td>
</tr>
</tbody>
</table>

* Based on the mean daily intake from 3-day food records  ** ≤50 y (n=17), >50 y (n=11)

a Dietary Reference Intakes, Eating Well with Canada’s Food Guide, b Range of estimated energy requirement for the sample (Esha Research, Salem, Oregon); c American Dietetic Association/ Dietitians of Canada Position Statement, 2007.

Figures 4.1-4.3 show the percentage of women whose intake of protein, carbohydrate and total fat (% energy) fell below, within and above the AMDR ranges (Health Canada, 2006).
Protein intake was within the AMDR for all women and most women (79%) were within the acceptable range for carbohydrates. Similarly, most women were within the recommendation for total fat, with 10% of women below and 11% above the AMDR. These findings are consistent with the CCHS data for protein, however a larger proportion of women from the national survey were below the AMDR for carbohydrates (25.3%) and above the AMDR for total fat (25.4%).

Figure 4.1 Distribution of Protein Intake (% energy) Relative to the AMDR (n=28)

Figure 4.2 Distribution of Carbohydrate Intake (% energy) Relative to the AMDR (n=28)
Figure 4.3 Distribution of Total Fat Intake (% energy) Relative to the AMDR (n=28)

Figure 4.4 shows that 61% and 39% were below and above the <10% guideline respectively, for saturated fat intake as a percentage of total energy.

Figure 4.4 Distribution of Saturated Fat Intake (% energy) (n=28)

In the absence of an estimated average requirement (EAR) for dietary fibre, it is not possible to determine the prevalence of inadequate intake. However, the median intake (27.1 g) for the sample (data not shown) was above the AI for both age groups, suggesting that the prevalence of inadequate intakes in this group of women is low (Health Canada, 2006).
Furthermore, since the Canadian Nutrient File does not contain data on functional fibre (Health Canada, 2009), the current analysis reflects naturally occurring fibre only and may therefore represent an underestimate of actual fibre intake.

Figures 4.5-4.7 show the distribution of vegetables and fruit, dark green vegetable and orange vegetable intake. Many women (61%) did not meet the minimum recommendation for total vegetables and fruit (7 servings/day), with 36% and 79%, respectively not meeting Health Canada’s recommendation (2007) to eat at least one dark green and one orange vegetable each day. Twenty-three percent of women in this sample reported less than five total vegetable and fruit servings per day, compared to almost 50% of women in the CCHS.

**Figure 4.5 Distribution of Total Vegetable and Fruit Intake (n=28)**

**Figure 4.6 Distribution of Dark Green Vegetable Intake (n=28)**
Figure 4.8 shows the distribution of milk and alternative intakes for women ≤ 50 y (n=17) and >50 y (n=11), relative to the recommended servings per day, based on Eating Well with Canada’s Food Guide. Sixty-five percent of women ≤ 50 y did not meet the recommended number of servings (2/day), while 91% of women > 50 y reported less than the recommended number of servings for their age group (3/day). These findings are similar to data from the CCHS, in which 72 and 80% of women respectively, were below minimum recommendations.

* Current recommendation ≤ 50 y = 2 servings/day, >50 y = 3 servings/day
Figure 4.9 shows the distribution of calcium intakes from foods relative to the Dietary Reference Intakes for women ≤ 50 y and > 50 y. Based on the EAR cut-point method (Health Canada, 2006), the prevalence of inadequate calcium intake from foods alone was high in this sample, with 47% of women ≤ 50 y and 55% of women > 50 y below the EAR for their age group (800 and 1000 mg, respectively). Figure 4.10 shows the distribution of total calcium intake from foods and supplements. The prevalence of inadequate intake based on combined intake from food and supplements, drops to 18% among women in both age categories.

**Figure 4.9 Distribution of Calcium Intakes from Foods (n=28) **

* EAR cut-point ≤ 50 y = 800 mg, >50 = 1000 mg

**Figure 4.10 Distribution of Calcium Intakes from Foods and Supplements (n=28) **
Figures 4.11 and 4.12 show the distribution of vitamin D intakes, with and without supplements. Vitamin D intake from foods alone was low across the sample group, with 96% of women below the EAR cut-point for adult women (10ug). The prevalence of inadequate intake based on combined intake from food and supplements was 36%. It is important to keep in mind that vitamin D status is influenced by sun exposure as well, although less so in the Canadian climate during the winter months (Health Canada, 2007). The DRIs for vitamin D were established assuming minimal sun exposure (National Academy of Sciences, 2010).

**Figure 4.11 Distribution of Vitamin D Intakes from Foods (n=28) ***

![Figure 4.11](image)

* EAR cut-point = 10 ug

**Figure 4.12 Distribution of Vitamin D Intakes from Foods and Supplements (n=28)**

![Figure 4.12](image)
4.5 Discussion

This study describes both self-reported changes in diet among early stage breast cancer survivors after diagnosis and current dietary intake, within the first year of completing chemotherapy treatment. The majority of women in this sample reported that they had made changes to their diet after their breast cancer diagnosis. Most of the changes reported were consistent with current guidelines for cancer prevention, including an increase in vegetable and fruit intake, decreased meat consumption, increased fish intake and reduced alcohol intake. Negative changes were minimal, including an increase in desserts for a small proportion of women. Compared to their normal diet before diagnosis, 53% of women reported that they had been eating less since the completion of treatment, reflecting residual treatment effects (low appetite) in half of these women and weight loss efforts after treatment in others.

Based on 3-day food records, protein, carbohydrate and total fat intakes were within the AMDR for most women and 61% of women were below the recommendation for saturated fat intake. Median fibre intake was above the AI for women ≤ 50 y and > 50 y, suggesting low prevalence of inadequate intakes in this sample. Although 75% of women reported an increase in vegetable and fruit intake, 61% did not meet the minimum recommendation for total vegetables and fruit and many did not meet the minimum recommendation to include at least one dark green and one orange vegetable each day. Two-thirds of women ≤ 50 y and most women > 50 y did not meet the recommended number of milk and alternative servings for their age group. The prevalence of inadequate calcium and vitamin D intake from foods was high across the sample, but were substantially lower when total calcium and vitamin D intakes from food and supplements were considered.
Compared to the most recent national survey data (CCHS, 2004), mean energy, fibre and vegetable and fruit intake appear to be a higher in this sample, while total and saturated fat, as a percentage of total energy, are slightly lower. These findings appear to reflect awareness of current public health messages around healthy eating for breast cancer survivors (Canadian Breast Cancer Foundation, 2012, Canadian Cancer Society, 2012a). While these professional associations acknowledge the uncertainty concerning specific foods or dietary components on breast cancer risk, both suggest that increasing intake of vegetables and fruit and maintaining a healthy body weight may reduce the risk of breast cancer recurrence. These recommendations are consistent with key messages from the much publicized American Institute of Cancer Research/World Cancer Research Fund report (2007), which may also have caught the attention of breast cancer survivors in recent years. Among women > 50 y, the mean milk and alternative, calcium and vitamin D intakes were higher than those reported by women of similar age in the CCHS. Again, many women in the current study seemed to be aware of the importance of adequate calcium and vitamin D for bone health, especially after menopause (National Institutes of Health, 2011). Fifty-four percent of women were taking supplemental sources of these nutrients at the time of interview, with 32% introducing regular use of these supplements since their diagnosis.

Comparisons to previous findings in women with breast cancer are challenged by the limited number of studies in which dietary changes among breast cancer survivors have been reported, as well as differences in dietary assessment methods and timing of the measures relative to diagnosis. Energy intake derived from 3-day food records in the current study is higher than previous reports in this population. Based on a 114 item FFQ, mean energy intake was estimated at 1356-1458 kcals, in two large prospective cohorts (Health, Eating, Activity
and Lifestyle (HEAL) and Life After Cancer Epidemiology (LACE) studies) of breast cancer survivors (stage 0-IIIA), approximately two years after diagnosis (Wayne, Lopez, Butler et al., 2004; Caan et al., 2005). At a similar time point, based on repeated 24-hr recalls, baseline data from the Women’s Healthy Eating and Living (WHEL) study (Pierce, Natarajan, Caan et al., 2007) (n=3088, stage I-IIIA) revealed a mean energy intake of 1718 kcals; energy intake that is similar to mean kcals reported by the Women’s Intervention Nutrition (WINS) study (n=2437, stage I-IIIA) (Chlebowski, Blackburn, Thomson et al., 2006).

Mean protein intake as a percentage of total energy (17.9%) is similar to that reported in the HEAL and LACE studies (16.9-17.1%), while the amount of energy derived from carbohydrates is a little higher in the current study (52.2% vs. 47.4-48.6%). Total fat intake (28.5%) is consistent with data from the WHEL and WINS studies (28.5-29.6%), but lower than estimates from the HEAL and LACE cohorts (33.8-35.5%). Mean fibre intake (26.7 g) was high compared to WHEL (21.2 g) and LACE (15.2 g). Finally, total servings of vegetable and fruit per day was lower in the current study (6.0) compared to WHEL (7.2-7.4) but higher than those reported in LACE and HEAL (3.6-4.1).

Current dietary intake in this sample seems to be more closely aligned with baseline data from the WINS and WHEL intervention trials, suggesting that the precision of the instruments (food records and 24-hr recalls vs. FFQ) may explain some of the apparent differences that were observed. Key demographic and clinical characteristics were similar across studies (ethnicity, education, clinical stage, baseline BMI), however participants in the current study and the WHEL study were, on average, a little younger compared to the HEAL, LACE and WINS cohorts, which may help account for differences in dietary data across studies.
Overall, the women participating in the current study seemed to be quite health conscious, eager to adopt or maintain lifestyle behaviours that might influence disease recurrence and overall health. This is supported by lower fat intake, higher fibre intake and higher mean vegetable and fruit servings compared to women in the same age range from the general population. Furthermore, the nature of dietary changes reported in the current study are similar to those reported in previous studies among breast cancer survivors, however the proportion of women reporting dietary changes after diagnosis is higher in this sample.

Maunsell et al. (2002) described self-reported dietary changes in 250 women with newly diagnosed, non-metastatic breast cancer. In this study, 41% of women reported that they had initiated dietary changes in the first year after diagnosis, most common being an increase in vegetable and fruit intake and a decrease in meat and desserts. Similarly, in response to global interview questions on dietary habits, Wayne et al., (2004) found that 39% of women diagnosed with stage 0-IIIA disease (n=260) reported an increase in vegetable and fruit intake after diagnosis, while 45% reported a decrease in dietary fat. Self-reported changes in this study were consistent with data derived from FFQs one year before and two years after diagnosis, however the amount of change estimated by FFQ was small (<0.5 servings), with 76% of women still eating less than five servings of vegetable and fruits per day (Wayne et al., 2004). Thomson et al., (2002) asked women recruited to the WHEL study to indicate via questionnaire whether they had increased or decreased their intake of several foods after diagnosis. In this sample of early stage breast cancer survivors (n=3084), the most frequently reported change was an increase in vegetables and fruit (60% and 58%, respectively) followed by a decrease in red meat, cheese and other high fat foods (38-61%) and an increase in whole grains (39%) and fish (38%). Self-reported changes were consistent with baseline dietary data,
with an overall more healthful diet apparent among women reporting these dietary changes after diagnosis (Thomson et al., 2002).

This research adds to a limited number of studies reporting dietary change in breast cancer survivors and to the author’s knowledge is the first to report dietary change, in the context of dietary intake in the first 12 months after diagnosis. These findings address an important gap in the literature, since understanding dietary habits of women after breast cancer treatment is a critical first step in developing effective intervention strategies (Thomson et al., 2002). A few studies have evaluated dietary change and/or dietary intake within two to four years of diagnosis (Thomson et al., 2002; Wayne et al., 2004, Caan et al., 2005). While these studies have provided important insights, it is possible that dietary assessments in this time frame may miss changes that are made earlier, and may or may not endure up to four years after diagnosis.

Of particular interest was the finding that many women reported having initiated positive changes in diet during active treatment. It has been suggested in the literature, and supported by the current study, that some women may need time to recover from the turmoil of a cancer diagnosis and its treatment before they are ready for dietary change (Thomson et al., 2002). Our results demonstrate however, that some women may be willing and able to implement positive changes earlier in the treatment trajectory. These women reported some challenges in making these changes during treatment, however appeared to have supports in place (e.g. cooking, social support) to motivate and reinforce their efforts. This has important implications for dietary counseling, suggesting that early intervention may be effective in promoting dietary habits that will assist with weight management and overall health.

There is some evidence to suggest that a diagnosis of breast cancer may represent a “teachable moment”, in which women are highly motivated to make lifestyle changes that will
promote long-term disease free survival and overall wellness (Demark-Wahnefried, Peterson, McBride et al., 2000; McBride, Clipp, Peterson et al., 2000). It appears that many women report positive changes in diet that may support weight management, disease remission and overall health (Kroenke et al., 2005; Rock, Natarajan, Pu et al., 2009; Kwan et al., 2009; Hauner et al., 2011). The amount of change however, is modest (Wayne et al., 2004), with many women still below current recommendations for vegetables, fruit and fibre and above the guidelines for dietary fat (Wayne et al., 2004; Caan et al., 2005; Pierce et al., 2007). Moreover, our findings of high prevalence of inadequate calcium and vitamin D intakes from foods alone highlight the need for dietary counseling around food and supplemental sources of these nutrients. This is especially important among women who have undergone treatment for breast cancer, given that many of these women are postmenopausal at diagnosis (Canadian Cancer Statistics, 2012), and many others are expected to become menopausal as a result of treatment (Canadian Breast Cancer Foundation, 2012). Treatment-induced menopause could not be evaluated in this study (length of time from treatment <12 months), however with the Recommended Dietary Allowance linked to loss of calcium from bones at menopause, it is likely that the dietary recommendation for calcium for women \( \leq 50 \text{ y} \) (1000mg) would increase to those of women \( > 50 \text{ y} \) (1200 mg), within the first few months of treatment. While “best practice” dietary guidelines after a breast cancer diagnosis are not yet known, these findings suggest possible targets for dietary intervention in this population.

This study has some limitations. First, the survey used to evaluate self-reported changes in diet is not a validated research instrument. It is noteworthy however, that data on dietary changes appear to be consistent with current dietary intake, with a high proportion of women reporting an increase in vegetables and fruit for example, reflected in relatively high intake of
vegetable and fruit servings, compared to national survey data. Moreover, earlier studies have reported good concordance between self-reported changes in diet and dietary changes captured by FFQ before and after diagnosis (Wayne et al., 2004) and current dietary intake assessed by repeated 24-hr recalls (Thomson et al., 2002). This survey has been used with breast cancer survivors (Maunsell et al., 2002), thus affording the opportunity to provide direct comparisons.

We did not quantify dietary change in this study, however self-reported changes were evaluated in the context of current dietary intake estimated from 3-day food records; an important link in understanding how these changes impact on the overall quality of the diet. In addition, we did not have baseline dietary data, which may have influenced the perception of dietary change data. For example, 39% of women reported a reduction in alcohol intake, however many others reported that they had consumed little or no alcohol before diagnosis and reported no change in alcohol consumption since their diagnosis. Once again, a precise measure of current dietary intake provided context for dietary change data.

It is possible that self-reported dietary change and dietary intake were subject to the well documented limitations of social expectation bias and under-reporting (Hill & Davies, 2001, Caan et al., 2000). Energy intake in this sample however, was higher than previous reports in breast cancer survivors and women of similar age from the general population, suggesting that social desirability and under-reporting may be less pronounced in this study. Two weekdays and one weekend day were included in each 3-day record, to control for possible day-of-the-week effects, but it is possible that seasonal variation in eating patterns may have influenced dietary intake. Data collection took place over a 14 month period however, with diet records equally dispersed across the summer and winter seasons, suggesting that seasonal variation likely did not have a significant impact on the data.
Lastly, dietary data in the current study may be associated with a self-selection bias, reflecting systematic differences in the type of women who might choose to participate in a study of this nature, and may not be representative of the population of breast cancer survivors. The age distribution of women in this sample appears to be a little younger than the distribution of Canadian women who are diagnosed with breast cancer (Canadian Cancer Statistics, 2012). This may have had an impact on generalizability of our results, since there is some evidence to suggest that younger women are more likely to make dietary changes after a diagnosis of breast cancer (Thomson et al., 2002; Wayne et al., 2004). Although many of the women who volunteered for this study appeared to have a strong interest in healthy eating and exercise, this is consistent with other studies in which breast cancer survivors are described as highly motivated to make positive changes in lifestyle. The study sample was part of a larger study, in which women were participating in qualitative interviews. In keeping with the in-depth nature of qualitative analysis, the sample size was relatively small.

In summary, the majority of women in this sample of early stage breast cancer survivors reported positive changes in diet since their diagnosis. Dietary changes were largely consistent with current recommendations for cancer prevention, however some women were still above the recommendations for dietary fat and many were below the minimum recommendation for vegetables and fruit, and milk and alternatives. The prevalence of inadequate calcium and vitamin D intakes from foods was high in the sample. Our findings add to a limited number of studies in which dietary changes among breast cancer survivors have been reported in the context of current dietary intake and may serve to guide dietetic practice and nutrition intervention in this population (see Chapter 6).
CHAPTER 5: FOREWARD

Chapter 5 presents the findings from study 2 (objectives 1, 2 and 5) and is focused on physical and psychological distress (past week), current dietary intake, changes in diet after diagnosis, and weight change since the completion of chemotherapy treatment. The data for this chapter, with the exception of current dietary intake, were collected in conjunction with the qualitative interviews for study 1.
CHAPTER 5: Weight Change, Physical Distress, Psychological Distress and Food Intake among Early Stage Breast Cancer Survivors.

The work presented in this chapter will be submitted to the European Journal of Cancer Care:

Vance V, Campbell S, McCargar L, Mourtzakis M and Hanning R. Persistent Treatment Effects, Food Intake and Weight Gain among Early Stage Breast Cancer Survivors.

5.1 Overview

Objectives: The purpose of this study was to describe weight change; symptoms of physical distress, psychological distress and fatigue; diet and dietary change in early stage breast cancer survivors within 12 months of completing chemotherapy. Relationships among weight change since the completion of treatment and composite scores for physical and psychological distress, fatigue, current dietary intake and changes in diet since diagnosis were investigated.

Methods: Symptoms of physical distress, psychological distress and fatigue (past week) were assessed in 28 early stage breast cancer survivors, using the Rotterdam Symptom Checklist (RSCL), the Distress Thermometer (DT) and the Fatigue Symptom Inventory (FSI). Current dietary intake was estimated from 3-day food records. Changes in diet were assessed using a self-reported survey in which women identified whether they had introduced, increased, decreased or eliminated foods/food groups since their diagnosis. Weight at the end of treatment was based on self-report. Current weight was measured at the time of interview.

Results: Weight change since the completion of treatment (mean=6.4±4.4 months) ranged from -6.0 kg to +5.2 kg (mean=-0.4±3.2). Among women who gained >2.0 kg (n=6), the mean weight gain was 3.5 kg. Psychological distress scores ranged from a low of 0 to a high of 76.1, out of 100 (mean=27.1±16.9) and were higher than physical distress scores (17.5±9.0, p<0.01). The DT rated the distress level as moderate to severe (≥4, scale=0-10) in 35% of women, according to guidelines from the National Comprehensive Cancer Network. Fatigue intensity was rated from 0 to 7.5 out of 10 (mean=3.5±2.2), was experienced from 0 to 7 days in the previous week (mean=4.5±2.6) and was present for 0 to 50% (mean=28±16%) of the daytime. The level of interference associated with fatigue ranged from 0 to 7, out of 10 (mean=2.4±2.0). The mean energy intake for the sample was 1883±359 kcals/day. Most women (84%) reported dietary changes since diagnosis, most common being an increase in vegetable and fruit intake. Fatigue duration (proportion of daytime) was negatively correlated with weight change (p=-0.46, p<0.05). No associations were observed between dietary factors and weight change during this time frame. Although symptoms were highly variable, the mean levels of physical and psychological distress in this sample were similar to previous reports among early stage breast cancer patients in active treatment and appear to be markedly higher than previous reports of distress among cancer-free adults. Despite relatively high levels of fatigue, 71% of women described their quality of life in the past week as “good” or “excellent”.

Conclusions: Symptoms of physical and psychological distress seem to persist for many breast cancer survivors in the first year after completing chemotherapy and may associate with weight change. These findings may serve to guide dietary counseling within a growing population of breast cancer survivors and to aid in the development of effective nutrition interventions.
5.2 Introduction

Weight gain and unfavourable changes in body composition, including fat gain and loss of lean tissue, are common among a growing population of breast cancer survivors (Canadian Cancer Statistics, 2011; National Cancer Institute, 2011). These changes have been well documented during chemotherapy treatment (see review, Vance et al., 2011), however weight gain is also known to be a progressive and persistent problem for many women in the months and years after diagnosis (Demark-Wahnefried et al., 1997b; Irwin et al., 2005; Makari-Judson et al., 2007). Excessive weight gain, especially an increase in relative adiposity, predisposes breast cancer survivors to obesity-related disorders including cardiovascular disease and type II diabetes (Brown et al., 1993; Wingo et al., 1998) and may increase the risk of disease recurrence (Nichols et al., 2009; Chen et al., 2010; Thivat et al., 2010). Loss of lean tissue might further exacerbate the problem of weight gain and combined with gains in adipose tissue may lead to adverse metabolic consequences (Robinson & Graham, 2004), decreased strength and functional impairment (Prado et al., 2008). Furthermore, weight gain after diagnosis is distressing for many breast cancer survivors and may contribute to poor quality of life and loss of self-esteem, especially among women who were not overweight before diagnosis (Knobf, 1986; Halbert et al., 2008).

The role of diet in promoting these changes is not yet clear, however it as been suggested that behavioural changes affecting energy balance, likely influenced by fatigue and psychosocial factors, may play an important etiologic role (Demark-Wahnefried et al., 1993; Rock et al., 1999). At this time, little is known about the potential influence of treatment-related side effects, many of which may persist beyond the period of chemotherapy treatment (Canadian Breast Cancer Foundation, 2012b), on diet and weight gain after treatment.
The purpose of this study was to describe 1) weight change 2) symptoms of physical distress, psychological distress and fatigue 3) diet and dietary change in early stage breast cancer survivors within 12 months of completing chemotherapy. Relationships among weight change since the completion of treatment and composite scores for physical and psychological distress, fatigue, current dietary intake and changes in diet since diagnosis were investigated.

5.3 Participants and Methods

5.3.1 Study Sample

The women in this sample group were participants in a qualitative study designed to explore individual experiences of food intake and weight change during chemotherapy. At the time of the qualitative interview, women provided survey data and 3-day food records to be used in the current analysis. Participants were recruited from the Waterloo, Guelph, Hamilton and London, Ontario regions. Eligibility requirements included female breast cancer survivors >18 y, clinical stage I-IIIA, within 12 months of completing chemotherapy treatment, able to communicate freely in English (oral and written) and capable of providing informed consent.

5.3.2 Procedures

Participants were made aware of the study by posting a recruitment letter at local events (e.g., Canadian Breast Cancer Run for the Cure), businesses and community support programs, as well as online through the Waterloo Region Registered Dietitian’s network and the Canadian Breast Cancer Network (Bulletin Board and Newsletter). The recruitment letter was also posted at the Grand River Regional Cancer Centre, Kitchener, Ontario and the University of Waterloo’s Well-Fit Centre (group exercise program for cancer patients) and advertisements were placed in several local, community newspapers.
Those who were interested in participating were asked to call a local telephone number or to contact the researcher via email, at which time they were screened for eligibility and provided with a detailed information letter. These women were contacted by the researcher by telephone or email within one week of initial contact, to review study details and respond to questions. Interviews were scheduled within the next two weeks in the participant’s home or at the University of Waterloo, based on participant preference. This research project received ethics clearance through the Office of Research Ethics at the University of Waterloo. All women provided written consent before participating.

**Measures**

A demographic and medical questionnaire was completed with the researcher, to collect background data on age, marital status, education and employment status, medical and treatment information and weight history. Current weight was measured on the same portable scale (Tanita, BF680, Arlington Heights, Illinois), calibrated against a standard platform balance scale, with participants wearing one light layer of clothing and no shoes. Participants were also asked to self-report their weight at the end of treatment and their current weight. In the event of uncertainty regarding medical or treatment information, participants referred to official medical documents in their possession or consulted with their medical oncologist.

Symptoms of physical and psychological distress were assessed using the Rotterdam Symptom Checklist (RSCL); a multidimensional tool which has been used and validated in breast cancer survivors (deHaes et al., 1996). The RSCL provides sub-scales for physical distress, psychological distress and global quality of life (QOL). Using this tool, participants were asked to indicate the extent to which they have been bothered by a series of common symptoms (e.g., lack of appetite, tiredness, worrying, depressed mood) in the past week.
Symptoms of physical and psychological distress were interspersed, with responses ranging from 1 (not at all) to 4 (very much). A single global QOL item asked the participants to respond to the question “all things considered, how would you describe your quality of life during the past week?”. This item was scored on a 7 point scale ranging from 1 (excellent) to 7 (extremely poor). The sums of physical and psychological symptom scores were calculated to provide a summary estimate (composite score) of overall physical and psychological distress, respectively. All raw scores (physical distress, psychological distress, global QOL) were transformed ([raw score – minimum raw score / maximum – minimum score] X 100) to provide a standardized score on a 100 point scale for each domain (Appendix J). This transformation adjusts for differences in the number of items for each sub-scale and allows for comparisons of the level of impairment across domains (deHaes et al., 1996). Lower scores imply better functioning or well-being.

Participants also completed the Distress Thermometer (National Comprehensive Cancer Network, 2012). The Distress Thermometer (DT) is a simple self-report measure developed and validated for the evaluation of distress in cancer patients (Jacobsen et al., 2005; Hegel et al., 2008; Yong et al., 2012), in which participants were asked to circle the number (0-10) on a visual scale that best describes the amount of distress they have been experiencing in the past week (0 = no distress, 10 = extreme distress). The DT has been reported in recent breast cancer survivorship literature (Hegel et al., 2006; Dabrowski et al., 2007; Hegel et al., 2008; Yong et al., 2012) and was included to allow for comparisons of findings.

The Fatigue Symptom Inventory (FSI) was used to conduct a more comprehensive assessment of current fatigue (Hann et al., 1998). The FSI is designed to measure the intensity and duration of fatigue and the extent to which fatigue impacts on quality of life. This
symptom was of particular interest since it is the most commonly reported symptom among breast cancer survivors and has been reported to persist for several months (Meeske et al., 2007). The FSI consists of four items related to intensity, in which participants were asked to rate their level of fatigue at its most, least and “on average” in the last week, as well as current fatigue, on an 11 point rating scale ranging from 0 (not at all) to 10 (extreme fatigue). Participants were also asked to rate how much, in the last week, fatigue had interfered with daily living (e.g., general activity, work activity, concentration, relationships) in a 7-item subscale, with responses ranging from 0 (no interference) to 10 (extreme interference). Two final items related to duration evaluated how many days in the past week participants were fatigued for any part of the day (range = 0-7) and how much of the day, “on average” they felt fatigued in the past week (range = 0 - none of the day to 10 - the entire day). Single scores were reported for most, least, mean and current fatigue (intensity), number of days and how much of the day (duration), with a composite score calculated for the level of “interference” associated with fatigue (Hann et al., 1998).

Current dietary intake (energy, % energy from protein, carbohydrate and fat) was assessed using 3-day food records (2 weekdays, 1 weekend day). Detailed verbal and written instructions for recording food intake and a “sample day” were provided. Participants were encouraged to provide as much detail as possible and to use household measures (teaspoons, measuring cups, scales) and food labels to estimate serving sizes. Completed records were reviewed with participants, for clarification and completeness. Nutrient analysis was conducted using The Food Processor SQL version 10.5.2 (Esha Research, Salem, Oregon), including the current Canadian Nutrient File Database (Health Canada, 2010).
Changes in diet after diagnosis were assessed via a questionnaire asking women to identify changes in food intake since their diagnosis. Nine food groups or diet components, adapted from previous research with breast cancer survivors (Maunsell et al., 2002) and grounded in current dietary recommendations for healthy eating (Health Canada, 2007), were evaluated including vegetables and fruit, legumes, meat, fish, dairy products, breads/cereals, desserts, alcohol and supplements. Participants were asked to indicate whether they had “introduced”, “increased”, “decreased” or “eliminated” these items from their diet since their diagnosis. In addition, four items were further explored to determine if there had been a “change in type” including meat, dairy products, breads/cereals and supplements. Based on the work of Maunsell et al. (2002), changes were categorized as positive if intake of vegetables and fruit, legumes and fish were reported as increased (or introduced) and if intake of meat, desserts and alcohol were reported as decreased (or eliminated). Changes in dairy products or meats, and breads/cereals were considered positive if women report consuming products with a lower fat content or higher fibre content, respectively.

5.3.3 Data Analysis

Descriptive statistics were used to characterize the sample in terms of demographic, medical and treatment background. Weight at end of treatment and current weight were used to categorize participants by weight change (weight gain, weight loss, weight stable) since the completion of treatment. Given that normal short-term fluctuations in body weight may be as high as 2.0 kg in some adults (Groff & Gropper, 2000), weight gain or loss was defined as a change in body weight greater than 2.0 kg. Body mass index (BMI) was calculated as weight (kg)/height (m²) and used to categorize participants as underweight (BMI<18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9) or obese (BMI ≥30).
Descriptive statistics were used to present self-reported symptoms of physical and psychological distress, global quality of life, intensity and duration of fatigue and the extent to which fatigue interfered with daily activities. Paired t-test was used to compare composite scores for physical and psychological distress. The mean scores for individual items on the physical distress, psychological distress and fatigue interference sub-scales were calculated in order to rank individual items from most to least distressing. Finally, mean scores for physical and psychological distress, quality of life, intensity of fatigue (“on average”) and level of interference associated with fatigue are presented in the context of normative data, including breast cancer patients in active treatment, a comparison group of healthy women and a random sample of cancer-free adults from the general population (deHaes et al., 1996; Hann et al. 1998; Hegel et al., 2006; Yong et al., 2011).

Current dietary intakes are presented as means, standard deviations and ranges. Descriptive statistics were used to identify the nature and extent of self-reported changes in diet since diagnosis.

Pearson’s correlations were used to investigate relationships between weight change (kg) since the completion of treatment and composite scores for physical and psychological distress, intensity of fatigue, duration of fatigue, level of interference associated with fatigue, current dietary intake (energy, macronutrients) and the number of positive changes in diet since diagnosis. In order to identify women more likely to gain weight since the completion of treatment, crude odds ratios compared women who gained weight to those who were weight stable or lost weight, on the basis of physical and psychological distress, fatigue, current dietary intake and changes in diet since diagnosis.
Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS version 20 IBM, Armonk, New York). Statistical significance was set at p< 0.05.

5.4 Results

5.4.1 Sample Characteristics

A total of 28 women consented to participate, over a 14 month recruitment period between Oct, 2010 and Nov, 2011. The mean time from completing treatment was 6.4±4.4 months. Demographic, clinical and treatment characteristics are summarized in Table 5.1.

Table 5.1: Demographic, Clinical and Treatment Characteristics of the Participants

<table>
<thead>
<tr>
<th>Characteristic (n=28)</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>49.8±8.5</td>
<td>33-69</td>
<td>25 (89%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td>White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black, Asian, West Asian</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>6 (21%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>7 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>15 (54%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>6 (21%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>7 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>15 (54%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employment Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>10 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leave of Absence</td>
<td>7 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed/Retired</td>
<td>11 (39%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living Arrangements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives with Significant Others</td>
<td>20 (72%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives alone</td>
<td>8 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (11%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>15 (53%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>10 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menopause Status (at diagnosis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>19 (68%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>9 (32%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment History</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumpectomy</td>
<td>15 (53%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastectomy</td>
<td>10 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planned (Mastectomy)</td>
<td>3 (11%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Cycles</td>
<td>5.9 (1.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of Treatment (weeks)</td>
<td>15 (4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time from Treatment (months)</td>
<td>6.4 (4.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiation Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (57%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planned</td>
<td>7 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>17 (61%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aromatase Inhibitor</td>
<td>5 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6 (21%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Weight History**

The mean BMI at the end of treatment was 26.2±5.5 kg/m², with 11 women (39.3%) in the normal weight category and 16 (57.1%) classified as overweight or obese. The mean weight change since the completion of treatment was -0.4±3.2 kg (range = -6.0 - +5.2). Among women who gained >2.0 kg (n=6), the mean weight gain was 3.5±1.0 kg. Seven women lost an average of 5.1±0.8 kg during this time frame. At the time of interview, the mean BMI was 26.1±5.7 kg/m² with 11 women (39.3%) in the normal weight category and 15 (53.5%) classified as overweight or obese. Weight history is summarized in table 5.2.

**Table 5.2: Weight History**

<table>
<thead>
<tr>
<th>Weight Status (end of treatment)</th>
<th>Mean (SD)</th>
<th>Range</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>72.9 (14.6)</td>
<td>48.2-101.8</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 (5.5)</td>
<td>17.1-36.7</td>
<td></td>
</tr>
<tr>
<td>Body Weight Classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (BMI &lt; 18.5)</td>
<td></td>
<td></td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>Normal Weight (BMI 18.5-24.9)</td>
<td></td>
<td></td>
<td>11 (39.3%)</td>
</tr>
<tr>
<td>Overweight (BMI 25-29.9)</td>
<td></td>
<td></td>
<td>9 (32.1%)</td>
</tr>
<tr>
<td>Obese (BMI ≥30)</td>
<td></td>
<td></td>
<td>7 (25.0%)</td>
</tr>
</tbody>
</table>

| Weight Change After Treatment    |           |           |          |
| All participants (kg)            | -0.4 (3.2)| -6.0 - +5.2| 6 (21.4%)|
| Women Who Gained Weight (kg)     | +3.5 (1.0)| +3.1 - +5.2| 7 (25%)  |
| Women Who Lost Weight (kg)       | -5.1 (0.8)| -3.5 - -6.0|          |

| Weight Status (current)          |           |           |          |
| Body Weight (kg)                 | 72.5 (15.1)| 49.5-103.4|          |
| BMI (kg/m²)                      | 26.1 (5.7) | 17.4-37.0 |          |
| Body Weight Classification       |           |           |          |
| Underweight (BMI < 18.5)         |           |           | 2 (7.2%) |
| Normal Weight (BMI 18.5-24.9)    |           |           | 11 (39.3%)|
| Overweight (BMI 25-29.9)         |           |           | 9 (32.1%) |
| Obese (BMI ≥30)                  |           |           | 6 (21.4%) |

**5.4.2 Symptoms of Physical and Psychological Distress**

The mean scores for physical and psychological distress (past week), based on the RSCL were 17.5±9.0 (range = 5.8-37.7) and 27.1±16.9 (range = 0-76.1), respectively. Based on these standardized scores, the level of psychological distress in this sample of women, at the time of interview, was significantly higher than the overall level of physical symptoms (p<0.01).
Figures 5.1 and 5.2 show the distribution of scores for physical and psychological distress across the sample group. These figures highlight the degree of variability in physical and psychological symptoms experienced by breast cancer survivors, in the first 12 months after completing chemotherapy treatment.

* Note: All RSCL results (physical distress, psychological distress and QOL) represent the standardized scores (100 point scale), for ease of comparison across domains.

**Figure 5.1: Physical Distress among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).**

* CV = Coefficient of Variation

**Figure 5.2: Psychological Distress among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).**
Based on the mean scores across participants for individual items on the physical distress scale, symptoms rated as most distressing included difficulty sleeping, decreased sexual interest, tiredness and difficulty concentrating (Table 5.3). The scores for psychological distress reflect a high level of burden reported for “worrying”, “irritability” and “despairing about the future” in particular (Table 5.4). * Scores range from 1 (not at all) to 4 (very much).

**Table 5.3: Ranking of RSCL Physical Symptoms by Mean from Most to Least Distressing among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment.**

<table>
<thead>
<tr>
<th>Symptoms of Physical Distress (n=28)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty Sleeping</td>
<td>2.20 (0.91)</td>
</tr>
<tr>
<td>Decreased Sexual Interest</td>
<td>2.18 (0.98)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>2.16 (0.58)</td>
</tr>
<tr>
<td>Difficulty Concentrating</td>
<td>2.09 (0.82)</td>
</tr>
<tr>
<td>Tingling Hands or Feet</td>
<td>1.95 (1.09)</td>
</tr>
<tr>
<td>Lack of Energy</td>
<td>1.91 (0.61)</td>
</tr>
<tr>
<td>Sore Muscles</td>
<td>1.86 (0.76)</td>
</tr>
<tr>
<td>Shivering</td>
<td>1.68 (0.82)</td>
</tr>
<tr>
<td>Low Back Pain</td>
<td>1.52 (0.79)</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>1.50 (0.64)</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.46 (0.74)</td>
</tr>
<tr>
<td>Burning/Sore Eyes</td>
<td>1.39 (0.57)</td>
</tr>
<tr>
<td>Lack of Appetite</td>
<td>1.36 (0.68)</td>
</tr>
<tr>
<td>Headaches</td>
<td>1.36 (0.68)</td>
</tr>
<tr>
<td>Acid Indigestion</td>
<td>1.29 (0.60)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.25 (0.44)</td>
</tr>
<tr>
<td>Abdominal (Stomach) Aches</td>
<td>1.25 (0.44)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1.21 (0.50)</td>
</tr>
<tr>
<td>Shortness of Breath</td>
<td>1.21 (0.42)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.11 (0.32)</td>
</tr>
<tr>
<td>Loss of Hair</td>
<td>1.11 (0.57)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.04 (0.19)</td>
</tr>
<tr>
<td>Sore Mouth/Pain when Swallowing</td>
<td>1.00 (0.00)</td>
</tr>
</tbody>
</table>

**Table 5.4: Ranking of RSCL Psychological Symptoms by Mean from Most to Least Distressing among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment.**

<table>
<thead>
<tr>
<th>Symptoms of Psychological Distress (n=28)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worrying</td>
<td>2.07 (0.66)</td>
</tr>
<tr>
<td>Irritability</td>
<td>1.86 (0.65)</td>
</tr>
<tr>
<td>Despairing About the Future</td>
<td>1.86 (0.59)</td>
</tr>
<tr>
<td>Tension</td>
<td>1.82 (0.82)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.82 (0.72)</td>
</tr>
<tr>
<td>Depressed Mood</td>
<td>1.70 (0.90)</td>
</tr>
<tr>
<td>Nervousness</td>
<td>1.54 (0.75)</td>
</tr>
</tbody>
</table>
The mean score for QOL (past week) was 19.6±20.3 (range = 0-83). Variability in this measure was high across the sample group, with 20 women (71%) describing their QOL in the past week as “good” or “excellent”, 4 (14%) as “moderately good” and 3 (11%) as “neither good nor bad”. One participant rated their quality of life as “poor” (Figure 5.3).

**Figure 5.3: Self-reported Quality of Life among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).**

![Quality of Life Scores](chart1.png)

The mean score on the Distress Thermometer (past week) was 3.1±2.9 (range = 0-9.5). The DT was added to the study protocol after recruitment was initiated and was completed by 26 of 28 participants. Nine of these women (35%) rated their distress level as moderate to severe (≥4), according to the National Comprehensive Cancer Network guidelines (2012).

**Figure 5.4: Distress Thermometer Scores among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=26).**

![Distress Thermometer Scores](chart2.png)
The mean score for intensity of fatigue ("on average") was 3.5±2.2 (range = 0-7.5), with fatigue reported across a mean of 4.5±2.6 days (range = 0-7) in the previous week. On a scale of 0 (none of the day) to 10 (the entire day), the mean score for the proportion of the daytime “on average” participants reported feeling fatigued was 28±16% (range=0-50%). Figures 5.5-5.7 show the distribution of scores for intensity and duration of fatigue (past week), highlighting wide variability in measures of fatigue across the sample group.

**Figure 5.5: Intensity of Fatigue among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).**

![Figure 5.5: Intensity of Fatigue among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).](image)

* 0 = not at all fatigued, 10 = extreme fatigue

**Figure 5.6: Duration of Fatigue (number of days/past week) among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).**

![Figure 5.6: Duration of Fatigue (number of days/past week) among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).](image)
Figure 5.7: Duration of Fatigue (proportion of daytime) among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).

The mean level of interference associated with fatigue was 2.4±2.0 (range=0-6.9). Figure 5.8 shows the distribution of scores across participants. This sample of women reported higher levels of interference for “general activity”, “ability to concentrate” and “mood” (Table 5.5).

Figure 5.8: Level of Interference Associated with Fatigue * among Early Stage Breast Cancer Survivors in the First Year after Completing Chemotherapy Treatment (n=28).

Table 5.5: Ranking of RSCL Fatigue Interference Sub-scale Items * by Mean from Most to Least Amount of Interference among Early Stage Breast Cancer Survivors (n=28).

<table>
<thead>
<tr>
<th>Interference with Daily Activities (n=28)</th>
<th>Mean</th>
<th>(SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Activity</td>
<td>3.36</td>
<td>2.77</td>
</tr>
<tr>
<td>Ability to Concentrate</td>
<td>3.21</td>
<td>2.90</td>
</tr>
<tr>
<td>Mood</td>
<td>2.86</td>
<td>2.53</td>
</tr>
<tr>
<td>Normal Work Activity</td>
<td>2.57</td>
<td>2.38</td>
</tr>
<tr>
<td>Enjoyment of Life</td>
<td>2.32</td>
<td>2.21</td>
</tr>
<tr>
<td>Relations with Other People</td>
<td>2.29</td>
<td>2.49</td>
</tr>
<tr>
<td>Ability to Bathe and Dress Yourself</td>
<td>0.46</td>
<td>1.23</td>
</tr>
</tbody>
</table>

* Scores range from 0 (no interference) to 10 (extreme interference)
5.4.3 Symptoms of Physical & Psychological Distress Relative to Previous Findings

Although true comparisons are not possible, it appears that on average, indicators of physical and psychological distress in this sample of early stage breast cancer survivors are comparable to reports of breast cancer patients in active treatment and higher than comparison groups of healthy adults (de Haes, et al., 1996; Hegel et al., 2006; Yong et al., 2012; Hann et al., 1998). Figure 5.9 (a-f) shows the means scores for physical distress, psychological distress, quality of life, the distress thermometer and fatigue relative to previous findings among breast cancer survivors and normative data from cancer-free adults. (see discussion)

Figure 5.9: Comparison of Mean Scores for Physical and Psychological Distress Indicators Between Early Stage Breast Cancer Survivors Post-treatment and Comparison Groups of Breast Cancer or Healthy Individuals from the Literature.
5.4.4 Dietary Intake and Dietary Change

Based on 3-day food records, the mean energy intake for the sample was 1883±359 kcals, with protein, carbohydrates and fat providing 17.9%, 52.2% and 28.5% of energy, respectively. Eighty-four percent of women (n=24) reported that they had made changes to their diet since diagnosis, the majority of which were categorized as positive. The most common change was an increase in vegetables and fruit (75% of total sample), followed by a decrease in overall meat consumption or a change to lower fat options (decreased red meat, increased chicken, 57.1%), increased intake of fish (46.4%) and reduced alcohol intake (39.3%). Reports of negative dietary changes were minimal in this sample, most common among them being an increase in desserts (14.3%). Among women reporting any dietary change, the mean number of positive changes was 3.88±1.4 (range = 0-6).

5.4.5 Relationships between Symptoms of Physical and Psychological Distress, Diet and Weight Gain Since the Completion of Treatment

Treating weight change (kg) as a continuous variable, there were no significant associations between weight change since the completion of treatment and each of physical and psychological distress scores, intensity of fatigue, duration of fatigue (number of days in the
past week) or level of interference associated with fatigue. Fatigue duration, based on the proportion of daytime fatigue was reported, was significantly correlated with weight change (r=-0.46, p<0.05), with fatigue over a larger proportion of the day associated with weight loss since the completion of treatment. Dietary factors, including current intakes and number of positive changes in diet since diagnosis, were not associated with weight change since the completion of treatment. Odds ratios comparing women who gained weight to women who did not gain weight (loss or stable) after treatment on the basis of treatment-related (physical and psychological distress, fatigue) and dietary factors (energy, macronutrients, number of positive changes in diet since diagnosis) were non-significant.

5.5 Discussion

This study provides an intensive investigation into weight change and symptoms of physical distress, psychological distress and fatigue, as reported by early stage breast cancer survivors within 12 months of completing chemotherapy treatment. Relationships among physical and psychological distress, fatigue, current dietary intake, changes in diet and weight gain since the completion of treatment were investigated.

Overall weight change in this sample, since the completion of treatment, was minimal. Six women (21.4%) however, gained an average of 3.5 kg, while 15 (53.6%) were weight stable and 7 (25%) lost weight during this time frame. Based on previous findings (Demark-Wahnefried et al. 1997a; Makari-Judson et al., 2007; Kutynec et al. 1999), it was expected that as many as 50% of women would gain weight in the first 12 months of completing treatment, however, the mean time from treatment in this sample was 6.4 months and 32% (n=9) of women were within three months. This relatively short follow-up period yielded a narrow range of weight change and a small proportion of women who gained weight during this time.
frame. While this may have limited capacity to detect significant relationships, the removal of six participants from the analysis who were \( \leq 1 \) month from completing chemotherapy did not alter our findings and no significant association was observed between weight gain and length of time from treatment (data not shown).

The current results suggest that levels of both physical and psychological distress associated with cancer and its treatment may persist for many breast cancer survivors in the first year after completing treatment. Although symptoms were highly variable across the sample group, based on the same instrument, the mean levels of physical and psychological distress in these women were similar to a large sample of early stage breast cancer patients in active treatment (\( n=653 \), age \(< 51 \) y) and appear to be markedly higher than previous reports of distress among a random sample of adults from the general population (\( n=201 \), 59\% female, mean age = 45 y) (de Haes, et al., 1996). The ranking of physical symptoms from most to least distressing is consistent with the findings of Stein, Denniston, Baker et al. (2003), who reported consistently high ratings for “tiredness”, “lack of energy”, “difficulty sleeping” and “decreased sexual interest” among 1005 male and female cancer patients (mean age = 58±14 y), 18\% of whom were still in active treatment.

Comparisons to breast cancer patients in active treatment or cancer-free populations were not available, however compared to newly diagnosed breast cancer patients awaiting treatment (\( n=236 \), stage I-III, mean age = 57 y), the mean DT score in this sample of women appears to be lower (Hegel et al., 2006). This finding is consistent with evidence that psychological distress may be higher immediately after diagnosis but recedes somewhat once treatment has been initiated (deHaes et al., 1996). The mean Distress Thermometer score seems to suggest marginally higher levels of distress in this sample, compared to a previous report of early stage
breast cancer survivors (n=150, stage I-II, mean age = 49 y) after treatment (Yong et al., 2012). However, since the time frame was not reported in the earlier study, it is possible that the comparison sample group was further removed from the completion of treatment, thus allowing more time to recover from the residual effects of treatment.

The mean intensity of fatigue (“on average”) in this sample, was comparable to the mean intensity of fatigue reported by breast cancer patients in active treatment (n=117, mean age = 52 y) and appears to be higher than an age-matched comparison group of healthy women (n=94) (Hann et al., 1998). Similarly, the extent to which fatigue interfered with daily activities was consistent with women in active treatment, but suggested a higher degree of burden associated with fatigue, compared to healthy women. Additional findings reported by Hann and colleagues (1998) are consistent with our results, in women who have completed treatment. Also based on the FSI, Hann et al. (1998) reported a mean intensity of fatigue of 3.4 (vs. 3.5 in the current study) among 113 women (mean age = 53 y) who were at least three months post-treatment for early stage breast cancer. In this sample, the mean duration of fatigue was 4.0 (days/week) and 31% (proportion of daytime), respectively compared to 4.5 and 28% in the current study. The mean score for fatigue “interference” was also comparable across studies (2.1 vs. 2.4).

Despite relatively high levels of physical and psychological distress at the time of interview, 71% of women in this sample rated their quality of life in the past week as “good” or “excellent” Based on interview responses to the qualitative portion of the larger study, this finding seemed to reflect a gradual adjustment to their cancer diagnosis over time, a strong sense of relief at having completed treatment and a commonly expressed desire to “seize the moment” and enjoy life after the stress and worry of this “life changing experience”. The mean
Score for global QOL appears to be comparable to a random sample from the general population but lower (implying better QOL) than early stage breast cancer patients in active treatment (de Haes, et al., 1996).

Scores for physical distress, psychological distress, fatigue and QOL were highly variable across the sample group. This finding is supported by previous reports among breast cancer survivors, in which the inter-individual variability for indicators of physical and psychological distress (CVs=54%-96%) and QOL (CV=67%), at various time points in the cancer trajectory, were high (deHaes et al., 1996; Hegel et al., 2006; Yong et al., 2011; Hann et al., 1998). In the current sample, scores for these survey variables were not significantly correlated with demographic or clinical characteristics, or length of time from treatment (data not shown).

Comparisons to previous findings and normative data must be considered within the context of similarities and differences in sample characteristics and study design. First, all comparisons were based on the same validated instruments and are strengthened by similarities in demographic and clinical characteristics of the participants. Breast cancer specific comparisons (RSCL, DT, FSI) were drawn from samples of women who were similar in age and stage of disease (de Haes, et al., 1996, Hegel et al., 2006; Yong et al., 2011; Hann et al., 1998). Cancer-free comparison groups included a sample of healthy women of similar age (Hann et al., 1998) and a random sample from the general population, of which 59% of participants were female (de Haes, et al., 1996). Differences in the timing of measures (Yong et al., 2011) and changes in treatment protocols over time, may however have impacted on the level of physical and psychological distress among clinical populations. It should also be noted that most of these studies, including the current investigation, were conducted with predominantly
white, married, well-educated women, suggesting caution in extrapolating the findings to the population of breast cancer survivors.

It is noteworthy that, without repeated measures in the same sample group, we cannot be certain that physical and psychological distress reported at the time of interview actually reflect persistent effects of cancer treatment. However, qualitative interviews with the same sample group, in which physical and psychological distress and pervasive fatigue were reported during treatment, suggest that current symptoms may represent residual effects of cancer and its treatment for many women. This is supported by comparisons of current findings to cancer-free populations, which suggest that the levels of distress in this sample of women were substantially higher.

Energy intake from 3-day food records (1883±359 kcals) in the current study is higher than previous reports in this population. In two large prospective cohorts of early stage breast cancer survivors (Health, Eating, Activity and Lifestyle (HEAL) and Life After Cancer Epidemiology (LACE) studies), mean energy intake based on a 114 item FFQ was estimated at 1356-1458 kcals (Wayne et al., 2004; Caan et al., 2005). Using 24-hr recalls, baseline data from the Women’s Healthy Eating and Living (WHEL) study (Pierce, Natarajan, Caan et al., 2007) (n=3088, stage I-IIIA) revealed a mean energy intake of 1718 kcals; energy intake that is similar to mean kcals reported by the Women’s Intervention Nutrition (WINS) study (n=2437, stage I-IIIA) (Chlebowski et al., 2006). Mean protein intake as a percentage of total energy (17.9%) is similar to that reported in the HEAL and LACE studies (16.9-17.1%). Total fat intake (28.5%) is consistent with data from the WHEL and WINS studies (28.5-29.6%), but lower than estimates from the HEAL and LACE cohorts (33.8-35.5%). The amount of energy derived from carbohydrates is a little higher in the current study, compared to those reported in
both HEAL and LACE (52.2% vs. 47.4-48.6%). Differences in dietary assessment methods and timing of the measures relative to diagnosis may explain apparent differences in dietary intake data. Although key demographic and clinical characteristics were similar across studies (ethnicity, education, clinical stage, baseline BMI), participants in the current study and the WHEL study were, on average, a little younger compared to the HEAL, LACE and WINS cohorts, which may help account for differences that were observed (Thomson et al., 2002; Wayne et al., 2004).

Our finding that higher scores for fatigue duration (proportion of daytime) were negatively correlated with weight change is of interest. This is consistent with findings from an earlier qualitative analysis with this sample group, suggesting that extreme and persistent fatigue during chemotherapy treatment may associate with reduced food intake and weight loss in some women (Chapter 3). In this study, participants who reported unrelenting fatigue between cycles, described that they were “too tired to eat”, “couldn’t be bothered” or didn’t have the energy to prepare food, especially if they were living alone. Given that fatigue has been shown to persist for many breast cancer survivors in the months and years after diagnosis (Meeske et al., 2007), the apparent relationship between fatigue and lower food intake may endure for some women. These findings contrast with those of Kumar et al. (2004) who found that, based on the FSI, duration of fatigue was positively correlated with weight gain in breast cancer survivors (n=198, stage I-IIIB) in the six month period after treatment; a relationship that may be mediated by lower levels of physical activity during this time (Irwin et al., 2003). Although fatigue is common in this population, these results highlight wide inter-individual variation in behavioural responses to this pervasive side effect of breast cancer treatment.
Beyond the observed association between fatigue duration and weight change, relationships between symptoms of physical and psychological distress, current dietary intake, changes in diet and weight gain since the completion of treatment were non-significant. There are a number of factors which may have influenced these null findings. First, data for this analysis were collected in conjunction with a qualitative study designed to explore the recalled experiences of food intake and weight change during treatment. In keeping with the in-depth nature of qualitative analysis, the sample size was relatively small and may have limited the ability to detect significant relationships after treatment. Based on the observed effect size in this study ($r=.46$), and a desired power level of 0.8, it is estimated that a sample size of 38-40 would be necessary to detect significant correlations between psychosocial and treatment-related factors and weight gain since the completion of treatment. A longer mean follow-up period, based on this sample size, may produce more variability in weight change and sufficient statistical power for further study.

In addition, this study was limited by the cross-sectional design, as it is not known if the level of physical and psychological distress reported at the time of interview (past week) accurately reflects the level of distress experienced since the completion of treatment. While normative data derived from women with similar characteristics allowed for meaningful comparisons to the current findings, and suggested enduring symptoms of physical and psychological distress after treatment, these comparisons would be strengthened by repeated measures within the same study population, across the cancer trajectory.

The current findings point to factors that may influence dietary choices and energy balance in the first year after breast cancer treatment. This is an important first step in developing dietary guidelines and interventions in this population, since efforts to promote healthy eating
and weight management are unlikely to be effective without appropriate supports in place to address potential barriers. Evidence of persistent physical and psychological distress among breast cancer survivors raises awareness of ongoing challenges that may influence eating behaviour after treatment. This is important given that psychological distress in particular, is common in cancer survivors but often goes unrecognized (National Comprehensive Cancer Network, 2012) and is now endorsed nationally and internationally as the “6th vital sign” (Howell & Olsen, 2011). Residual effects of cancer and its treatment, including distress should be recognized in the clinical and research settings for their effects on overall health and their potential impact on food intake and energy imbalance after treatment.

In summary, our results suggest that symptoms of physical and psychological distress may persist for many breast cancer survivors in the first 12 months following primary treatment and may be associated with weight change. These findings may serve to guide dietary counseling within a growing population of breast cancer survivors and to aid in the development of effective nutrition interventions.
CHAPTER 6: GENERAL DISCUSSION

The purpose of this general discussion is to provide a summary of the overall results of this thesis, with an emphasis on the integration of qualitative and quantitative findings and weight history across studies 1 (Chapter 3-during treatment) and 2 (Chapters 4 and 5-after treatment). Key contributions of these findings toward expanding the field of research are reviewed, followed by a discussion of the relevance of these findings for clinical practice and recommendations for future research. Finally, some concluding remarks and a “personal post-script” are included as an effort to capture the depth of involvement offered by the women who participated in this study and to provide additional context for the interview process.

6.1 Overall Findings and Key Contributions

The purpose of study 1 was to gain an appreciation of the experience of chemotherapy from the perspective of breast cancer survivors; to describe the unique challenges related to diet and weight management and to investigate possible relationships among psychosocial and treatment-related factors, dietary intake and weight change during treatment. Since participants were interviewed within 12 months of completing chemotherapy, this timing offered an opportunity to explore whether factors that appear to associate with weight change during treatment (study 1), might persist in the first year after receiving chemotherapy and continue to exert an effect on food intake and energy balance after treatment (study 2). The use of qualitative methods, validated surveys and dietary records (at the time of interview) helped to overcome some of the methodological limitations associated with dietary assessment during breast cancer treatment and provided novel insights into diet and weight change after diagnosis, that have not previously been explored.
Qualitative findings (study 1) revealed common themes around food intake and eating patterns, and factors associated with changes in diet during treatment. As presented in Figure 3.1, changes in food intake relative to treatment day, changes in appetite and changes in food appeal (food cravings, comfort foods and food aversions) were common concerns in this sample of early stage breast cancer survivors. Based on women’s perceptions, fatigue, taste changes, gastrointestinal disturbance, family/social support and the emotional impact of cancer and its treatment were key factors contributing to changes in food intake and eating patterns during treatment (Figure 3.2).

While underlying themes were apparent across the sample group, these shared psychosocial and treatment-related issues produced a wide range of dietary responses. Taste changes, for example, produced both food cravings and food aversions in this sample, while gastrointestinal disturbance and emotional distress were associated with increased appetite and increased intake of energy dense comfort foods in some women and reduced appetite and lower food intake in others. Qualitative analysis, based on the constant comparative method, led to the development of two theoretical models. The first model was designed to explain how psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight gain during treatment (Figure 3.3). This model was expanded to include factors associated with weight loss during treatment (Figure 3.4), in light of emerging evidence that weight fluctuation, both gain and loss, may associate with adverse health effects.

The theoretical framework presented in Figure 3.3 shows that increased appetite, food cravings and intake of energy dense comfort foods seemed to be more prevalent and persistent among women who gained weight during treatment. Vivid recall of the chemotherapy experience in most women, suggested that changes in taste, nausea and emotional distress were
central in promoting these dietary responses. These qualitative findings are supported by a significant association between self-reported quantity of food intake (compared to usual intake before diagnosis) and weight gain during treatment, and the subjective perceptions of women concerning behavioural factors affecting energy balance during this time frame.

Figure 3.4 highlights possible relationships between treatment effects, food intake and weight loss during treatment. Women who lost weight in this sample group tended to report more severe and persistent side effects of treatment, leading to a more prolonged reduction in food intake after treatment. Fatigue, nausea, constipation and heartburn in particular, seemed to endure in these women well into the second and third weeks within cycles, producing decreased appetite and irregular eating throughout treatment. In this sample, weight loss also appeared to be more common among women who lived alone, perhaps reflecting the level of cooking support that was available in the home.

Findings from study 2 (Chapters 4 and 5) provide additional support for some of the qualitative results presented in study 1. In this sample of women, mean scores for physical distress, psychological distress and fatigue at the time of interview (mean = 6.4 months from completing treatment), were similar to women in active treatment but appeared to be consistently higher than normative data drawn from healthy comparison groups. Based on the Distress Thermometer, compared to a large sample of women with newly diagnosed early stage breast cancer, the level of distress reported in the current sample appears to be lower. This observation is consistent with the experience of women in the current study, with most women having reported lower levels of anxiety once a treatment plan was in place and chemotherapy was initiated.
As reported in previous studies, self-reported changes in diet after diagnosis were consistent with current dietary recommendations for cancer prevention, with many women reporting an increase in vegetable and fruit intake, decreased meat, increased fish and reduced alcohol consumption. The proportion of women reporting positive changes in diet after diagnosis was quite high in this sample, compared to earlier studies, however based on 3-day food records at the time of interview, many women did not meet minimum recommendations for vegetable & fruit servings or milk & alternatives and some were above the current guidelines for total and saturated fat. The prevalence of inadequate fibre intake appeared to be low.

A significant association between fatigue and weight loss in study 2 also lends support to qualitative findings from study 1. Based on the Fatigue Symptom Inventory, fatigue duration (past week) was negatively correlated with weight change since the completion of treatment. This is consistent with an apparent association between extreme fatigue and weight loss during active treatment. Associations between other survey variables, current dietary intake, changes in diet and weight gain since the completion of treatment were non-significant. These findings likely reflect insufficient statistical power, based on sample size and limited variability in weight change in the current study, however serve to estimate a required sample size of 38-40 for future studies.

Figure 6.2 (pg. 182) integrates the findings of study 1 and 2, to explain how psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight change after a breast cancer diagnosis. Factors that appear to associate with food intake both during and after treatment are bolded. This model suggests that emotional distress, fatigue and decreased appetite may persist for some women in the months following treatment and continue to exert an effect on weight change during this time frame. Based on
the RSCL, “tiredness” and “lack of energy” were ranked high on the list of individual symptoms of physical distress, at the time of interview. Although “lack of appetite” was ranked lower, based on the mean values for most to least distressing (table 5.3), 54% of women (n=15) reported that they had been eating less than they would normally eat since the completion of treatment, almost half of whom (n=7) attributed lower food intake to early satiety and reduced appetite. Five of these women had lost weight since the completion of treatment. Symptoms of psychological distress were relatively high in this sample, compared to cancer-free adults, and reflected higher scores for “worrying”, “despairing about the future”, “tension” and “anxiety”, in particular. Most women reported that other treatment-related factors associated with food intake and eating patterns during treatment (taste changes, food cravings/aversions, nausea, constipation, heartburn) had largely resolved by the time of interview.

Weight change during treatment and since the completion of treatment are provided in the results sections of chapters 3 and 5, however a closer look at weight history across the total study period (diagnosis to time of interview) may provide additional insights (Figure 6.1). Weight gain >2kg was observed in 57.1% of women (n=16) in this sample, during or after treatment. One woman gained weight in both of these time periods. Among women who gained weight during treatment (n=11), 64% (n=7) were still > 2kg above their baseline body weight, at the time of interview. Three additional women, who were weight stable during treatment, gained > 2kg since the completion of treatment. Between diagnosis and the time of interview, the mean weight change was +0.5±3.9 kg (range = -10.1 - +8.41); supporting the variability in weight change that has been observed in breast cancer survivors (Gu et al., 2010; Nissen et al., 2011). Among women who gained weight across the total study period (n=10, 35.7%), the mean weight gain was 4.0 kg. The mean BMI at the time of interview was
26.1±5.7 kg/m², compared to 25.9±5.7 kg/m² at diagnosis, with 53.5% of women (vs. 46.4%) now classified as overweight or obese. During this time frame, two women moved from the normal weight to overweight category and one woman, who was normal weight at diagnosis, was classified as underweight at the time of interview. These findings are consistent with earlier studies in which a general trend toward a reduction in overall weight gain in this population has been observed (Vance et al., 2011), however underscores that weight gain is nonetheless a persistent problem for a sizeable proportion of women.

The weight gain reported in this sample, over an average of 15 weeks of treatment (0.8±4.6 kg) is higher than would be expected in a healthy population (~0.2-0.55 kg/y) (Williamson et al, 1991; Guo et al., 1999), and was substantially higher in some women. Weight change during treatment, after treatment or across the study period were not associated with BMI at diagnosis (p = .20, .29 and .47, respectively); a finding that is supported by some (Goodwin et al., 1988; Costa et al., 2001; Lankester et al., 2002; Ingram & Brown, 2004; Irwin et al., 2005; Heideman et al., 2009; Tredan et al., 2010; Gordon et al., 2011) but not all (Gu et al., 2010; Nissen et al., 2011; Yaw et al., 2011) previous studies.

**Figure 6.1 Weight Change Across the Study Period (n=28)**

1 = Diagnosis to End of Treatment

2 = End of Treatment to Time of Interview

3 = Diagnosis to Time of Interview
Figure 6.2: Relationships between Psychosocial & Treatment-related Factors, Food Intake and Weight Change in Breast Cancer Survivors during and after Treatment.
These findings contribute to the current literature in a number of important ways.

1. **Food intake and eating patterns during treatment are influenced by a wide range of psychosocial and treatment-related factors that vary across women.**

Qualitative methods based on comprehensive interviews with breast cancer survivors provided a unique perspective on food intake and weight change during treatment. The exploration of food intake and eating patterns, in the context of psychosocial and treatment-related factors, identified dietary challenges that women face as they are undergoing chemotherapy treatment. Although nutrition-impact symptoms are well documented, the severity and persistence of these symptoms vary considerably between women and across the treatment trajectory, leading to a broad range of behavioural responses associated with both weight gain and weight loss. This data, based on the lived experience of women, will help to design healthy eating and weight management strategies that acknowledge and address potential barriers.

2. **Methodological challenges have limited the ability to detect relationships between food intake and weight change during treatment.**

Evidence of marked variability in food intake within cycles and across treatment, highlights the difficulty in accurately capturing dietary change and energy balance using quantitative assessment methods. A theoretical model based on the current findings supports several pathways by which psychosocial factors and treatment-related side effects might influence diet and eating patterns in ways that promote weight change during treatment. These findings may have important relevance for clinical practice (section 6.2) and future research (section 6.3).

3. **Many breast cancer survivors may not be meeting current dietary recommendations.**

Study 2 adds to a limited body of literature on dietary changes and dietary intake after breast cancer. Improving our understanding of dietary habits after diagnosis including dietary changes that women are making on their own, when these changes are initiated and how dietary intakes
compare to current recommendations, will inform appropriate targets/timing for intervention. For example, knowing that the majority of women (84%) are already making dietary changes and that many (36%) are making these changes during active treatment helps to direct the timing and provision of resources.

4. **Physical and psychological distress appear to persist for many breast cancer survivors in the first 12 months after completing chemotherapy treatment.**

This study is the first, to the author’s knowledge, to explore the potential influence of physical and psychological distress on diet and weight change after treatment. Further research with a larger sample size is needed to confirm relationships between survey variables, dietary data and weight change. Nonetheless, the relatively high levels of physical and psychological distress reported in this sample of breast cancer survivors, on average 6 months post-treatment, is an important finding. Health care providers should be alerted to the role that fatigue and emotional distress for example, may play in promoting energy imbalance after treatment.

**6.2 Clinical Applications**

Qualitative findings from study 1 may help the health care team to identify women who are most at risk of weight gain or loss during treatment. Moreover, understanding the unique challenges related to diet and weight management in this population may inform the development of effective guidelines and diet/weight management interventions after diagnosis.

A key lesson to be drawn from the experiences of women who participated in this study is an appreciation for the variability in dietary responses to common psychosocial and treatment-related issues that was evident during treatment. It is clear that the “anticipated” experience of early stage breast cancer patients receiving chemotherapy cannot be defined by a single set of guidelines. This is supported by wide variation in weight change during and after treatment, reported in this study and others. This suggests that health care providers should screen for
weight change and associated psychosocial and treatment-related factors regularly throughout treatment and refer to the appropriate supportive care personnel for guidance and counseling, as required. Dietitians should acknowledge the potential role of taste changes, nausea and emotional distress in promoting food cravings, increased appetite and weight gain and provide guidance around dietary strategies that will assist in maintaining energy balance during treatment. Given that weight loss may be equally concerning in terms of health outcomes, the apparent link between extreme fatigue and GI disturbance should be evaluated in the context of the level of cooking support that is available in the home, to ensure that women who are experiencing persistent symptoms have access to supportive services and adequate nutrition throughout treatment.

Evidence in the current study that some women may be willing and able to implement positive changes in diet during treatment suggests that supportive dietary services may be effective early in the cancer trajectory. This is supported by earlier studies in which it has been demonstrated that a diagnosis of breast cancer may represent a time when women are open to learning about food and nutrition and highly motivated to make lifestyle changes that will promote optimal health (Demark-Wahnefried et al., 2000; McBride et al., 2000). Although a full analysis is beyond the scope of this thesis, qualitative interviews included a question in which participants were asked to discuss their previous knowledge and level of concern about weight control during treatment, their use of dietary services and any recommendations they had for improving dietary supports after diagnosis. Most women expressed that weight management was on their mind during treatment but was a lower priority for them, as they coped with their diagnosis and the effects of treatment. Many were not aware that weight gain during treatment was a potential problem. A few women (n=4, 14%) attended general classes
offered by dietitians in the cancer centres where they were treated, but only two received individual counseling during this time. Many women expressed that they would have been open to meeting with a dietitian early in treatment to discuss food intake and weight management issues. Most of these women indicated that practical advice around dietary planning, coping with side-effects and foods that might increase or decrease the risk of recurrence was of particular interest. These services are in fact available in most major cancer centres, however it was apparent that many women were not aware of how to access them or were overwhelmed with information and medical appointments, such that attending a class on another day was impractical for them. During the study period, the Grand River Regional Cancer Centre, where 57% of the study sample were treated, was offering two classes to cancer patients; one focused on healthy eating in general, the other providing guidance around nutrition and cancer specifically. Individual diet consultations could also be arranged through supportive services. Although only two women exercised this option, several others (n=7, 25%) mentioned that a Registered Dietitian from supportive services had dropped in to see them in the chemotherapy suite. These meetings were generally brief, designed to explore how patients were coping with nutrition-related side effects of treatment. These findings suggest a need for improved integration of dietary support services, within the regular oncology schedule.

Although a large proportion of women in this study reported positive changes in diet after diagnosis, dietary data based on 3-day food records in the first 12 months after diagnosis, suggests that vegetable and fruit, milk and alternatives, dietary fat, calcium and vitamin D intakes may be targets for nutrition intervention in this population. This is consistent with current recommendations for breast cancer survivors. At this time, observational cohort studies
and two randomized trials (Chlebowski et al., 2006; Pierce et al., 2007), evaluating the effects of specific foods/nutrients on prognosis, have produced mixed results. Without clear evidence for the beneficial effects of individual dietary factors (Robien, Demark-Wahnefried & Rock, 2011), current findings suggest that a reduced fat, predominantly plant-based diet, that supports a healthy body weight will improve overall survival (Kroenke et al., 2005, Kwan et al., 2008) and may protect against recurrence (Rock et al., 2009; Hauner et al., 2011). Similarly, an association between calcium and vitamin D and breast cancer recurrence is equivocal (Jacobs, Thomson, Flatt et al., 2010), however the established role of these micronutrients in protecting against osteoporosis after menopause (National Institutes of Health, 2011), supports their place in nutrition intervention.

Lastly, evidence of progressive weight gain after treatment suggests that continued intervention and follow-up is warranted. Dietary supports are needed within the context of potential barriers to healthy eating and weight management during and after treatment. Relatively high levels of distress in this sample of women, who were on average 6.4 months from completing chemotherapy, underscores a need for ongoing cancer care and wellness programs across the cancer trajectory. Several women expressed anxiety about being outside the “circle of care”, meaning they were no longer seeing their oncologists on a regular basis or receiving routine diagnostic tests to monitor their disease. As a result, they were concerned that they would not know how to interpret new symptoms and that they would not know if their “cancer had come back”. Supporting the results of previous studies, most women were very interested in behavioural strategies that might reduce the likelihood of recurrence, once again highlighting the need for “rehabilitation” programs that will help patients to fully recover from cancer and its treatment, in the months and years after diagnosis.
There are undoubtedly lessons to be drawn from the long standing practices and established benefits of cardiac rehabilitation. Cardiac rehab programs aimed at recovery, secondary prevention and lifestyle change, have been in place since the 1960’s (Certo, 1985). The Cardiac Health Foundation of Canada (2012) defines cardiac rehab as “the enhancement and maintenance of cardiovascular health through individualized programs designed to optimize physical, psychological, social, vocational and emotional status”. Such programs, focused on diet, exercise, smoking cessation and stress management, are known to reduce risk factors associated with heart health, decrease pain, reduce the risk of morbidity and mortality and improve quality of life (National Institutes of Health, 2012).

While there is a critical need for further research to support cancer rehabilitation programs, for a growing population of breast cancer survivors, there is also a need to translate the best evidence to date into clinical practice. Elevated risk of co-morbid conditions among women who have been treated for breast cancer and the known benefits of diet and exercise in promoting overall health, support the need for lifestyle intervention in this vulnerable population (Robien et al., 2011). The “precautionary principle” endorsed by the Canadian Breast Cancer Foundation (2012) suggests that evolving evidence should be applied, with a view to “err on the side of caution” and put women’s health first.

Table 6.1 summarizes suggestions for caregivers working with women who are undergoing chemotherapy treatment for breast cancer. These suggestions are not meant to be exhaustive, or to reiterate well-established standards of dietetic practice, but rather represent “lessons” from the women who participated in this study that may help to provide guidance around healthy eating and weight management during treatment.
### Table 6.1: Suggestions for Caregivers Working with Women Undergoing Chemotherapy Treatment for Breast Cancer.

#### Before Treatment

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| **Fatigue**              | Very common for the first few days after treatments.  
|                          | May persist into the second week and may be cumulative across cycles. |
| **Changes in Taste**     | Many foods will likely taste “off” - metallic or chemical taste is common.  
|                          | May experience loss of taste sensation.  
|                          | Taste changes usually present with the first couple of days and may last through the first and second week after chemotherapy. |
| **GI Disturbance**       | May experience nausea, constipation, diarrhea, heartburn.  
|                          | Reinforce adherence to anti-nausea, laxative and acid reflux medication protocols, as prescribed. |
| **Changes in Appetite**  | Most women experience lower appetite for the first couple of days.  
|                          | Appetite generally improves in the second and third weeks.  
|                          | Some women experience an increase in appetite within a few days of treatment. |
| **Food Cravings/Food Aversions** | Both are common and are often associated with changes in taste.  
|                          | May want to avoid favourite foods around chemotherapy days. |
| **Mouth Sores**          | Reinforce careful oral hygiene and routine use of mouthwashes, as prescribed. |
| **Planning Ahead**       | Stock up on easy to prepare, well tolerated foods (e.g. pasta, soups, bananas, applesauce, puddings and yogurt).  
|                          | Bring snacks on treatment days in case of long waiting periods and limited availability of preferred foods. |
| **Social Support**       | Support of family and friends (e.g. treatment companion, food preparation) is especially helpful on treatment days and the first few days after chemotherapy. |

#### During Treatment

<table>
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<th>Screen for:</th>
<th>Suggest:</th>
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| **Fatigue** | Rest and daytime naps as required for the first few days.  
|             | May find it helpful to break down “must do” tasks into smaller increments.  
|             | Low intensity exercise (walking, yoga) as tolerated, may help to increase energy. |
| **Changes in Taste** | Adding lemon, salt or spices to foods as tolerated, may enhance flavour or mask unpleasant tastes. |
| **GI Disturbance** | Healthy dietary strategies for managing nausea (e.g. soda crackers), constipation (e.g. high fibre as tolerated, plenty of fluids), diarrhea (e.g. increase fluids, avoid fried foods/caffeine) and heartburn (e.g. avoid eating 3-4 hrs before bedtime). |
| **Changes in Appetite** | Increased appetite: Lower energy-dense food choices (e.g. fruit, yogurt, eggs).  
|                         | Reduced appetite: High protein, energy-dense food choices (e.g. smoothies, nuts). |
| **Food Cravings/Food Aversions** | Nutrient rich, lower energy-dense foods may satisfy cravings for starchy carbohydrates and sweets (e.g. whole grain pasta, fruit, yogurt, chocolate milk).  
|                         | Smaller portions of energy-dense cravings.  
|                         | Alternate protein sources for red meat aversions (e.g. fish, eggs, dairy, beans).  
|                         | Cooked vegetables, soups and juices may be tolerated in place of raw vegetables. |
| **Mouth Sores** | Soft foods if mouth sores are present.  
|               | Cool foods (e.g. applesauce, yogurt) may be especially well tolerated. |
| **Social Support** | Ask about food preparation and level of cooking support.  
|                   | Refer to appropriate supportive services as required. |
| **Emotional Distress** | Refer to appropriate supportive services as required. |

#### Advice for Family and Friends:

| Social Support | Practical assistance (e.g. accompanying patients to treatments, food preparation, childcare) contributes to emotional wellness. |
| Food Preparation | Check to see which foods are appealing and well-tolerated. May change over time. |
6.3 Future Research Directions

Given the adverse consequences of weight gain, fat gain and loss of lean tissue after diagnosis, continued efforts to identify the relative contribution of diet in promoting these changes are justified. Qualitative methods show promise as an effective means of capturing dietary change and associated psychosocial and treatment-related factors across the treatment trajectory, however the integrity and transferability of key themes should be tested in breast cancer populations representing a wider range of demographic characteristics (age, ethnicity, education), treatment protocols and stage of disease. Since multiple days of record keeping are problematic and may be impractical during treatment, future energy balance studies should, as a minimum, be designed to account for the timing of diet assessment relative to treatment day. Intra-individual variation in food intake across treatment is a confounder, however overall patterns of dietary intake in this sample suggest that food records or 24 hr recalls in the first, second and third weeks after treatment will provide a more accurate picture of dietary change, compared to the more common use of before and after measures only.

Evidence that both weight gain and weight loss may be associated with poor prognosis suggests that underlying metabolic disturbances associated with changes in body composition may be responsible for poor health outcomes (Healy, Ryan, Carroll et al., 2010). Since fat gain and loss of lean tissue may occur with or without weight gain (Cheney et al., 1997; Kutynec et al., 1999), it will be important to measure changes in body composition and to evaluate the effect of these changes on intermediate metabolic biomarkers (e.g., insulin, blood lipids).

At this time it seems probable that diet and physical activity patterns interact with a range of secondary factors (psychosocial, treatment effects, hormonal changes) to promote energy imbalance after diagnosis. These behavioural factors, which appear to play a significant role
during treatment, may continue to exert an effect in the months and years after diagnosis. As such, further research is needed to test the efficacy, optimal timing and delivery of combined diet and exercise interventions after diagnosis (Robien et al, 2011), along with long-term studies designed to examine the effects of these interventions on prognosis and overall health.

6.4 Concluding Remarks

Although there is more research to be done to evaluate the impact of diet and exercise intervention on disease recurrence and survival, I conclude this thesis with a personal testament to the benefits of adopting a healthy lifestyle after diagnosis. A cancer diagnosis, and the treatment that follows, is clearly a time when patients must relinquish control over many aspects of their life. Diet and exercise may help to restore a sense of control and may have a significant role to play in overall wellness.

Valerie: I know that everyone's journey is so very different, but focusing on fitness and nutrition is the one thing that had the most positive physical and psychological impact on my recovery. It really made me feel strong and in control again - something that cancer tries to steal. I also had an incredible network of support that encouraged me to do whatever I needed to do to recover, so I felt very fortunate.

Current dietary advice for patients seems to include a message to “eat whatever you want” or to “just get through it”, however, it was suggested by a few women that this was not a very positive message.

Heather: When you’re in treatment, they just said “eat whatever you want, just eat, you want to have 10 donuts, eat 10 donuts” and I thought, yeah right.

Ursala: They said, “you eat anything that you want to eat”. That was bad to tell me, you know for when I started feeling better.

Connie: I didn’t want my weight to go up for sure. I saw it as an opportunity to make some changes that I could carry through after chemo and treatments were done.

Findings from this study suggest that proactive advice for preventing weight gain during treatment may be appropriate and well received. Although several women acknowledged that
they may or may not have been able to adhere to weight management advice in the face of treatment-related side effects, they would have appreciated more information at the time. It is clear however, that weight management guidelines should be flexible and delivered with a sensitivity and respect for the challenges that women face as they are undergoing treatment.

In keeping with the constructivist theoretical position adopted for this research, it is important to keep in mind that each woman’s experience with chemotherapy will be different. While there were common themes around diet and eating patterns and factors associated with food intake during treatment, there were many different perspectives and behavioral responses, reflecting individual reactions to cancer and its treatment. Moreover, with much variability in psychosocial and treatment-related factors affecting food intake, it was apparent that *a priori* “sensitizing concepts” should be held lightly, to ensure that the theoretical framework that was generated was grounded in the reality that breast cancer survivors “construct” for themselves.

**Personal Post-Script**

The women who participated in this study appeared to be wholly invested in the research, exhibiting a level of commitment that I believe influenced the quantity and quality of the data that were obtained. The opportunity for “kitchen table” conversation, where I often had the privilege of meeting significant others and children, and their willingness to openly share their personal stories, provided an atmosphere for comfortable discussion and rich context.

Most of the participants seemed very eager to provide as much information as possible. It is noteworthy that many women appeared to be more at ease discussing how unwell they felt during treatment as the interviews progressed, suggesting the importance of developing a comfortable rapport. The interviews usually approached or exceeded the 90 minute target, with participant questions and concerns interspersed throughout. In addition, a few women offered
their personal diaries from the treatment period, in the event that additional information contained there would assist with the research. Food records were very detailed, often accompanied by food labels and/or personal recipes.

In the days and weeks following the interviews, I received several follow-up emails indicating how much they had enjoyed the opportunity to participate, and expressing interest in hearing about the results. In one case, I received an email update (with pictures) from a participant who wanted to share that she had accomplished a major lifestyle goal she had set for herself during treatment. This high level of interest and commitment to provide quality data reflected a strong motivation to “give back” in a way that might assist future breast cancer patients, and provided personal insights that could only derive from a qualitative approach.
REFERENCES


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Appendix A – Pilot Study Overview and Preliminary Findings

Information Letter: Overview of Methods and Procedures

Nutrition and Metabolic Evaluation of Breast Cancer Patients

Principal Investigator: Dr. Marina Mourtzakis  
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Co-Investigators:  
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Dr. Mala Bahl, Grand River Hospital  
Ms. Caryl Russell, University of Waterloo

Student Investigators  
Megan Bedbrook, University of Waterloo  
Vivienne Vance, University of Waterloo

Purpose of Study:

There are several changes that occur in your body when you are receiving treatment for breast cancer. You have been asked to take part in a research study designed to evaluate the nutrition and metabolic changes that occur with exercise training in breast cancer patients. Patients with breast cancer who receive chemotherapy tend to gain fat and lose lean mass. These changes may increase your risk of cardiovascular disease and diabetes. Exercise can reduce the risk factors leading to these diseases. Many breast cancer patients exercise to reduce fatigue and enhance their quality of life; however, the metabolic benefits of exercise in breast cancer patients are not known. During the time that you are receiving treatment, we will evaluate the changes that take place in your nutrition and metabolism. We will be studying 20 breast cancer patients who are receiving chemotherapy. Of these 20 patients, 10 will undergo exercise training for 16 weeks while 10 will be studied in the same way without undergoing an exercise program. You have an equal chance of being in either the exercise training or non-exercise training group. If you are in the non-exercise group, you will have the option, at the end of the study, to receive a similar exercise training program through the Well-Fit Centre at the University of Waterloo that will be 12 weeks long and be customized to activities that you enjoy. The information from this study will help us design future studies to better understand the benefits of nutrition and exercise for patients with breast cancer.

Procedures Involved in this Study for All Participants:

If you participate in this study, regardless of whether you are in the exercise or non-exercise group, you will be scheduled for nutrition, blood and fitness evaluations at the University of Waterloo at 3 different times over the 16-week duration of the study. You will have the following tests and procedures
On each of the 3 occasions (Weeks 0, 8, and 16), the total time that the evaluation will require at the Well-Fit Centre is 4.5 hours as well as 2 hours for the completion of the 3-Day Food Diary and Physical Activity Surveys prior to your evaluation at wks 0, 8 and 16.

If you are in the exercise group, you will also participate in a 16-week exercise training program (3 sessions / week for 1 to 1 ½ hours each session) and you will be supervised by an exercise physiologist at each session at the Well-Fit Centre at the University of Waterloo.

**Explanation of Procedures and Risks for All Participants:**

For the evaluations at Weeks 0, 8, and 16, you will be asked to come to the Well-Fit Centre at the University of Waterloo (See attached brochure or go to www.uwfitness.uwaterloo.ca) after an overnight fast (about 8 hours without food or drink except water). You will be able to take your usual medication in the morning. Upon arrival at the Well-Fit Centre, you will be asked if you have taken any medications that morning and then one of our personnel will take your weight and height (without shoes). The amount of fat in your body will also be estimated using skin-fold test with callipers and girth measurements.

**3-Day Food Diary & Nutritional Consult (~30 minutes per day):**

The purpose of the dietary analysis is to examine the quality and quantity of nutrients that are you eating or drinking. You will be provided with instructions and material to complete a 3-day food diary (~30 minutes per day). To complete the food diary, you will be asked to record everything you eat and drink for a period of 3 days (2 weekdays, 1 weekend day). You will also need to indicate the medications, vitamins and supplements that you are taking. It is important that you do not try to alter your diet during this period of time. You should eat as you would normally do if you were not recording your nutritional intake.

A sample day is provided with the instructions so that you can see the amount of detail needed in filling out the diary. During the time that you are completing the dietary record, we will contact you by telephone to check if you have any questions about the food diary. After you have completed the document, you will be asked to bring it with you to your next scheduled visit at the University of Waterloo.

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<thead>
<tr>
<th>Procedure</th>
<th>Week 0 (beginning of the study)</th>
<th>Week 8</th>
<th>Week 16</th>
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<tr>
<td>3-Day Food Diary</td>
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<tr>
<td>Physical Activity Surveys</td>
<td>X</td>
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<tr>
<td>Blood Test</td>
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<td>Oral Glucose Tolerance Test</td>
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<td>Snack</td>
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<tr>
<td>Incremental Exercise Test</td>
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<tr>
<td>Strength Test</td>
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**Physical Activity Surveys (30 minutes):**

You will be asked to complete 2 physical activity surveys to provide us with information about your level of activity during the time that you are recording information for your food diary. This will allow us to understand the amount of energy you use compared to the amount of food energy you take in. Please do not alter your activity during this period of time. After you have completed the document, you will be asked to bring it with you to your next scheduled visit at the University of Waterloo.

**Blood Tests and Oral Glucose Tolerance Test (about 3 hours 30 minutes):**

You will be asked to arrive at the Well-Fit Centre after an overnight fast (about 8 hours without food or drink except water). We encourage you to drink water the morning of these tests. You may take your medications the morning of the tests but please inform us of the medications that you are taking. You will have your finger pricked to attain a small amount of blood (a couple of drops) for a quick measure of your blood glucose. If your fasting blood glucose is above 7.0mM, we will not be able to carry out the study and we will also notify your physician of this result. If your fasting blood glucose is above 6.0mM, but less than 7.0mM, you will still be able to participate in the study, but we will make your doctor aware of your results. After the finger prick, a catheter attached to saline will be inserted by someone who is certified to draw blood for a series of blood samples. The catheter will be inserted into a suitable vein in the forearm. A blood sample (~20 mL which is about 1.5 tablespoons) will be taken for the analysis of several different compounds that are not routinely measured at the cancer clinic. The sample will provide us with information about how your metabolism is changing during treatment. After this initial blood sample, a second sample will be taken 30 minutes later (about 5 mL or 1 teaspoon) and this will be the baseline for the oral glucose tolerance test. An oral glucose tolerance test will allow us to determine how sensitive your body is to sugar. You will then ingest a drink (orange-flavoured) that contains 75g of sugar. For this test, a blood sample of about 5 mL (1 teaspoon) will be taken at 8 additional time points over a 3 hour period. The insertion of a catheter may, on occasion, result in some bruising or discomfort at the site of insertion.

**Snack Break (15 minutes):**

A small snack will be provided to you after you have completed the blood tests and prior to the exercise tests. One of our personnel will meet with you to review your food diary. When a food diary is completed in detail, valuable information is obtained and appropriate recommendations for changes in your diet can be made.

**Incremental Exercise Test (20 minutes):**

The risks of doing incremental exercise to your functional limit are very similar to the risks of doing heavy voluntary exercise. There is a very slight chance that an apparently healthy individual will have a cardiovascular complication that has not been previously detected during normal medical examinations. There is no way to predict this potential complication.
**Heart Rate** – Heart rate will be continuously monitored by an electrocardiograph (ECG) by placing 3 spot electrodes on the skin surface. The electrodes are normally placed in the lower portion of the chest. This procedure is entirely safe. In a very small group of individuals, a skin rash might occur due to the adhesive on the electrodes. There is no way of knowing this ahead of time. The rash, if it develops, will resolve itself within a day or so. However, you are asked to avoid scratching any rash and to keep it clean.

**Oxygen Uptake** – We measure the amount of oxygen you take from the air you are breathing by having you breathe through a face mask. Attached to the face mask will be a sensor to determine the volume of air that moves into and out of your lungs, and a sample line that takes a small quantity of the air to a gas analyzer system. The facemask and the volume measurement device are sterilized before each person’s use to eliminate any risk of spread of infection. If you are allergic to rubbing alcohol, then you should not participate in this study.

**Incremental Exercise** – This test will begin with a four-minute warm-up period in which you will pedal against a very low resistance. The work rate will then increase progressively but you will not be asked to reach your maximal effort. Instead, 2-3 submaximal efforts will be recorded. The total test duration will be approximately 10-15 minutes. For participants who will be in the exercise training program, this test will allow us to design an exercise program and to evaluate your progress over 16 weeks.

Incremental exercise does have some risk. We will not include individuals who have high blood pressure (resting diastolic pressure over 90 mmHg during a measurement in our lab) or who have been told by their doctor that they have some form of cardiovascular disease. It is impossible to predict whether apparently healthy individuals might have some previously undetected cardiovascular disease that might cause a heart attack or arrhythmia (irregular heart beat) during strenuous exercise. The Well-Fit Centre is equipped with an Automated External Defibrillator on site. In the case of a medical emergency, all researchers and Well-Fit Centre staff have First Aid training.

The sensation of fatigue that you experience during incremental exercise will probably be similar to that experienced previously during some voluntary activities. The sensation of fatigue should quickly disappear after the test.

**Stopping the Exercise Session:**

If you experience any sensation that appears to be unusual to you (i.e. not what you would expect during voluntary maximal exertion), then you can stop the exercise and inform the researchers of this.

**Strength Test (about 25 minutes):**

This test will begin after your muscles have warmed up following your incremental exercise test. We will test the muscles of your upper-body and lower-body for their maximal strength. You will be shown how to perform each exercise safely. You will start with a relatively low weight that you can easily and safely lift one time (based on your reported activity levels). You will have 1-2 minutes break before we add weight gradually and ask you to lift the weight one
time, correctly and safely. You may experience some soreness and fatigue in the muscles that were tested, but this will disappear within a couple of days after the test. This information will allow us to design an exercise training program and test your progress.

Treatment Evaluation

When you see your doctor at the Grand River Hospital for your routine follow-up appointment while you are receiving chemotherapy, your doctor will ask you a series of questions and will also provide us with your blood analysis from your treatment evaluation.

Explanation of Procedures and Risks for Participants in the Exercise Training Group

Exercise Training (1 - 1 ½ hours per session; 3 sessions per week):

The exercise training program will take place 3 times / week and will consist of 30 minutes of cardiovascular exercise (either bike or treadmill depending on your preference) at 60% of your maximal performance. The rest of the exercise session will consist of lifting weights at 60% of your maximal strength (3 sets of 10 repetitions for each exercise with 1-2 minute break between sets). If you experience any sensation that appears to be unusual to you, then you can stop the exercise and inform the researchers of this. You may feel some soreness in your muscles for the first week of this exercise program, but this will be less or may disappear entirely after the first 2 weeks of the program.

Heart rate will be monitored by chest band heart rate monitor for the duration of the exercise training protocol. The band is placed in the lower portion of the chest. This procedure is entirely safe. The band is sterilized between uses. In the case of a medical emergency, all researchers and Well-Fit Centre staff have First Aid training.

Personal Benefits of Participation:

Participation in this study may or may not be of personal benefit to you. Exercise has been shown to reduce fatigue while receiving chemotherapy. Based on the evaluations done in this study, we will provide you with personalized nutritional information that may or may not be helpful in managing your dietary intake and weight. However, based on the results of this study, it is also hoped that, patient care can be improved in the future.

Additional Instructions:

- Participants are asked to refrain from drinking alcohol in the 24-hour period immediately prior to scheduled evaluations at Weeks 0, 8 and 16.
- For the blood test and oral glucose tolerance test, please arrive following an overnight fast (about 8 hours without food or drink except water). We encourage you to drink water the morning of these tests. You may take your medications the morning of the tests but please inform us of the medications that you are taking.
• The 3-Day Food Diary should include 2 weekdays and 1 weekend day. Please record everything you eat and drink as precisely as possible.
• The Physical Activity Surveys should be completed during the time that you complete your 3-Day Food Diary.
• Regardless of which group you are in (exercise or non-exercise group), for your evaluations at Weeks 0, 8 and 16, please wear comfortable pants/shorts, a short sleeve shirt and running shoes. If you are part of the exercise training group, you will also be asked to wear comfortable pants/shorts, a short sleeve shirt and running shoes for each of your training sessions.

Medical Screening Form:

This questionnaire asks some questions about your health status. This information is used to guide us with your entry into the study. Contraindications to participation in this study include any injury that makes exercise uncomfortable, any kidney problems, known diabetes, or any cardiovascular diseases including bleeding disorders, or any respiratory diseases.

Participation in the study:

You may choose not to participate in this study. Choosing not to participate in this study will not compromise the medical care that you receive from your doctor.

You may withdraw from this study at any time without penalty. You may be asked why you have chosen to withdraw so that the researchers have an understanding of how to improve enrolment in this study. To withdraw from the study, indicate this to the researcher or one of the research assistants by saying, "I no longer wish to participate in this study". Withdrawing from the study will not compromise the medical care that you receive from your doctor.

Confidentiality and Security of Data:

Identifying health information will be collected during this study. Information from your medical records including: date of birth, cancer diagnosis, current medications, treatments and blood analysis done as part of your routine medical care for the duration of this study. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances.

Your identifiable health information may need to be inspected from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:
  • Tri-Hospital Research Ethics Board
  • University of Waterloo Research Ethics Board
To ensure the confidentiality of individuals’ data, each participant will be identified by a participant identification code known only to the principal investigator and her research assistants. If we identify abnormal results from your blood glucose and lipid tests, we will contact your doctor to make him or her aware of these results. Any publications or reports that result from this study will be presented as group data. In the case where individual data is presented and data that is analyzed by students, your information will not be identifiable. Your information will be stored in Dr. Marina Mourtzakis’ locked office (BMH building at the University of Waterloo) and secure computer. The information will be stored for an indefinite time but the links that identify you will be destroyed after 10 years.

Although absolute confidentiality can never be guaranteed, we will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

As a participant of this study, you have the right to ask the researchers about the data being collected about you for the study and the purpose of this data. You also have the right to ask the study doctor to let you see your personal information and to make any necessary corrections to it.

**Participant Feedback:**

After the study is completed, you will be provided with a feedback sheet that will include a summary of your dietary intake and exercise results. We will discuss your nutrition and exercise results and provide recommendations for your nutritional and activity needs.

**Remuneration:**
Your participation in this study is greatly appreciated and while monetary remuneration will not be provided, we will cover:

- the cost of parking for your scheduled visits to the University of Waterloo,
- the cost of a nutrition and exercise consult

For patients who were in the non-exercising group, they will be offered a similar exercise program when the study is completed. This program will be 12 weeks long and suited to the activities that the patients enjoy at the Well-Fit Centre.

**Contact Information:**
If you have any questions about the study at any time, please contact Dr. Marina Mourtzakis at her office 519-888-4567 ext. 38459.

**Concerns about Your Participation:**

I would like to assure you that this study has been reviewed and received ethics clearance through the Office of Research Ethics at the University of Waterloo and the Tri-Hospital Research Ethics Board. Please be aware that you may contact the Director, Office of Research Ethics at the University of Waterloo, Dr. Susan Sykes at 519-888-4567 ext. 36005 or the Chair of the Tri-Hospital Research Ethics Board, Dr. Michael Coughlin at 519-749-4300 ext. 5367. The final decision about participation is yours.
Preliminary Findings

Mean Energy Intake by Treatment Week (n=6)

Mean Energy Intake by Weeks from Treatment (n=6)
Appendix B - Chemotherapy Protocols for Early Stage Breast Cancer

Classification of Chemotherapy Drugs Used to Treat Breast Cancer

<table>
<thead>
<tr>
<th>Class</th>
<th>Mode of Action</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating Agents</td>
<td>damages the proteins that control growth in the genes of the tumor cell</td>
<td>cyclophosphamide</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>acts as false building blocks in the genes of cancer cells, causing cell death as it prepares to divide</td>
<td>5-flourouracil</td>
</tr>
<tr>
<td></td>
<td></td>
<td>gemcitabine</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>inhibits gene replication</td>
<td>doxorubicin, epirubicin</td>
</tr>
<tr>
<td>Antimiotic Agents</td>
<td>prevents genes from reproducing themselves during cell division</td>
<td>vincristine, vinorelbine</td>
</tr>
<tr>
<td>Antimicrotubule</td>
<td>interferes with cell structure and cell division</td>
<td>taxol, taxotere</td>
</tr>
</tbody>
</table>

Common Chemotherapy Combinations Used to Treat Breast Cancer

AC – doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan, Procytox)
- usually given every 21 days for 4 cycles
- treatment lasts ~3-4 months

AC + T – doxorubicin, cyclophosphamide + paclitaxel (Taxol) or docetaxel (Taxotere)
- usually given every 21 days – 4 cycles of AC, followed by 4 cycles of paclitaxel or in the case of docetaxel, every 21 days for 6 cycles
- Note: AC with docetaxel often requires colony-stimulating factor drugs (i.e. filgrastim (Neupogen) treatment lasts ~ 4-6 months

FAC (or CAF) – cyclophosphamide (orally or IV), doxorubicin and 5-flourouracil (5-FU, Adrucil)
- usually given every 21 days for 6 cycles
- treatment lasts ~4-6 months
- Note: when cyclophosphamide is given orally, FAC is usually given every 28 days for 6 cycles

CEF – cyclophosphamide (orally), epirubicin (Ellence) and 5-flourouracil
- usually given every 28 days for 6 cycles
- treatment lasts ~ 4-6 months

FEC - 5-flourouracil, epirubicin and cyclophosphamide (IV)
- usually given every 21 days for 6 cycles
- treatment lasts ~ 4-6 months

CMF – cyclophosphamide (orally or IV), methotrexate and 5-flourouracil
- usually given every 28 days for 6 cycles
- treatment last ~ 6 months
- Note: this protocol is now used rarely

In some cases, single drugs including vinorelbine (Navelbine), capecitabine (Zeloda), paclitaxel (Taxol), docetaxel (Taxotere) or gemcitabine (Gemzar) are used to treat metastatic or recurrent disease

Adapted from Canadian Cancer Society (2009), American Cancer Society (2009), Breastancer.org (2008)
PARTICIPANTS NEEDED

RESEARCH IN NUTRITION AMONG WOMEN WITH BREAST CANCER

ARE YOU A BREAST CANCER SURVIVOR?

Have you completed CHEMOTHERAPY TREATMENTS within the LAST 12 MONTHS?

As a participant in this study, you would be asked to:

- Participate in an individual interview (approximately 60-80 minutes) to discuss the unique challenges associated with chemotherapy treatment in relation to food intake and weight management.

- Complete 2 questionnaires related to ongoing side effects of treatment.

- Record your food intake for 3 days.

Participants will receive a personal nutritional assessment, $30.00 honorarium and a breast cancer bracelet in appreciation for your time.

For more information or to volunteer for this study, please contact:

Vivienne Vance, R.N., MSc, PhD (Candidate)
Department of Health Studies & Gerontology
University of Waterloo
Telephone: (519) 654-2538
Email: vavance@uwaterloo.ca

This study has been reviewed and received clearance through the University of Waterloo Office of Research Ethics.
Appendix D: Sample Newspaper Advertisement

ARE YOU A BREAST CANCER SURVIVOR?

Have you completed chemotherapy treatments within the last 12 months?

PARTICIPANTS NEEDED: Research in Nutrition among Women with Breast Cancer (stage I - IIIA).
As a participant in this study, you would be asked to participate in an individual interview (approximately 60-80 minutes) to discuss the unique challenges associated with chemotherapy treatment in relation to food intake and weight management, complete 2 questionnaires related to ongoing side effects of treatment and record your food intake for 3 days. Participants will receive a personal nutritional assessment, a $30.00 honorarium and a breast cancer bracelet in appreciation for their time.
For more information or to volunteer for this study, please contact:

Vivienne Vance, University of Waterloo at (519) 654-2538 or vavance@uwaterloo.ca.

"This study has been reviewed and received clearance through the University of Waterloo Office of Research Ethics.

UNIVERSITY OF WATERLOO
Appendix E: News Release – UW Daily Bulletin

UNIVERSITY OF WATERLOO

WATERLOO | DAILY BULLETIN

Monday, March 7, 2011

- Project studies chemo patients’ eating
- With four weeks to go in the winter term

Editor:
Chris Redmond
Communications and
Public Affairs
bulletin@uwwaterloo.ca

Project studies chemo patients' eating

by Michelle Douglas-Mills, faculty of applied health sciences

Waterloo researchers want to hear from women who have recently completed treatment for breast cancer to help better understand the unique food intake and weight management challenges associated with chemotherapy.

Unlike with some cancers, weight gain is a common and persistent problem for many breast cancer survivors, both during treatment and in the months and years after diagnosis.

"Most of the women I have spoken to have expressed considerable disruption to their normal eating patterns during chemotherapy treatments and many have experienced significant weight gain," explains doctoral student Vivienne Vance of Waterloo’s department of health studies and gerontology, who is leading the study. She’s at centre in the photo of a team from the "Run for the Cure" breast cancer fund-raiser last October.

"We are very concerned about the potential health consequences of weight gain and the additional distress that changes in body weight may cause, at a time when breast cancer patients are already under a great deal of stress," Vance says.

Changes in eating patterns and energy expenditure — whether the result of stress, fatigue, or other side effects of treatment — can contribute to weight gain. Research suggests that loss of lean tissue in some women may exacerbate the issue. When combined with gains in body fat, these changes in body composition increase the risk of chronic conditions including cardiovascular disease and diabetes and may lead to treatment complications and poor clinical outcomes.

While weight gain is a problem for many breast cancer survivors, not all are affected. Vance and her advisor, Rhona Hanning, are exploring possible differences in the experience of chemotherapy and food intake for women who gain weight compared to
those who do not gain weight during and after treatment. They hope their findings will help other women and their health care teams better understand food issues related to treatment and the role that changes in diet may have in promoting weight gain.

They are seeking female breast cancer survivors who have completed chemotherapy within the last 12 months. The study involves a personal interview, approximately 60 to 80 minutes, to discuss the challenges associated with chemotherapy treatment in relation to food intake and weight management. Participants will be asked to complete two questionnaires related to ongoing side effects of treatment and to record their food intake for three days. In appreciation, participants will receive a $30 honorarium, a breast cancer bracelet, and the opportunity for a personal nutritional assessment. The study has been reviewed and received ethics clearance through Waterloo’s office of research ethics. Anyone wanting more information can e-mail vavance@uwaterloo.ca or call 519-654-2538.

Approximately one in nine Canadian women will develop breast cancer in her lifetime, and one in 28 will die of the disease. While improved screening and advances in treatment have resulted in a decline in breast cancer mortality, the growing population of breast cancer survivors — at least 166,000 Canadian women and 2.5 million American women — are faced with aftereffects of treatment and questions about how best to promote disease remission and long-term health: questions Vance and Hanning hope to help answer.

“We believe that breast cancer survivors can provide important insights that could lead to the development of more helpful diet and weight management guidelines, improvements in patient care, and a healthier future,” Vance says.
Appendix F– Information Letter

Relationships among Psychosocial Factors, Treatment-Related Side Effects, Dietary Intake and Weight Gain in Women Treated with Adjuvant Chemotherapy for Early Stage Breast Cancer

Principal Investigator:  Dr. Rhona Hanning  
Department of Health Studies and Gerontology, University of Waterloo  
(519) 888-4567, ext 35685 - rhanning@uwaterloo.ca

Co-Investigators:  Dr. Marina Mourtzakis, University of Waterloo  
Dr. Sharon Campbell, University of Waterloo  
Dr. Linda McCargar, University of Alberta

Student Investigator:  Vivienne Vance, MSc., PhD (Candidate)  
Department of Health Studies and Gerontology, University of Waterloo  
(519) 654-2538 - vavance@uwaterloo.ca

Purpose of Study:

Weight gain is a common problem for many breast cancer survivors during treatment and in the months and years after diagnosis. Weight gain is distressing for most women and may lead to an increased risk of heart disease, diabetes and disease recurrence. Although it appears that many women experience changes in diet during and after treatment, we do not know if these changes play a role in weight gain after diagnosis. We are very interested in gaining a better understanding of the unique challenges associated with chemotherapy in relation to nutrition and weight management in breast cancer survivors.

You have been asked to participate in a research study designed to investigate changes in your food intake and eating patterns during and after treatment and to identify factors that may have influenced these changes. We will be interviewing approximately 30 breast cancer survivors within 12 months of completing chemotherapy treatment, including those who have gained weight and those who have not gained weight, since diagnosis. The information from this study will help us to develop nutrition guidelines and programs to support healthy eating and weight management during and after treatment.

Procedures Involved in this Study:

If you participate in this study, you will be scheduled for a 60-80 minute individual interview with the student investigator. Interviews will take place in your home or at the University of
Waterloo, based on your personal preference. In this interview, you will be asked to discuss your experience of chemotherapy, in terms of food intake and eating patterns and to identify factors which may have influenced changes in your diet during treatment. You will also be asked to complete two brief questionnaires related to quality of life and ongoing side effects of treatment. The first questionnaire will ask you to indicate the extent to which you have been bothered by 30 common physical and emotional symptoms in the past week. For example: “Have you been bothered in the past week by lack of appetite, nausea, difficulty sleeping, irritability, anxiety - not at all, a little, quite a bit or very much”. The second questionnaire will ask you to rate the intensity and duration of fatigue and how much fatigue has interfered with your daily activities, during the previous week. In addition, you will be asked to identify any changes in diet that you have made since the completion of treatment and to discuss changes in physical activity and any concerns you have regarding weight management since diagnosis. A brief background questionnaire will collect information on age, marital status, education and employment, as well as medical (date & age at diagnosis), treatment (surgery, chemotherapy, radiation, other medications) and weight history (weight change since diagnosis). Current weight will be measured at the time of interview. You may choose to not answer any interview question or questionnaire item, at your discretion.

At the completion of the interview you will be provided with a diet record and asked to record everything you eat and drink for a period of 3 days (2 weekdays, 1 weekend day). The purpose of the diet record is to examine the quality and quantity of nutrients in your current diet. Each day of recording is expected to take about 30 minutes in total. Detailed written instructions and a “sample day” will be provided. It is important that you do not alter your diet during the recording period – simply eat as you would normally eat. Arrangements will be made for your completed diet record to be picked up at your home, within one week. During the time that you are recording your food intake, we will contact you by telephone to see if you have any questions or concerns.

Follow-Up Contact:

Once your personal information is analyzed, we may re-contact you to clarify any information and ensure that our interpretation of your interview responses accurately reflects your experience. You may choose at that time to participate or not participate in further discussion.

Explanation of Benefits and Risks:

Participation in this study may or may not be of personal benefit to you. During the interview, you will have opportunity to discuss any concerns you have about your current diet and exercise patterns and written resources on healthy eating and exercise will be provided, at your request. Based on your 3-day food record, we will provide you with a personalized nutrition assessment and a summary of the research findings at the end of the study, which may be helpful in managing a healthy diet and a healthy body weight. It is hoped that the findings from this study will improve patient care in the future. We do not anticipate any risks associated with participation in this study.
Confidentiality and Security of Data:

Personal health information will be collected during this study. Direct access to this information will be restricted to the researchers who are directly involved in the study. To ensure the confidentiality of personal data, each participant will be identified by a participant identification code, known only to the listed investigators. Any publications or reports that result from this study will be presented as group data and your personal information will not be identifiable. Your information will be stored in a locked cabinet and secure computer. The information will be stored for an indefinite time but the links that identify you will be destroyed after 10 years. As a participant in this study, you have the right to ask the researchers about the data being collected about you for the study and the purpose of this data. You also have the right to ask the student investigator to see your personal information and to make any necessary corrections to it.

Withdrawal from the Study:

You may withdraw from this study at any time without penalty. You may be asked why you have chosen to withdraw so that the researchers have an understanding of how to improve enrolment in this study. To withdraw from the study, please indicate this to the researcher by saying, "I no longer wish to participate in this study".

Participant Feedback:

At the completion of the study, you will be provided with a personalized nutritional assessment, based on your 3-day food record, and a summary of the research findings.

Remuneration:

All participants in this study will receive a small honorarium of $30 and a breast cancer bracelet, as a token of appreciation. The cost of parking ($4) will be covered, for those opting to be interviewed at the University of Waterloo.

Contact Information:

If you have any questions or concerns about the study at any time, please contact:
- Vivienne Vance (519) 654-2538 - vavance@uwaterloo.ca or
- Dr. Rhona Hanning (519) 888-4567 ext. 35685 - rhanning@uwaterloo.ca

Ethics Review:

This study has been reviewed and received ethics clearance through the Office of Research Ethics at the University of Waterloo. Please be aware that you may also contact the Director, Office of Research Ethics, University of Waterloo Dr. Susan Sykes (519) 888-4567 ext. 36005 ssykes@uwaterloo.ca with any concerns or questions about your participation in this study.
Appendix G - Consent Form

CONSENT FORM

I agree to participate in a research study being conducted by Vivienne Vance, PhD (Candidate) under the direction and supervision of Dr. Rhona Hanning, Dr. Marina Mourtzakis and Dr. Sharon Campbell of the University of Waterloo and Dr. Linda McCargar of the University of Alberta.

Yes  No

I have made this decision based on the information I have read in the information letter. All of the procedures and any risks and benefits have been explained to me. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted. I am aware that I may withdraw from the study or decline answering any interview question or questionnaire item without penalty at any time by advising the researcher of this decision.

This project has been reviewed and received ethics clearance by the Office of Research Ethics at the University of Waterloo. I am aware that I may contact the Director, Office of Research Ethics at the University of Waterloo, Dr. Susan Sykes at 519-888-4567, ext. 36005 or Dr. Rhona Hanning of the Department of Health Studies and Gerontology (519-888-4567, ext 35685) if I have any questions or concerns resulting from my involvement in this study.

Printed Name of Participant  Signature of Participant  Date

__________________________  ___________________________  ____________________

Printed Name of Witness  Signature of Witness  Date

__________________________  ___________________________  ____________________

Printed Name of Investigator  Signature of Investigator  Date

__________________  ______  ___________________________  ____________________
Appendix H - Demographic/Medical Questionnaire

Demographic/Medical Questionnaire

Participant #: ___________________________ Date: ___________________________

Age: ______

Ethnicity: White ______ Black ______ Hispanic ______ Asian ______ Other ______

Marital status: Single ______ Married ______ Divorced/Separated ______ Widowed ______

Education - highest level completed: ________________________________________

Employment Status:

Working outside the home before diagnosis? Yes ______ No ______ PT ______ FT ______

Working outside the home during treatment? Yes ______ No ______ PT ______ FT ______

Working outside the home currently? Yes ______ No ______ PT ______ FT ______

Length of time away from work (if applicable) ____________________________

Medical/Treatment History

Age at Diagnosis: ___________________________ Stage at Diagnosis: ____________

Surgery: Yes ______ No ______ Type: ________________________________

Chemotherapy: Yes ______ No ______ Type: ____________________________ Don’t know ______

Date of Last Treatment: ____________ Location of Treatments: ________________

Number of Cycles ______ Total Duration ____________________________

Other Medications: Yes ______ No ______ Type: ____________________________ Don’t know ______
  (e.g., Decadron/Neupogen)

Radiation: Yes ______ No ______ Number of Treatments ______ Total Duration ______

Hormonal Therapy: Yes ______ No ______ Type: ____________________________ Don’t know ______
  (e.g., Tamoxifen, Aromatase Inhibitors)

Menopause Status: At diagnosis: Pre _____ Peri _____ Post _____ Current: Pre _____ Post _____

Weight History: In the year before diagnosis: Weight stable______ Weight Gain______ Weight Loss______

Weight at Diagnosis______________________ Weight at the Completion of Treatment______________________

Current Weight: ___________________________ Height: ___________________________
Appendix I - Interview Script

Interview Script - Study 1

Participant #: ___________________________ Date: ___________________________

Introduction:

Thank you for agreeing to meet with me today. We are very interested in gaining a better understanding of the unique challenges associated with chemotherapy in relation to dietary intake among women treated for early stage breast cancer. We are especially interested in learning about any changes in your food intake and eating patterns during treatment and identifying factors that may have influenced these changes. As you may know, weight gain is a problem for many women during and after treatment but we don’t really understand yet, if and how changes in diet after diagnosis might play a role. Because of this, we would also like to explore if there are differences in the experience of chemotherapy and nutrition related issues for women who gain weight compared to women who do not gain weight. The information from this study will help us to develop nutrition guidelines and programs to support healthy eating and weight management during and after treatment. I believe that women who have been through breast cancer treatment can provide much needed insight and I am looking forward to hearing about your experience.

1. From the perspective of food intake and eating patterns, can you tell me about your experience during chemotherapy treatment?

Probe for: a) changes in appetite?
   b) food cravings?
   c) changes in eating patterns?
      (frequency, time of day, increase or decrease in intake of particular foods or food groups, “comfort” foods or beverages?)
   d) usually eat alone with others, prepare food for yourself/others?

2. During treatment, compared to your normal diet before diagnosis, do you feel you ate:

   the same amount as you would usually eat? _______

   more than you would usually eat? _______

   less than you would usually eat? _______

Probe for: a) changes in intake relative to treatment days?
   b) duration of acute treatment effects on diet
   c) any consistent patterns in intake within treatment cycles?
   d) changes in intake across treatment?

3. Next I’d like to explore how you were feeling during treatment and what factors you think might have influenced your food intake and eating patterns during this time.

Probe for: a) treatment-related side effects?
   (nausea/vomiting, changes in taste/smell, constipation/diarrhea, mouth sores, heartburn)
   b) fatigue?
   c) emotional distress, mood, coping style
   d) family/social support – who shopped, cooked?
   e) burden of treatment (diagnostic tests, consults, treatments)? – concerns re: loss of income?

Note: link to question #1 – e.g., you mentioned that you experienced nausea for a few days after treatment. Can you elaborate on this (frequency, severity, duration) and talk about how this side effect influenced your food intake?
4. During treatment, compared to your normal physical activity level before diagnosis, do you feel you:

- were as active as usual? __________
- were more active than usual? __________
- were less active than usual? __________

Probe for: a) changes in work, leisure activities and structured exercise – determinants?
- a) changes in activity relative to treatment days?
- b) duration of acute treatment effects on activity
- c) any consistent patterns in activity within treatment cycles?
- d) changes in activity across treatment?

Note: link to employment status – demographic/medical questionnaire

5. Were you aware when you started treatment that weight gain might be an issue?

Probe for: a) source of information? (physician, nurse, dietitian, other patients, patient materials, websites)
- b) weight related advice/recommendations (medical, family/friends)

6. Were you concerned about weight control during treatment? Any weight control strategies?

Probe for: a) experience with weight change (loss, gain, stable)
- b) reaction to weight change – distress, health concerns?
- c) previous dieting? weight management concerns?
- d) weight management efforts during treatment?
- e) availability and utilization of dietary supportive services?
Interview Script - Study 2

Participant #: ___________________________ Date: ___________________________

Introduction
The next section of our interview involves collecting information about how you’re feeling, now that you’ve completed chemotherapy treatments. We are also interested in your current food intake and any changes you may have made in your diet since the completion of treatment.

1. Rotterdam Symptom Checklist – in this brief questionnaire (31 items) you will be asked about your current symptoms. For each symptom, please circle the answer most applicable to you to indicate the extent to which you have been bothered by it during the past week. Provide example.

   Completed: yes_________ no:_________
   If not completed: provide brief explanation

2. Fatigue Symptom Inventory – this questionnaire asks you more specifically, to rate the intensity and duration of fatigue during the past week and to indicate the extent to which fatigue has interfered with your normal activities. There are 13 items in total. Provide example.

   Completed: yes_________ no:_________
   If not completed: provide brief explanation

3. Since the completion of treatment compared to your normal diet before diagnosis, do you feel you have been eating:
   the same amount as you would usually eat?_________
   more than you would usually eat?_________
   less than you would usually eat?_________

4. Since diagnosis have you made any changes to the kinds of foods you eat? Yes_______No_______
   If yes, were these changes initiated: During treatment?_______ Since the completion of treatment?_______

5. If yes, probe for specific changes re: food groups/dietary components
   1) Fruits & Vegetables: introduced_______ increased_______ reduced_______ eliminated_______
   2) Legumes: introduced_______ increased_______ reduced_______ eliminated_______
   3) Meat: introduced_______ increased:_______ reduced_______ eliminated_______
   Change in type?____________________________________

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4) Fish: introduced ______ increased ______ decreased ______ eliminated ______

5) Dairy products: introduced ______ increased: ______ reduced ______ eliminated ______
   Change in type?

6) Breads/Cereals: introduced ______ increased ______ decreased ______ eliminated ______
   Change in type?

7) Desserts: introduced ______ increased ______ decreased ______ eliminated ______

8) Alcohol: introduced ______ increased ______ decreased ______ eliminated ______

9) Supplements: introduced ______ increased ______ decreased ______ eliminated ______
   Change in type?

6. Since the completion of treatment, compared to your normal physical activity level before
diagnosis, do you feel you:
   have been as active as usual? ______
   have been more active than usual? ______
   have been less active than usual? ______

Probe for: a) changes in work, leisure activities and structured exercise – determinants?
   b) changes in activity since the completion of treatment compared to during treatment
   c) current level of exercise? regular? (type, frequency, duration)

7. Have you been concerned about weight control since the completion of treatment?
   Any weight control strategies?

Probe for: a) experience with weight change since the completion of treatment (loss, gain, stable)
   b) reaction to weight change – distress, health concerns?
   c) weight management efforts since the completion of treatment?
   d) availability and utilization of dietary supportive services?

8. Looking back on your experience of chemotherapy treatment, are there any additional nutrition
   supports that you feel would be useful in assisting patients with healthy eating and weight
   management in particular, after diagnosis?

Probe for: a) information (written, individual counseling, group meetings)
   b) specific guidelines for weight management (supports and monitoring)
   c) optimal time to intervene? (before, during, after treatment)
   d) meal provision?

9. Review of 3 day food record – recording instructions, sample day, pick up or mailing instructions

Remuneration Received? Bracelet - Date: ______________ Participant Signature ______________
   Honorarium ($30) - Date ______________ Participant Signature ______________
   (cash / cheque)
Appendix J: Rotterdam Symptom Checklist

Rotterdam Symptom Checklist - Confidential

Participant #: __________ Date of Completion: ________________

In this questionnaire you will be asked about your symptoms. Would you please, for all symptoms mentioned, indicate to what extent you have been bothered by it, by circling the answer most applicable to you. The questions are related to the past week.

Example: Have you been bothered, during the past week, by

<table>
<thead>
<tr>
<th>Headaches</th>
<th>not at all</th>
<th>a little</th>
<th>quite a bit</th>
<th>very much</th>
</tr>
</thead>
</table>

Have you, during the past week, been bothered by:

- lack of appetite
- irritability
- tiredness
- worrying
- sore muscles
- depressed mood
- lack of energy
- low back pain
- nervousness
- nausea
- despairing about the future
- difficulty sleeping
- headaches
- vomiting
- dizziness
- decreased sexual interest
- tension
- abdominal (stomach) aches
- anxiety

<table>
<thead>
<tr>
<th></th>
<th>not at all</th>
<th>a little</th>
<th>quite a bit</th>
<th>very much</th>
</tr>
</thead>
</table>

231
<table>
<thead>
<tr>
<th>Symptom</th>
<th>not at all</th>
<th>a little</th>
<th>quite a bit</th>
<th>very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>constipation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diarrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>acid indigestion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>shivering</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>tingling hands or feet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>difficulty concentrating</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sore mouth/pain when swallowing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>loss of hair</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>burning/sore eyes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>shortness of breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dry mouth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please circle the number (0-10) that best describes how much distress you have been experiencing in the past week, including today.

![Thermometer Image]

**Sample Raw Score Transformation**

\[
(\text{raw score} - \text{minimum raw score}) \times 100 \\
(\text{maximum} - \text{minimum score})
\]

Psychological raw score = 15  
Minimum raw score = 7  
Maximum raw score = 28  

Calculation:
\[
(15-7) \times 100 = 8 \times 100 = 38.1 \\
(28-7) \quad 21
\]

All things considered, how would you describe your quality of life during the past week?

- excellent
- good
- moderately good
- neither good nor bad
- rather poor
- poor
- extremely poor
Appendix K: Fatigue Symptom Inventory

Fatigue Symptom Inventory - Confidential

Participant #: __________________ Date of Completion: _______________________

In this questionnaire you will be asked about your level of fatigue during the past week.

Intensity:

Questions 1-4 ask you to rate the intensity of fatigue during the past week. Please indicate the response most applicable to you, using the following scale:

<table>
<thead>
<tr>
<th>0</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>“not at all fatigued”</td>
<td></td>
<td>“extreme fatigue”</td>
</tr>
</tbody>
</table>

1. Rate your level of fatigue on the day you felt most fatigued during the past week
   ________

2. Rate your level of fatigue on the day you felt least fatigued during the past week
   ________

3. Rate your level of fatigue on the average in the last week
   ________

4. Rate your level of fatigue right now
   ________

Interference:

Questions 5-11 ask you to indicate the extent to which fatigue has interfered with your daily activities. Please indicate the response most applicable to you, using the following scale:

<table>
<thead>
<tr>
<th>0</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>“no interference”</td>
<td></td>
<td>“extreme interference”</td>
</tr>
</tbody>
</table>

5. Rate how much, in the past week, fatigue interfered with your general level of activity
   ________

6. Rate how much, in the past week, fatigue interfered with your ability to bathe and dress yourself
   ________

7. Rate how much, in the past week, fatigue interfered with your normal work activity (includes both work outside the home and housework)
   ________

8. Rate how much, in the past week, fatigue interfered with your ability to concentrate
   ________

9. Rate how much, in the past week, fatigue interfered with your relations with other people
   ________

10. Rate how much, in the past week, fatigue interfered with your enjoyment of life
    ________

11. Rate how much, in the past week, fatigue interfered with your mood
    ________
Duration:

Questions 12-13 ask you to rate the duration of fatigue during the past week.

12. Indicate how many days (0-7) in the past week, you felt fatigued for any part of the day _______.

13. Using the following scale, rate how much of the day, on average, you felt fatigued _______.

<table>
<thead>
<tr>
<th>0</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>“none of the day”</td>
<td>“the entire day”</td>
<td></td>
</tr>
</tbody>
</table>
Appendix L – 3-Day Food Record

3-DAY FOOD DIARY

Participant #: ______________________________

Phone Number: ____________________________

Record Dates: ___________ (DD/MM/YY)
____________ (DD/MM/YY)
____________ (DD/MM/YY)

Your Most Recent Treatment Date: ___________ (DD/MM/YY)

University of Waterloo
Department of Health Studies & Gerontology
INSTRUCTIONS FOR RECORDING
DAILY FOOD INTAKE

Your food diary will provide information for studying everything you eat and drink during a 3-day period. From this record, we can obtain information on total calories, types of foods, amount of protein, carbohydrates or fats, as well as types of nutrients. It is important to 
record ALL foods, beverages, and supplements — whether it is a full course meal at home or a quick can of pop at work. Before you start recording your intake, please read the following instructions and the Sample Day.

The 3-Day Food Diary has a separate section for every day (see Day 1, Day 2, Day 3 on top each page). Each day is divided into 6 possible eating times: (though you may not eat at all 6)

1. Morning meal 2. Mid-morning snack
3. Mid-day meal (lunch) 4. Afternoon snack
5. Evening meal 6. Evening snack

Please include the following information on your food record:

1. FOOD AND BEVERAGE ITEMS: Enter all foods and beverages consumed at the meal or snack time. Please record the specific type of food (example: WHOLE WHEAT bread, FROSTED FLAKES cereal). In the same column, record all items added (examples: sugar, syrup, jam, butter, mayonnaise, gravy, milk, salt). For combination foods (e.g. sandwich, lasagna), please include detailed information on each item. For example: If you had a tuna sandwich, you would list the following detailed information: white bread, mayonnaise, carrot, solid white tuna, salt.

2. DESCRIPTION OF ITEM: For every food or beverage item listed, include the following (if applicable):
   - Brand: MIRACLE WHIP mayonnaise, PIZZA HUT DEEP DISH pizza, OREO cookie
   - Type of flavor: BLUEBERRY muffins, STRAWBERRY yogurt
   - Method of cooking: FRIED, BAKED, BBQ'D

   All relevant information on food label: LOW FAT ranch salad dressing, 28% M.F. cheddar cheese, LEAN Ground Beef, WATER PACKED tuna.

3. UNIT OF MEASURE: For every item consumed, enter the unit of measure you are using for this item. For example: enter the word "cup", "grams", "piece", "ounce", "teaspoon", or "tablespoon". Enter a unit of measure not only for the menu item, but for toppings or items added as well. Each entry must have its own unit of measure. Use measuring cups and spoons whenever possible.

4. NUMBER OF UNITS: In this area, record the number of units consumed. Include the amount of the food or beverage item and the amount of any topping or items added.

5. Fill in the blanks on the bottom of each record. Indicate the time of your meal or snack and where it was eaten (for example: at home, at a restaurant). If you did not eat a meal or snack, please place a check mark (✓) in the space provided on the bottom of the page, so that we do not think you forgot to record it.

6. Daily check: In the evening, go back over your entries to make sure you have included as much detail as possible for each item. At the end of each Day 1, 2, and 3, there are 2 questions that inquire about how the day you recorded compares to your normal diet. Don't forget to answer these questions.

All foods and beverages you consume are important (including water). Please be as accurate as possible. Please do not change your eating habits because of the survey. The information provided will be most useful to you and to this research study, if it is a reflection of how you actually ate on the recording days.

Thank you for your participation in this study. Please look closely at the Sample Day before you start. If you have any questions, please contact: Vivienne Vance (519) 654-2538 or varance@uwaterloo.ca

Tips:
1. Carry your Food Diary with you and record your entries soon after you eat
2. Please record foods and beverages (including alcohol) consumed away from home (i.e. at the mall, at work, at a restaurant) these are just as important as those eaten at home
3. Don't forget to fill out the last 2 pages on supplements that you are currently taking and the nutritional questionnaire.

236
# Sample Day

## FOOD AND BEVERAGE ITEMS

<table>
<thead>
<tr>
<th>FOOD AND BEVERAGE ITEMS</th>
<th>DESCRIPTION OF ITEM</th>
<th>UNIT OF MEASURE</th>
<th>NO. OF UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enter all foods and beverages consumed. For combination foods, please include detailed information on each item.</td>
<td>Include a detailed description of each food and drink item consumed including: - Brand name - Flavour - Method of cooking - All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice)</td>
<td>Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon</td>
<td>Enter number of units</td>
</tr>
</tbody>
</table>

### Spaghetti with tomato/meat sauce:
- **Pasta**: Spaghetti, cooked - Cup - 2
- **Tomato sauce**: Hunt’s canned sauce, roasted garlic flavor - Cup - 1
- **Meat balls**: Made with extra lean ground beef - Number (1 oz/ball) - 5
- **Parmesan cheese, grated**: Kraft, 30% Milk Fat (M.F.) - Tablespoon - 1

### Garlic Bread:
- **Italian Bread**: Toasted - Piece (large slice) - 3
- **Garlic Butter**: Teaspoon - 3

### Caesar salad:
- **Lettuce**: Romaine - Cup - 1
- **Croutons**: Safeway brand, garlic flavor - Tablespoon - 2
- **Bacon bits**: Simulated flavour, No Name Brand - Tablespoon - 2
- **Caesar salad dressing**: Kraft, Fat free - Tablespoon - 2

### Milk
- **1%**: Cup - 1

### Tiramisu
- **Sarah Lee**: Slice - 1

### Coffee
- **Black**: Cup - 1

---

**Fill in blanks: Time of meal/snack:** 6:00 pm  
**Location meal/snack was consumed:** at home  
**Please CHECK (✓) if you did not eat or drink at this meal or snack time:**
### Day 1 – Morning Meal

<table>
<thead>
<tr>
<th>FOOD AND BEVERAGE ITEMS</th>
<th>DESCRIPTION OF ITEM</th>
<th>UNIT OF MEASURE</th>
<th>NO. OF UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enter all foods and beverages consumed. For combination foods, please include detailed information on each item.</td>
<td>Include a detailed description of each food and drink item consumed including: - Brand name - Flavour - Method of cooking - All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice)</td>
<td>Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon</td>
<td>Enter number of units</td>
</tr>
</tbody>
</table>

Fill in blanks: Time of meal/snack: ______________ Location meal/snack was consumed: ________________________
Please CHECK (✓) if you did not eat or drink at this meal or snack time: __________
## Day 1 – Mid-Morning Snack

<table>
<thead>
<tr>
<th>Food and Beverage Items</th>
<th>Description of Item</th>
<th>Unit of Measure</th>
<th>No. of Units</th>
</tr>
</thead>
</table>
| Enter all foods and beverages consumed. For combination foods, please include detailed information on each item. | Include a detailed description of each food and drink item consumed including:  
- Brand name  
- Flavour  
- Method of cooking  
- All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice) | Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon | Enter number of units |

Fill in blanks: Time of meal/snack: __________ Location meal/snack was consumed: __________________________

Please CHECK (✓) if you did not eat or drink at this meal or snack time: __________
# Day 1 – Mid-day Meal (lunch)

<table>
<thead>
<tr>
<th>FOOD AND BEVERAGE ITEMS</th>
<th>DESCRIPTION OF ITEM</th>
<th>UNIT OF MEASURE</th>
<th>NO. OF UNITS</th>
</tr>
</thead>
</table>
| Enter all foods and beverages consumed. For combination foods, please include detailed information on each item. | Include a detailed description of each food and drink item consumed including:  
- Brand name  
- Flavour  
- Method of cooking  
- All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice) | Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon | Enter number of units |

Fill in blanks: Time of meal/snack: __________ Location meal/snack was consumed: __________________________

Please CHECK (✓) if you did not eat or drink at this meal or snack time: __________
## Day 1 – Mid-Afternoon Snack

<table>
<thead>
<tr>
<th>FOOD AND BEVERAGE ITEMS</th>
<th>DESCRIPTION OF ITEM</th>
<th>UNIT OF MEASURE</th>
<th>NO. OF UNITS</th>
</tr>
</thead>
</table>
| Enter all foods and beverages consumed. For combination foods, please include detailed information on each item. | Include a detailed description of each food and drink item consumed including:  
- Brand name  
- Flavour  
- Method of cooking  
- All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice) | Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon | Enter number of units |

Fill in blanks: Time of meal/snack: ____________ Location meal/snack was consumed: ____________________  
Please CHECK (✓) if you did not eat or drink at this meal or snack time: ____________
## Day 1 – Evening Meal

### Food and Beverage Items

<table>
<thead>
<tr>
<th>Food and Beverage Items</th>
<th>Description of Item</th>
<th>Unit of Measure</th>
<th>No. of Units</th>
</tr>
</thead>
</table>
| Enter all foods and beverages consumed. For combination foods, please include detailed information on each item. | Include a detailed description of each food and drink item consumed including:  
- Brand name  
- Flavour  
- Method of cooking  
- All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice) | Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon | Enter number of units |

---

Fill in blanks: Time of meal/snack: ____________ Location meal/snack was consumed: __________________________

Please CHECK (✓) if you did not eat or drink at this meal or snack time: _________
**Day 1 – Evening Snack**

<table>
<thead>
<tr>
<th>FOOD AND BEVERAGE ITEMS</th>
<th>DESCRIPTION OF ITEM</th>
<th>UNIT OF MEASURE</th>
<th>NO. OF UNITS</th>
</tr>
</thead>
</table>
| Enter all foods and beverages consumed. For combination foods, please include detailed information on each item. | Include a detailed description of each food and drink item consumed including:  
- Brand name  
- Flavour  
- Method of cooking  
- All other relevant information on food/drink label (e.g. fortified, low fat, 1%, 2% milk fat, 100% juice) | Enter unit of measure:  
for example: cup, grams, ounce, piece, teaspoon, tablespoon | Enter number of units |

Fill in blanks: Time of meal/snack: ___________ Location meal/snack was consumed: ____________________

Please CHECK (✓) if you did not eat or drink at this meal or snack time: ___________
Day 1 Meals

Compared to my normal diet, I ate:

☐ The same amount as I would usually eat

☐ More than I would usually eat

☐ Less than I would usually eat

Please circle how you felt today for each of the symptoms below:

Best Appetite

Not nauseated

Not Tired

Worst Possible Appetite

Worst possible Nausea

Worst possible Tiredness

NOTE: Compared to my “normal” diet refers to how you have been eating over the last couple of weeks. In other words, does this day of recording represent how you have been eating lately?
VITAMINS, MINERALS & OTHER HERBAL / NUTRITIONAL SUPPLEMENTS

<table>
<thead>
<tr>
<th>SUPPLEMENT BRAND (EXAMPLE: CENTRUM)</th>
<th>TYPE (EXAMPLE: MULTIVITAMIN 50+, CALCIUM)</th>
<th>NUMBER OF PILLS PER DAY</th>
<th>DAYS PILLS WERE TAKEN (EXAMPLE: DAY 1, 2 OR 3)</th>
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Appendix M – Ethics Approvals

UNIVERSITY OF WATERLOO
OFFICE OF RESEARCH ETHICS

Notification of Ethics Clearance of Application to Conduct Research with Human Participants

Principal/Co-Investigator: Rhona Hanning
Principal/Co-Investigator: Marina Mourtzakis
Principal/Co-Investigator: Sharon Campbell
Principal/Co-Investigator: Linda McCergar
Faculty Supervisor: Rhona Hanning
Student Investigator: Vivienne Vance

Department: Health Studies & Gerontology
Department: Health Studies & Gerontology
Department: Health Studies & Gerontology
Department: Department of Agriculture, Food and Nutritional Science, University of Alberta
Department: Health Studies & Gerontology

ORE File #: 16679

Project Title: Relationships among psychosocial factors, treatment-related side effects, dietary intake and weight gain in women treated with adjuvant chemotherapy for early stage breast cancer

This certificate provides confirmation that the additional information/revised materials requested for the above project have been reviewed and are considered acceptable in accordance with the University of Waterloo’s Guidelines for Research with Human Participants and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. Thus, the project now has received ethics clearance. This clearance is valid for a period of four years from the date shown below and is subject to an annual ethics review process (see Note 2). A new application must be submitted for on-going projects continuing beyond four years.

Note 1: This project must be conducted in accordance with the description in the application and revised materials for which ethics clearance has been granted. All subsequent modifications to the application must be submitted for prior ethics review using ORE Form 104 and must not be initiated until notification of ethics clearance has been received.

Note 2: All ongoing research projects must undergo annual ethics review. ORE Form 105 is used for this purpose and must be submitted by the Faculty Investigator/Supervisor (FIFS) when requested by the ORE. Researchers must submit a Form 105 at the conclusion of the project if it continues for less than a year.

Note 3: FIs and FSs also are reminded that they must immediately report to the ORE (using ORE Form 106) any events related to the procedures used that adversely affected the participants and the steps taken to deal with these.

Susan E. Sykes, Ph.D., C.Psych.
Director, Office of Research Ethics

OR
Susanne Santi, M. Math
Senior Manager, Research Ethics

OR
Julie Joza, B.Sc.
Manager, Research Ethics

Date 9/20/2010

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UNIVERSITY OF WATERLOO
OFFICE OF RESEARCH ETHICS

Request for Ethics Clearance of a Revision or Modification
to an Ongoing Application to Conduct Research with Human Participants

Principal Investigator(s): Rhona Hanning, Marina Mourtzakis, Sharon Campbell, Linda McCargar,
Department: Health Studies & Gerontology, Kinesiology, Agriculture, Food & Nutritional Science
ORE #: 16679
Date of Full Ethics Clearance: September 20, 2010
Faculty Supervisor(s): Rhona Hanning, Health Studies & Gerontology
Student Investigator: Vivienne Vance, Health Studies & Gerontology
Title of Project: Relationships among Psychosocial factors, Treatment-Related Side Effects, Dietary
Intake and Weight Gain in Women Treated with Adjuvant Chemotherapy for Early Stage Breast Cancer

1. Previous Modifications Associated with this ORE 104 Application
Have you previously submitted an ORE 104 for this project? Yes [X] No [ ]
If Yes, please provide the clearance dates for each previous modification under this ORE 104.

2. Information Letter and Consent Form
Do the proposed revised procedures require any change(s) to the Information Letter-Consent Form
currently in use? Yes [X] No [ ]
If Yes, briefly describe these changes on the following table and attach a copy of the revised version of
the Information Letter-Consent Form.

3. Summary of the Nature, Description and Rationale for Proposed Modifications
On the following summary table, describe the nature of each modification requested under the current
ORE 104 and provide a rationale for each proposed change.

4. Revised ORE 104 Pages
Attach all pages from the ORE Form 101 that have been revised due to the proposed modification.

Signature of Principal & Co-Investigators
Investigator(s):______________________________

Signature of Faculty
Supervisor(s):______________________________

Signature of Student
Investigator(s):______________________________
Date: Jan 6/11

FOR OFFICE OF RESEARCH ETHICS USE ONLY

[ ] The current modification request to an ongoing project involving human participants has been reviewed
and received ethics clearance as submitted.
[ ] The current modification request to an ongoing project involving human participants has been reviewed
and requires revisions as outlined in the attached email.

Date: 1/14/2011

Susan E. Sykes, Ph.D., C. Psych.
Director, Research Ethics
or
Susanne Santi, M.Math.
Senior Manager, Research Ethics
or
Julie Joza, BSc.
Manager, Research Ethics

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UNIVERSITY OF WATERLOO
OFFICE OF RESEARCH ETHICS

Request for Ethics Clearance of a Revision or Modification
to an Ongoing Application to Conduct Research with Human Participants

Principal Investigator(s): Rhona Hanning, Marina Mourtzakis, Sharon Campbell, Linda McCarron
Department: Health Studies & Gerontology, Kinesiology, Agriculture, Food & Nutritional Science
ORE #: 16679
Date of Full Ethics Clearance: September 20, 2010
Faculty Supervisor(s): Rhona Hanning, Health Studies & Gerontology
Student Investigator: Vivienne Vance, Health Studies & Gerontology
Title of Project: Relationships among Psychosocial factors, Treatment-Related Side Effects, Dietary Intake and Weight Gain in Women Treated with Adjuvant Chemotherapy for Early Stage Breast Cancer

1. Previous Modifications Associated with this ORE 101 Application
Have you previously submitted an ORE 104 for this project? Yes [X ] No [ ]
If Yes, please provide the clearance dates for each previous modification under this ORE 101.
- January 25, 2011

2. Information Letter and Consent Form
Do the proposed revised procedures require any change(s) to the Information Letter-Consent Form currently in use Yes [ ] No [X ]
If Yes, briefly describe these changes on the following table and attach a copy of the revised version of the Information Letter-Consent Form.

3. Summary of the Nature, Description and Rationale for Proposed Modifications
On the following summary table, describe the nature of each modification requested under the current ORE 104 and provide a rationale for each proposed change.

4. Revised ORE 101 Pages
Attach all pages from the ORE Form 101 that have been revised due to the proposed modification.

Signature of Principal & Co-Investigators
Investigator(s):

Signature of Faculty
Supervisor(s):

Signature of Student Investigator(s):

Date: June 29, 2011

FOR OFFICE OF RESEARCH ETHICS USE ONLY
[ ] The current modification request to an ongoing project involving human participants has been reviewed and received ethics clearance as submitted.
[ ] The current modification request to an ongoing project involving human participants has been reviewed and requires revisions as outlined in the attached email.

Date: 7/5/2011

Susan E. Sykes, Ph.D., C. Psych.
Director, Research Ethics
or
Susanne Santi, M.Math.
Senior Manager, Research Ethics

Julie Joza, BSc.
Manager, Research Ethics

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Appendix N – Participant Feedback Letter

Date:

Dear [Name],

Thank you for participating in our study, designed to investigate the unique challenges associated with chemotherapy in relation to nutrition and weight management in breast cancer survivors. This study will help us to develop nutrition guidelines and programs to support healthy eating and weight management during and after treatment. It is hoped that the findings from this study will improve patient care in the future.

I am attaching a summary and personal nutritional assessment based on your 3-day food record. We have identified areas of nutrition in which you are doing well and pointed out some areas that could be improved. We hope this information will be helpful in planning a healthy diet. Some additional resources are provided at the end of your personal assessment. If you have any questions or concerns, please feel free to contact me using the email or telephone number listed at the bottom of the page. The full study is expected to be completed by December 2011, at which time I will be pleased to send you a summary of the research findings.

Please be assured that your results are identified by a specific code, known only to the investigators and will be kept confidential. Direct access to this information will be restricted to the researchers who are directly involved in the study. Any publications or reports that result from this study will be presented as group data and your personal information will not be identifiable.

As with all University of Waterloo projects involving human participants, this project was reviewed by and received ethics clearance through the Office of Research Ethics at the University of Waterloo. Should you have any comments or concerns resulting from your participation in this study, please contact Dr. Susan Sykes in the Office of Research Ethics at 519-888-4567, Ext., 36005 or ssykes@uwaterloo.ca.

Thank you once again for your valuable contribution.

Sincerely,

Vivienne Vance
Department of Health Studies and Gerontology, University of Waterloo
vavance@uwaterloo.ca (519) 654-2538
Appendix O – Personal Nutritional Assessment

PERSONAL NUTRITIONAL ASSESSMENT

Name: ______________________________ Date: ___________________________

Height: ________________

Weight: ________________

Weight Change:

Body Mass Index (BMI):

Body mass index is a basic measure of body size based on your height and weight. The normal range for BMI is between 18.5 and 24.9.

Current BMI: ________________

BMI Status:

Nutrition Summary

Estimated Daily Calorie Requirement:

Actual Daily Caloric Intake (based on your 3-day food record):

Daily Caloric Intake Status:

Estimated Daily Protein Requirement: 0.8 g/kg (~ /day), 10-35% of total calories

Actual Daily Protein Intake (based on your 3-day food record):

Grams:
% of total calories:

Your current intake…..

Protein is a source of calories that is important for cell growth, repair, and maintaining a healthy immune system. Ensuring adequate protein intake will help to protect against loss of lean tissue after treatment. Try to include a little protein at each meal/snack (low fat milk, cheese or yogurt, eggs, lean meats, fish, poultry, legumes, tofu, nuts & seeds). Protein also helps to create and maintain a feeling of “fullness” and stabilizes blood sugar for longer periods of time throughout the day.
**Estimated Daily Carbohydrate Requirement:** minimum of 130 g/day, 45-65% of total calories

**Actual Daily Carbohydrate Intake (based on your 3-day food record):**

Grams:
% total calories:

Your current intake …..

Dietary carbohydrates provide the body with energy and in their less processed forms, come packed with important nutrients including fibre, vitamins and minerals.

A carbohydrate rich diet includes plenty of whole grains, fruits, vegetables, legumes and low fat dairy. Eating Well with Canada’s Food Guide provides an excellent resource for serving sizes and healthy ways to incorporate these food groups into your daily diet.

**Estimated Daily Fat Requirement:** total fat: 20-35% of total calories, saturated fats < 10%

**Actual Daily Fat Intake (based on your 3-day food record):**

Total fat:
Saturated fat:

Your current intake of total fat and saturated fat…..

Some fat in the diet is critical for good health. Dietary fats provide the body with energy, insulation and protection for vital organs. Fat is also needed for the absorption and use of fat-soluble vitamins, structure of cell membranes and to make several important body compounds.

Current guidelines suggest that we should increase our intake of heart healthy fats (vegetable oils, fatty fish, nuts & seeds) and limit our intake of saturated fats (red meats, whole milk, cream, butter, cheese, coconut and palm oils) and trans fats (processed and deep-fried foods, cakes, cookies, pastries, imitation cheese, some margarines)

**Things you are doing well:**

**Name:**
Areas to work on:

Nutrition Goals:
Reminder: a balanced diet means eating a variety of foods from each of the four food groups every day and enjoying “extras” or other foods in moderation. Be sure to adjust your total calorie intake according to your activity level for the day. e.g.) eat a little lighter on days when you are less active and ensure that you eat enough to support your exercise on more active days.

Resources:
Guelph and Wellington Breast Cancer Support Group  
http://communitylinks.cioc.ca/record/GCL0512

Canadian Breast Cancer Network  www.cbcn.ca

Canadian Breast Cancer Foundation  www.cbcf.org

http://www.bccancer.bc.ca/PPI/TypesofCancer/Breast/breastcakit.htm

www.cancer.ca


Eating Well with Canada’s Food Guide (2007). Health Canada,  
Appendix P - Participant Feedback Letter - Results Summary

June, 2012.

Dear “name of participant”,

Thank you once again for participating in our study on nutrition, weight change and chemotherapy in breast cancer survivors. All of the data for this study have now been collected and analyzed. Below is a summary of the research findings:

1. A total of 28 women participated in this study. Weight change during chemotherapy was highly variable ranging from a loss of ~12 kg (27lbs) to a gain of ~9 kg (20 lbs).
2. Food intake was highly responsive to the day of treatment, with most women reporting lower food intake and irregular eating patterns for the first few days after chemotherapy.
3. Participants who lost weight tended to report more severe and persistent side effects of treatment, leading to a more prolonged reduction of food intake after each cycle.
4. Increased appetite, food cravings and intake of calorie dense comfort foods seemed to be more common among women who gained weight during treatment. These dietary changes were associated with changes in taste, nausea and emotional distress.
5. Most women reported a reduction in physical activity during treatment.
6. Weight change after treatment was also quite variable (range = -6 kg to + 5 kg).
7. Most women (84%) reported changes in diet after diagnosis. Most changes were positive (e.g. ↑ veggies/fruit) and consistent with current recommendations for cancer prevention.
8. Despite these changes, some women were still above the guidelines for total fat and saturated fat and many were below recommendations for vegetables/fruit and milk/alternatives. Many women were not receiving adequate calcium and vitamin D from foods alone, however intakes were improved considerably through the use of supplemental sources of these nutrients.
9. Based on survey responses, symptoms of physical and psychological distress after treatment (including fatigue) were highly variable across women, however “on average” scores were similar to previous reports of women in active treatment and higher than women who have not been treated for breast cancer.
10. These findings suggest that changes in food intake and eating patterns may play an important role in weight change after a breast cancer diagnosis.
11. Comprehensive interviews with breast cancer survivors provided a unique perspective on food intake and weight change during treatment, helping to advance our understanding of dietary challenges that women face as they are undergoing treatment.
12. A key lesson drawn from your personal stories is an appreciation for the fact that each woman’s experience with chemotherapy is different. This finding, combined with data on dietary habits of women after breast cancer and evidence of persistent treatment effects in the first year after completing chemotherapy, will help to guide future research and to design effective healthy eating and weight management programs.

We sincerely appreciate your contribution to this research and hope that it was an interesting experience for you. Please feel free to contact me if you have any questions or concerns, using the email or telephone number listed below.

Best wishes!

Vivienne Vance
School of Public Health and Health Systems, University of Waterloo
vavance@uwaterloo.ca (519) 654-2538
Diagnostic In Obesity and Complications

Weight gain in breast cancer survivors: prevalence, pattern and health consequences

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Received 28 May 2010; revised 30 July 2010; accepted 5 August 2010

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Summary

Weight gain is a common and persistent problem for many breast cancer survivors and is associated with adverse health consequences. A comprehensive review of the English language literature was conducted to investigate the frequency, magnitude and pattern of weight gain among breast cancer survivors, to identify factors that are associated with these changes and to review the clinical significance of weight gain on disease-free survival and overall health. While there appears to be a general trend toward a reduction in the magnitude of weight gain in recent years, as many as 50–96% of women experience weight gain during treatment and many, including some women who remain weight stable during treatment, report progressive weight gain in the months and years after diagnosis. Weight gain is more common in women receiving adjuvant chemotherapy, especially for women receiving longer duration treatments and seems to be especially pronounced in premenopausal women. With or without weight gain, unfavourable changes in body composition including fat gain and loss of lean tissue are prevalent. This unique pattern of weight gain and change in body composition is distressing for most women, poses significant risk for the development of co-morbid conditions and may impact on long term disease-free survival.

Keywords: breast cancer, recurrence, survival, weight gain.

obesity reviews (2011) 12, 282-294

Introduction

Breast cancer is the most common female malignancy in the world, accounting globally for 23% of all new cancer cases in women and 14% of all female cancer related deaths (1). While improved screening, combined with advances in treatment has resulted in a decline in breast cancer mortality, an increasing number of women are living with a diagnosis of breast cancer. This population of breast cancer survivors, currently estimated to include at least 166 000 Canadian women (2) and 2.5 million American women (3), underscores a critical need to investigate modifiable risk factors that will positively impact overall health, disease remission and long-term survivorship.

Obesity at diagnosis associates with increased risk of disease recurrence (4,5), breast cancer death (6,7), and all-cause mortality (8,9,10). A recent meta-analysis incorporating more than 8000 women, found that obesity at diagnosis was associated with poor prognosis, with a combined effect size of 1.56 for all-cause mortality (10). This effect is evident in both pre and postmenopausal women (5,11). While the evidence for a relationship between pre-morbid body weight and prognosis is compelling, it is not clear if weight gain after diagnosis, a common problem for many breast cancer survivors (6) impacts independently on breast cancer specific outcomes. Weight gain, however, is linked to poor quality of life and an increased risk of developing comorbid conditions (6), emphasizing
the potential therapeutic relevance of weight management after diagnosis (5).

The relationship between obesity and prognosis is complex, seemingly influenced by several possible metabolic and hormonal pathways. Proposed mechanisms include an increase in adipose tissue derived circulating oestrogens resulting from the conversion of androgens in peripheral fat stores (12). Oestrogen is known to play a role in the initiation and promotion of breast cancer by stimulating cell division, increasing the potential for DNA mutations and promoting the growth of oestrogen dependent tumours (6). Body fatness also increases circulating levels of insulin, insulin-like growth factor and leptin, which may also promote cell proliferation and breast cancer development (9,12). Insulin also down-regulates plasma concentrations of sex hormone binding globulin, resulting in an elevation of available bioactive estradiol and potential increases in angiogenesis and breast epithelial cell proliferation (12). Increased body fat may be related to physical inactivity and dietary factors, before or after diagnosis.

Thus, obesity may also serve as a marker for lifestyle behaviours that contribute to poor prognosis (9). Furthermore, poor outcomes in obese women may be related to more advanced disease at diagnosis, systematic under-treatment and/or poor treatment response (9).

Adjuvant chemotherapy is linked to weight gain; however, the underlying mechanisms contributing to energy imbalance after diagnosis are unclear. Fatigue and other treatment-related side effects, psychological distress and the demands of multiple treatment days may affect diet and physical activity patterns in ways that promote weight gain. At this time, there is little support for a reduction in basal metabolic rate (13-18); however, metabolomic research suggests limited oxidative capacity in those who gain weight (19), which implies compromised energy balance.

With a growing population of breast cancer survivors and an established link between obesity and prognosis serving as the rationale, the purpose of this review was to investigate the frequency, magnitude and pattern of weight gain among breast cancer survivors and to examine factors that most consistently correlate with weight gain in this population. Adverse health consequences associated with weight gain are reviewed, with a particular focus on evidence for a relationship between weight gain after diagnosis and disease free survival.

Results

Frequency and magnitude of weight gain

Weight gain is a common problem among breast cancer survivors; a finding that was initially unexpected since many forms of cancer and its treatment are typically associated with weight loss (20). Two extensive reviews of weight gain after diagnosis were conducted during the 1990s (20,21). At that time, combined results suggested that 50–96% of early stage breast cancer patients experience significant weight gain during treatment. Weight gains in the range of 2.5–6.2 kg were most commonly reported but gains of 10 kg or more were not unusual. Since 1997, many additional studies have addressed weight gain during and after breast cancer treatment; 23 studies are summarized in Table 1.

While there appears to be a trend towards reduced magnitude of weight gain since the mid 1990s (22), the majority of recent investigations continue to show a high frequency of weight gain among women with early stage disease (13,14,23–31). A 2002 retrospective chart review of 100, stage I-IIIA breast cancer patients, e.g. found that 64% of women gained more than 2 kg during six cycles of adjuvant or neoadjuvant treatment (27). Defining ‘significant’ weight change as a gain or loss of greater than 2.5 kg, Ingram and Brown (22) concluded that only 34.2% of premenopausal women gained weight during chemotherapy treatment. The mean weight change among all women was 1.4 kg; however, those who were classified as ‘gainers’ (>2.5 kg) experienced a mean weight gain of 5.0 kg.

Some of the more recent investigations have not reported significant weight change during active treatment, possibly owing to shorter duration chemotherapy regimes (15,16,32); however, longer follow-up data in these studies and others have reported progressive weight gain after the completion of treatment. For example, in women with early stage breast cancer, Kutyniec et al. (16) found that while body weight was unchanged over 12 weeks of adjuvant chemotherapy or radiation, follow-up data for 13 participants revealed that four out of seven women treated with chemotherapy (mean follow-up 66 weeks) and four out of six women treated with radiation (mean follow-up 103 weeks) had gained an average of 4.7 kg and 4.1 kg, respectively. Similarly, Demark-Wahnefried et al. (15) found no significant change in mean body weight among 18 premenopausal women during treatment, however in the
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample (size, key characteristics)</th>
<th>Follow-up</th>
<th>Weight measures</th>
<th>Frequency of weight gain</th>
<th>Mean Weight Gain</th>
<th>Additional finding/observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflato et al. 2009 (33)</td>
<td>n = 25, age 26–73 years (mean = 67 years), Pre-Menop (80%), Post-Menop (20%), stage I-III, CMF chemotherapy (6 months)</td>
<td>6 months</td>
<td>measured height and weight day 1 of cycles 2 and 6</td>
<td>7%</td>
<td>3.55 kg</td>
<td>Weight gain in pre-menopausal women vs. post-menopausal women</td>
</tr>
<tr>
<td>Campbell et al. 2007 (14)</td>
<td>n = 10, mean age = 46.9 years, Pre-Menop (70%), Post-Menop (30%), stage I-III A, AC or CEF chemotherapy (3-6 months)</td>
<td>3–6 months</td>
<td>measured height and weight before and after treatment</td>
<td>70%</td>
<td>1.69 kg</td>
<td>Trend toward higher weight gain in pre-menopausal women but N/S</td>
</tr>
<tr>
<td>Caan et al. 2004 (25)</td>
<td>n = 315, mean age = 55.3 years, Pre-Menop (25%), Post-Menop (5%) Stage I-III A, chemotherapy and/or radiation (15% surgery only)</td>
<td>5–7 years</td>
<td>self-reported weight 1 yr before diagnosis and at study enrollment (~2 years from diagnosis)</td>
<td>44% (+5%)</td>
<td>2.4 kg</td>
<td>5.6%</td>
</tr>
<tr>
<td>Chen et al. 1997 (23)</td>
<td>n = 34, age 30–73 years (mean = 51–56 years), Pre-Menop (44%), Post-Menop (56%), Stage I-III A, current chemotherapy or surgery and/or chemotherapy 1 yr ago</td>
<td>6–12 months</td>
<td>measured (24%) or chart review of weight at diagnosis (46 months) and after treatment (6–12 months)</td>
<td>71%</td>
<td>0.91%</td>
<td>Median gain among women who gained weight = 3.2–3.3 kg</td>
</tr>
<tr>
<td>Costa et al. 2002 (26)</td>
<td>n = 10, age 26–76 years (median = 49 years), Pre-Menop (47%), Post-Menop (53%), Stage I-III (20% palliative), CMF, FAO, FEC or AC chemotherapy</td>
<td>4.9 months</td>
<td>chart review of patients with act. weight records (1 or 2 months apart) during chemotherapy</td>
<td>81%</td>
<td>2.8 kg</td>
<td>Weight gain data excludes women receiving palliative treatment</td>
</tr>
<tr>
<td>Del Rio et al. 2002 (13)</td>
<td>n = 30, mean age = 56 years, Post-Menop (100%), Stage III 5 cycles of CMF chemotherapy</td>
<td>6 months</td>
<td>measured weight before and after treatment</td>
<td>100%</td>
<td>2.8 kg</td>
<td>No change in mean body weight during treatment</td>
</tr>
<tr>
<td>Dammik-Wahnenfeld et al. 1997 (15)</td>
<td>n = 20, age 27–52 years (mean = 39.9 years), Pre-Menop (100%), Stage I-II A, Adjacent chemotherapy = 12–24 weeks</td>
<td>12 months</td>
<td>measured weight before and after treatment chart review at 12 months</td>
<td>3.8 kg</td>
<td>Mean weight gain at 6 months 0.5-2.2 kg</td>
<td></td>
</tr>
<tr>
<td>Dammik-Wahnenfeld et al. 2001 (16)</td>
<td>n = 53, age 27–54 years (mean = 41 years), Pre-Menop (100%), Stage III Surgery with or without radiation, adjacent chemotherapy</td>
<td>12 months</td>
<td>measured weight before and after treatment (6 months) and 12 months</td>
<td>10%</td>
<td>2.1 kg</td>
<td>Modest weight gain in 6 months period after treatment (1.9 kg) offset by small N/S loss during treatment</td>
</tr>
<tr>
<td>Friedman et al. 2004 (32)</td>
<td>n = 20, mean age = 46.2 years, Pre-Menop (30%), Post-Menop (50%), Stage I-IIIA, Adjacent chemotherapy</td>
<td>10.5 months</td>
<td>measured height and weight before treatment, 2 weeks after treatment and 6 months post-treatment</td>
<td>40–50%</td>
<td>0.27 kg</td>
<td>2.4 kg</td>
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</tbody>
</table>

256
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample (size, key characteristics)</th>
<th>Follow-up</th>
<th>Weight measures</th>
<th>Frequency of weight gain</th>
<th>Mean Weight Gain</th>
<th>Additional findings/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al.</td>
<td>n = 535, mean age = 53.3 years</td>
<td>12 months</td>
<td>measured height and weight before or during 1st 6 months of treatment and 12 months (n= 446)</td>
<td>64%</td>
<td>1.6 kg</td>
<td>Onset of menopause was a significant independent predictor of weight gain (P &lt; 0.05)</td>
</tr>
<tr>
<td>Ert et al.</td>
<td>n = 34, mean age = 57.4 years</td>
<td>DNR Mean = -6 years</td>
<td>self-reported height and weight before diagnosis and at study enrollment (1-6 years from diagnosis)</td>
<td>47%</td>
<td></td>
<td>Mean gain among women who gained weight = 7.3 kg</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 260, mean age = 47 years</td>
<td>2 years</td>
<td>chart review of height and weight before and after (3, 6, 12, 24 months) treatment</td>
<td>47%</td>
<td>0.30 kg</td>
<td>Mean gain among women who gained weight at 12 months = 1.01 kg Weight gain in pre-menop vs. post-menop = NS</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 17, mean age = 46 years</td>
<td>12 months</td>
<td>measured height and weight before, mid (3rd cycle) and after treatment (1 month and 9,12 months from diagnosis)</td>
<td>55%</td>
<td>5.0 kg</td>
<td>Mean weight gain after treatment (1-6 months) = 3.3 kg</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 27, mean age = 54 years</td>
<td>Median = 3.1 years</td>
<td>chart review of height and weight at diagnosis, 1 year after diagnosis and -6 years after diagnosis</td>
<td>55%</td>
<td>2.4 kg</td>
<td>Mean gain among women who gained weight = 5.4 kg</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 76, age 36-64 years</td>
<td>6 months</td>
<td>measured height and weight before, during (every other cycle) and after treatment</td>
<td>36%</td>
<td>1.4 kg</td>
<td>Mean gain among women who gained weight = 5.6 kg</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 51, mean age = 56 years</td>
<td>3 years</td>
<td>measured height and weight within first year of diagnosis (-6 months) and 2 years after baseline (within third year of diagnosis)</td>
<td>66%</td>
<td>1.7 kg</td>
<td>Mean gain among women who gained weight = 3.9 kg, 18% gained &gt;10 kg</td>
</tr>
<tr>
<td>et al.</td>
<td>n = 202, mean age = 56-62 years</td>
<td>Mean = 40 months</td>
<td>chart review of height and weight at diagnosis, after treatment (mean = 34 months for tamoxifen) and final followup</td>
<td>1.2 kg</td>
<td></td>
<td>No systemic chemotherapy treatment</td>
</tr>
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## Table 1 Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample (size, key characteristics)</th>
<th>Follow-up</th>
<th>Weight measures</th>
<th>Frequency of weight gain</th>
<th>Mean Weight Gain</th>
<th>Additional findings/comments</th>
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<tr>
<td>Kumar et al. 2004 (23)</td>
<td>n = 196, mean age = 49 years</td>
<td>–12 months</td>
<td>measured height and weight before and after treatment – self-reported 6 months</td>
<td>3.1 kg</td>
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<tr>
<td></td>
<td>Pre-Menop (47%), Post-Menop (53%)</td>
<td></td>
<td>post-treatment</td>
<td>(6 months)</td>
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<td></td>
<td>Stage I-II, Adjuvant chemotherapy</td>
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<td>(6 months)</td>
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<td></td>
<td>with or without radiation</td>
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<td></td>
<td>(6 months)</td>
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<tr>
<td>Kelyea et al. 1989 (14)</td>
<td>n = 18, mean age = 42–44 years</td>
<td>12 weeks</td>
<td>measured height and weight before and after treatment</td>
<td>0.0–1.0 kg</td>
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<td>Pre or perimenopausal (100%)</td>
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<td>Stage I-II, AC chemotherapy</td>
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<td>(44%) or radiation only (56%)</td>
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<td>Lankaster et al. 2002 (27)</td>
<td>n = 100, age 29–73 years</td>
<td>–6 months</td>
<td>chart review of height and weight before and after treatment</td>
<td>6% (&gt; 2 kg)</td>
<td>3.07 kg</td>
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<td></td>
<td>(mean = 60 years), Pre-Menop (59%),</td>
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<td>(5%–6%)</td>
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<td>Post-Menop (41%), Stage I-II, 6</td>
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<td>cycles of adjuvant or</td>
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<td>neoadjuvant FEC or CMF chemotherapy</td>
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<tr>
<td>Muller-A ihtiya et al.</td>
<td>n = 195, age 24–91 years</td>
<td>3 years</td>
<td>chart review of height and weight diagnosis and 1, 2, 3 years after diagnosis</td>
<td>71% (1 year)</td>
<td>1.5 kg (1 year)</td>
<td>Mean gain among women who</td>
</tr>
<tr>
<td>2007 (30)</td>
<td>(mean = 61 years), Pre-Menop (50%),</td>
<td></td>
<td></td>
<td>70% (2 years)</td>
<td>2.7 kg (2 years)</td>
<td>gained weight (1 year) = 3.7 kg</td>
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<td></td>
<td>Post-Menop (50%), Stage I-II,</td>
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<td>50% (3 years)</td>
<td>2.8 kg (2 years)</td>
<td>Among women who were</td>
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<td>Adjuvant chemotherapy and</td>
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<td>weight stable in year 1 = 32%</td>
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<td>hormone therapy, 4% no</td>
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<td>systemic treatment</td>
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<tr>
<td>McNees and Knobf, 2001 (20)</td>
<td>n = 44, age 29–75 years</td>
<td>3 years</td>
<td>chart review of height and weight diagnosis and 1, 2, 3 years after diagnosis</td>
<td>76% (1 year)</td>
<td>4.1 kg (1 year)</td>
<td>Mean gain among women who</td>
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<tr>
<td></td>
<td>(mean = 60 years), Pre-Menop (59%),</td>
<td></td>
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<td>82% (2 years)</td>
<td>4.2 kg (1 year)</td>
<td>gained significant weight</td>
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<td></td>
<td>Post-Menop (41%), Stage I-II,</td>
<td></td>
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<td>71% (3 years)</td>
<td>4.8 kg (2 years)</td>
<td>(1.2 kg).(1 year)</td>
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<td>Adjuvant chemotherapy with</td>
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<td>or without radiation</td>
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<tr>
<td>Rock et al. 1999 (24)</td>
<td>n = 1116, age 26–70 years</td>
<td>Mean= 26 months</td>
<td>self reported height and weight 1 year before diagnosis and study entry</td>
<td>60%</td>
<td>2.7 kg</td>
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<td></td>
<td>(mean = 51 years), Pre-Menop at</td>
<td></td>
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<td>24% (50 years)</td>
<td>2.4 kg</td>
<td>Postmenopausal women &lt;50</td>
</tr>
<tr>
<td></td>
<td>study entry (mean = 26 months</td>
<td></td>
<td></td>
<td>(50 years)</td>
<td>4.5 kg (1)</td>
<td>years were likely premenopausal</td>
</tr>
<tr>
<td></td>
<td>from diagnosis) (21%),</td>
<td></td>
<td></td>
<td>installation)</td>
<td>2.0 kg</td>
<td>at diagnosis</td>
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<tr>
<td></td>
<td>Post-menop at study entry (59%),</td>
<td></td>
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<td>(50 years)</td>
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<td>stages I-II, Adjuvant chemotherapy</td>
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<td>completed and/or anti-estrogen</td>
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<td></td>
<td>treatment</td>
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</table>

PostMenop = postmenopausal at diagnosis, Pre-Menop = premenopausal at diagnosis.

*P < 0.05 compared with postmenopausal, *P < 0.05 compared with premenopausal and postmenopausal >50 years.

NS, not significant.
year after treatment, 14 of 18 women for whom weight data were available, had gained an average of 3.8 kg.

Recent longitudinal data confirms that weight gain after treatment is progressive for many breast cancer survivors. A review of consecutive patient records found that, among 185 women diagnosed with stage I-III breast cancer, the mean weight change across all women was 1.5 kg at year one, 2.7 kg at year two and 2.8 kg at year three, suggesting that weight gain is persistent after diagnosis (30). Similarly, Irwin and colleagues (29) found that by the third year after diagnosis, 68% of women with stage I-IIIA breast cancer had gained an average of 3.8 kg.

While post-diagnosis weight gain is common, it is not universal. Among those who gain weight, the amount of weight gained at different time points in the cancer trajectory is highly variable. Moreover, it is possible that there are ethnic differences in the pattern of weight gain after a breast cancer diagnosis (33). A study of Korean women diagnosed with early stage disease, reported a mean weight gain of 0.3 kg at 3 months but no significant weight change at 6, 12 and 24 month follow-ups (33). In this study, 47% of patients experienced a mean gain of 1.9 kg at 12 months; however, only 10% were reported to have gained a ‘significant amount of weight’ (≥5% vs. baseline) during this time frame.

Estimating average weight gain in this population is confounded by the fact that weight change has been reported using a variety of methods (absolute change, % change, ‘significant change’, % change/day, median vs. mean). In addition, some studies have reported mean weight change across all participants (e.g. including those who are weight stable or lose weight) and others report by treatment group or menopause status (24,14,32).

Regardless of how the data are presented, based on more than 30 years of research, it is clear that among breast cancer survivors, weight gain is a common and persistent problem. The amount of weight gained is larger than would be expected in the general population and occurs at an accelerated rate compared to age-matched healthy women (14,24,29).

Patterns of weight gain and body composition changes

Weight gain in otherwise healthy women typically includes a gain in both adipose tissue and lean tissue (17,18). A growing body of research however, suggests that the pattern of weight gain typical of breast cancer patients is unique in that it generally occurs with no associated gains or perhaps even losses in lean tissue; changes which may lead to the body composition phenotype known as ‘sarcopenic obesity’ (6,34).

Using several modalities of body composition, including skin-folds (17,25), waist and hip circumference (17,25), dual energy X-ray absorptiometry (DXA) (14,16,18,32) and computed tomography (CT) (23), increases in fat mass after diagnosis are well documented. Using DXA, Demark-Wahnefried et al. (18) reported changes in body composition in 36 premenopausal breast cancer patients (stages 0-IIII) during the year after diagnosis. At 6 and 12 months, respectively, women treated with adjuvant chemotherapy had gained an average of 2.2 kg and 2.1 kg in body weight and 2.0 kg and 2.3 kg of fat mass (FM), representing a relative gain in body fat of 1.8% and 2.2%. During the same time frame, a small but non-significant decrease in fat free mass (FFM) and lean body mass in particular was noted.

Others have reported an increase in FM, accompanied by a significant loss (16,23) or no change (14,32) in FFM during treatment. Based on CT images, Cheney et al. (23) found that, regardless of weight change, seven out of eight early stage breast cancer patients gained body fat and lost lean tissue over 6 months of adjuvant treatment. Similarly, in the absence of significant weight gain, Kutynec et al. (16) reported a significant increase in percent body fat and a significant loss of lean body mass in 18 premenopausal women, over 12 weeks of chemotherapy or radiation. Once again, loss of lean tissue was especially pronounced in the leg region, for both chemotherapy and radiation treated women. Collectively, these findings suggest that, with or without weight gain, changes in body composition consistent with the development of sarcopenic obesity occur in some breast cancer survivors, during and after treatment.

Factors associated with weight gain and body composition changes

Treatment effects

There is considerable evidence that post-diagnosis weight gain among breast cancer survivors is highly correlated with the type and duration of treatment (20). Early research in this area suggested that systemic treatment (adjuvant chemotherapy) produced significantly more weight gain than localized treatment (surgery and/or radiation only) and that weight gain was higher among women treated with multi-agent regimes over longer periods of time (21). Findings from more recent investigations confirm an association between chemotherapy treatment and weight gain (24,25,18,30,35–37). A summary of common chemotherapy protocols and their abbreviations (e.g. AC, CEF), used in subsequent sections of this paper, are provided in Appendix A.

A large prospective study of pre and postmenopausal women with early stage breast cancer (25) demonstrated that weight gain in the first year after diagnosis was significantly greater in women treated with any form of chemotherapy (2.5 kg) compared to those who received no
adjuvant treatment (0.63 kg, P < 0.001). Similarly in 2001, Demark-Wahnefried et al. (18) reported a mean weight gain of 2.2 kg at 6 months and 2.1 kg at 1 year among premenopausal women treated with adjuvant chemotherapy versus corresponding weight gains of 0.5 kg and 1.0 kg in women receiving localized treatment only (surgery, with/without radiation). Adjusting for known confounders, data from the Women’s Healthy Eating and Living (WHEL) study revealed that women treated with chemotherapy were 65% more likely to gain weight during treatment compared with women who received no systemic treatment (36). In this sample, the type of chemotherapy did not impact on the amount of weight that was gained. There is some suggestion in the literature that the newer chemotherapy regimes containing anthracyclines (doxorubicin and etoposide) are associated with less weight gain (22); however, this has not been a consistent finding (25,28–30,36). The use of oral agents versus intravenous administration within these and other chemotherapy regimes has also been associated with higher weight gain (21).

Current evidence suggests that the duration of adjuvant treatment may be the more important predictive indicator.

A general trend towards shorter duration treatments since the mid 1990s may explain the reduction in the magnitude of weight gain observed in some of the subsequent research (22,25). Harvie et al., (17) reported a mean weight gain of 3.3 kg among pre and postmenopausal women treated with 6 months of FEC or CMF adjuvant therapy; a finding that is consistent with studies in which patients were treated with similar protocols (13,27,38). Others have reported that, when only four cycles of AC was the dominant therapy, weight gain during treatment was minimal and in most cases not significant (15,16,22,32). It is possible that lengthy protocols, often involving the use of multi-agent therapies, reflect longer and harsher exposure to the conditions that affect behaviour change.

Earlier suggestion that tamoxifen therapy may contribute to weight gain (21,39) is not supported by recent investigations (25,27,30,36,40). One of the largest of these studies (36) found that, over a 6-year follow-up, tamoxifen alone was not associated with significant weight gain, nor did the addition of tamoxifen to chemotherapy treatment modify the effect of chemotherapy on weight gain. The use of corticosteroids (dexamethasone, prednisone) to treat inflammation and nausea and vomiting associated with some chemotherapy agents and the use of megestrol acetate for advanced stage disease are known to produce significant weight gain during treatment (41,42). The wide range of chemotherapy protocols and other medications that are currently used in breast cancer treatment may explain some of the variability in weight gain that has been observed.

**Menopause status**

Studies conducted before the mid 1990s, suggested that weight gain after diagnosis seemed to be more pronounced among premenopausal women (20,21): a finding that is supported by some (14,23,25,26,32,35,37) but not all later investigations (14,27–29,33,38,43). In 2009, Heideman et al. (37) reported a mean weight gain of 2.0 kg and 2.4 kg, among women treated for stage 0-III disease, 1 year and 5 years after diagnosis, respectively. Stratification by menopause status however, demonstrated that weight gain in this sample was largely limited to premenopausal women who gained an average of 3.9 kg at 5 years versus 1.1 kg in postmenopausal women. Data from the Life After Cancer Epidemiology (LACE) and WHEL studies (35,44) revealed that women who were premenopausal at diagnosis gained significantly more weight (5.6 kg vs. 3.0 kg, P < 0.001) and were significantly more likely to gain at least 5% of their body weight between pre-diagnosis (~1 year) and study entry (mean = 23 months after diagnosis) compared with women who were postmenopausal at diagnosis (P < 0.01).

Higher weight gain in premenopausal woman may correlate with treatment-induced menopause. This effect is thought to be mediated by alterations in ovarian function and sex hormone concentrations which may produce an acceleration of the normal physiological changes associated with menopause including fat accumulation, changes in fat distribution and a decrease in lean body mass (45,46). Among 535 women treated for early stage disease, Goodwin et al. (25) found that premenopausal women who experienced treatment-induced menopause gained significantly more weight (2.65 kg) over a 1-year follow-up, compared with women who remained pre- or perimenopausal (1.07 kg) or who were postmenopausal (1.03 kg) at diagnosis. Controlling for age, initial body weight and adjuvant treatment, a multivariate analysis revealed that onset of menopause was a significant predictor of weight gain (P < 0.05) in the first year after diagnosis (25). In a small sample of women with early stage disease, Freedman et al. (32) found that while menopause status was not associated with weight gain during treatment, women who were premenopausal at diagnosis gained significantly more weight than postmenopausal women in the 6-month period after the completion of chemotherapy (+2.43 kg vs. –0.24 kg, P < 0.01). It is noteworthy that in this study, all but one of the women became a menorrhoeic within 6 months of completing chemotherapy. Small sample size may have been a methodological barrier for some studies in which a relationship between menopause status and weight gain after diagnosis was not evident (14,27,38). Other explanations for discordant findings include variation in timing of recruitment (24), length of follow-up (38) and the degree of control for potential confounding variables (e.g. diet, physical activity, resting energy expenditure). Although it appears that premeno-
Menopausal women may experience greater risk during and after treatment, it is important to recognize that weight gain is a persistent problem for many postmenopausal women as well.

### Lifestyle

While there is an established link between adjuvant chemotherapy and weight gain, especially for women on longer duration treatments, potential changes in diet and physical activity, in response to the stress of cancer and its treatment, is an area of active research. Evidence of weight gain among breast cancer patients who received no form of adjuvant treatment (41, 47), coupled with data clearly showing progressive weight gain in many breast cancer survivors after initial treatment, suggest that behavioral changes affecting energy balance may play an important etiologic role (24). Despite recent efforts to capture possible changes in dietary intake during and after treatment, empirical support for an increased energy intake after diagnosis and an association between increased energy intake and post-diagnosis weight gain is lacking (13, 15–18, 25, 43). Several studies however, have documented a significant reduction in physical activity during and after treatment, suggesting a role in post-diagnosis weight gain (15, 18, 43, 48, 49).

### Health consequences

Ten studies investigating the effects of weight gain after diagnosis on disease-free survival are equivocal (Table 2). For the purposes of this review “disease-free survival” (DFS) outcomes will include no breast cancer recurrence or breast cancer mortality over the follow-up period (range = 3.5–9.3 years).

Four studies have found a positive association (47, 50–52). Chlebowski et al. (50) reported an inverse relationship between weight gain and DFS; however, the absence of data concerning other prognostic indicators makes this results difficult to interpret. Perhaps more convincing are the findings of Camoriano et al. (47) who followed a large sample of node positive pre and postmenopausal women treated with or without adjuvant chemotherapy, for more than 6 years. Over 60 weeks of treatment, premenopausal women gained significantly more weight compared with postmenopausal women. Controlling for age, tumour characteristics, nodal status and initial body mass index (BMI), a median follow-up of 6.6 years revealed that premenopausal women who gained more than the median amount of weight were 50% more likely to experience disease recurrence and 60% more likely to die from their disease. Despite a similar trend, weight gain among postmenopausal women was not significantly associated with recurrence or overall survival.

Based on a sub-sample of women with breast cancer from the Nurses Health Study, weight gain among women who had never smoked was associated with poor outcomes (51). Compared with women who maintained a stable weight in the first 12–24 months after diagnosis, a multivariate model revealed that women who gained 0.5–< 2.0 BMI (kg/m²) units (median = 2.73 kg) and ≥2.0 BMI units (median = 7.73 kg) were 40% and 53% more likely to experience disease recurrence over a 9-year follow-up period. Similar findings were observed for breast cancer deaths and all-cause mortality. Weight gain among women who were overweight or obese at diagnosis was not associated with increased risk. Lastly, Nichols and colleagues (52) followed a large cohort of women with a diagnosis of invasive breast cancer [n = 3993] for an average of 6.3 years and found that among women who gained weight after diagnosis, each 5 kg gain was associated with a 13% increase in breast cancer death and a 12% increase in all-cause mortality. Cardiovascular disease mortality was similarly associated with weight gain (19% increase for each 5-kg weight gain, P < 0.05) suggesting the possibility of a graded increase in the risk of breast cancer and non breast cancer related death and emphasizing the potential for weight maintenance to improve long-term survival (52).

While these results are intriguing, six additional studies, failed to identify a relationship between post-diagnosis weight gain and prognosis (28, 30, 35, 41, 53, 54). Combined data from ≥8000 women from the LACE and WHEL studies (35), found that at 5- and 7-year follow-ups, respectively, after controlling for known prognostic indicators, weight gain after diagnosis was not associated with disease recurrence. A follow-up study of only LACE participants (44) found that after 7 years, weight gain was not associated with DFS or overall survival. While BMI before diagnosis was significantly associated with all-cause mortality, with a trend towards an increased risk of breast cancer death, weight gain after diagnosis did not seem to confer additional risk of recurrence, breast cancer death or death from any cause. It is possible that pre-morbid body weight, which may reflect longer exposure to the effects of overweight or obesity and may correlate with other lifestyle behaviours, may be more critical in predicting breast cancer outcomes (44). Other studies are less convincing because of relatively small sample sizes (28, 30, 55, 54) and short follow-up (30, 55, 54).

With conflicting results from two large carefully controlled, prospective studies (35, 52), it is clear that further research in this area is needed. Consistent timing of weight measures and definition of recurrence endpoints is needed (44). Most studies have been limited to weight gain in the year after diagnosis; however, possible effects of progressive weight gain after the first year, a well-documented problem for many breast cancer survivors, needs to be established (44).
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample size, key characteristics</th>
<th>Follow-up</th>
<th>Weight measure</th>
<th>Weight GAIN</th>
<th>Relationship between weight gain and DFS</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cammarano et al. 1991 (47)</td>
<td>n = 64, age 20-75 years, Node positive disease treated with or without adjuvant chemotherapy Minneapolis/USA</td>
<td>Median = 5.5 years</td>
<td>Body weight at randomization (within 6 weeks of surgery) and after treatment (60 weeks)</td>
<td>Median weight gain: Premenopausal = 5.9 kg Postmenopausal breast cancer = 3.6 kg Postmenopausal non-treated = 1.8 kg</td>
<td>Premenopausal women who gained more than median weight had higher risk of recurrence (HR = 1.5, ( P = 0.01 )) and death (HR = 1.6, ( P = 0.02 )); Postmenopausal women with weight gain had N/S effect on recurrence or survival</td>
<td>Controlled for lymph node status, age, nuclear grade, initial BMI, estrogen receptor status and tumour size</td>
</tr>
<tr>
<td>Cann et al. 2006 (36)</td>
<td>n = 3250, age 19-70 years (mean age at diagnosis = 66.3 years), Stage I-IV, Data from LACE and WHEL USA</td>
<td>Median = 5 years (LACE) 7 years (WHEL)</td>
<td>Body weight 1 year before diagnosis and at enrolment (mean = 23 months from diagnosis)</td>
<td>Mean weight gain = 2.4 kg Weight gain was progressive after diagnosis in both groups, stabilizing at ~ 3 years</td>
<td>No association between weight gain and risk of breast cancer recurrence No association between weight gain and DFS or all-cause mortality (LACE only - 7 year follow-up)</td>
<td>Controlled for age, stage, lymph node status and hormone-receptor status, treatment type, pre-diagnosis BMI</td>
</tr>
<tr>
<td>Ciakowski et al. 2006 (50)</td>
<td>n = 62, 44 positive nodes, Adjuvant chemotherapy Western USA</td>
<td>Median = 112 months (range: 0-138)</td>
<td>Body weight before and after treatment (12 months)</td>
<td>91% of CMF-treated women gained weight Mean = 3.7 kg 74% of 5-year treated women Mean = 2.0 kg</td>
<td>Weight gain &gt; 10 kg associated with poor prognosis - 85% of women who gained &gt; 10 kg had not survived at follow-up vs. 44% survival in women who gained &lt; 10 kg</td>
<td>All patients at high risk for recurrence, based on inclusion criteria</td>
</tr>
<tr>
<td>Costa et al. 2002 (28)</td>
<td>n = 106, age 36-78 years, (mean = 46 years), Adjuvant, neoadjuvant and palliative chemotherapy, Sao Paulo, Brazil</td>
<td>Median follow-up not &gt; 4 months</td>
<td>Body weight before and after one or more cycles of chemotherapy (mean = 49 months)</td>
<td>81% of women receiving adjuvant or neoadjuvant treatment gained weight Mean = 0.81 ± 1.39% / month</td>
<td>Tend toward decreased DFS for women who gained weight but N/S (( P = 0.08 ))</td>
<td>No association between weight gain and DFS or over all survival</td>
</tr>
<tr>
<td>Goodwin et al. 1985 (41)</td>
<td>n = 637, mean age across groups = 55-56.5 years, Localized disease treated with or without adjuvant chemotherapy, Toronto ON</td>
<td>Median follow-up recruitment (range: 1963-1984)</td>
<td>Body weight at diagnosis and 1 year after diagnosis</td>
<td>Body weight gain = 1.21-6.51 kg across 5 treatment groups</td>
<td>No association between weight gain (quintiles) and DFS or over all survival</td>
<td>Controlled for age, initial weight, lymph node status, menopause status and use of adjuvant therapy Weight lossing is up to 32% for some groups</td>
</tr>
<tr>
<td>Haasman et al. 1985 (53)</td>
<td>n = 237, age 25-70 years (mean = 47.0 years), Stage I adjuvant chemotherapy, Toronto ON</td>
<td>Median follow-up not &gt; 2 years</td>
<td>Body weight before and after treatment (12 months)</td>
<td>74% of patients gained weight during treatment Mean = 4.9 kg</td>
<td>No association between weight gain (quintiles) and DFS or over all survival</td>
<td>Controlled for lymph node status, menopause status and type of treatment</td>
</tr>
<tr>
<td>Reference</td>
<td>Sample (4 key characteristics)</td>
<td>Follow-up</td>
<td>Weight measures</td>
<td>Weight GAIN</td>
<td>Relationship between weight gain and DFS</td>
<td>Comments</td>
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<td>Kocanek et al. 2003 (51)</td>
<td>M = 5,004, age 30-45 years, Invasive non-metastatic disease. Sub-sample from the Nurses Health Study, USA</td>
<td>Median = 9 years (range 2-36 years)</td>
<td>Pre-diagnosis BMI and post-diagnosis BMI (most recent measure = 12 months)</td>
<td>33% of patients gained 0.5 to 2.9 kg/m². Mean = 2.73 kg. 34% of patients gained ≥ 2.9 kg. Median 18.2 kg.</td>
<td>Among breast cancer survivors, weight gain is associated with increased risk of recurrence. Weight gain &gt; 2.9 kg (HR = 1.42, P &lt; 0.001). Weight gain 6.5 to 2.9 kg (RR = 1.15, P &lt; 0.05). Similar findings for breast cancer death and all-cause mortality.</td>
<td>Controlled for age, pre-diagnosis BMI, oral contraceptive use, BMI, health index, menopause status, protein intake, tumor size, lymph node status and treatment.</td>
</tr>
<tr>
<td>Levine et al. 1991 (54)</td>
<td>M = 32, age 25-55 years (mean = 46 years), 40% lymph node involvement, Adjunct chemotherapy, Birmingham, AL</td>
<td>2 years</td>
<td>Body weight before and after treatment (3 months) and 2 years follow-up</td>
<td>69% of patients gained weight during treatment. Mean = 1.9 kg. 84% of patients gained weight at 2 years. Mean = 4.8 kg.</td>
<td>Women who lost weight at 2 years had 26% higher risk of recurrence, but this effect was not significant (P &gt; 0.05). Weight gain &gt; 2.5 kg at 1 year was not associated with DFS (any breast cancer event including new primary, relapse-free survival, recurrence or overall survival).</td>
<td>Stratified by menopause status and menopause status.</td>
</tr>
<tr>
<td>Malik et al. 2007 (23)</td>
<td>M = 185, age 25-91 years (mean = 50.5 years), Stages I-III, Adjunct chemotherapy and/or hormonal therapy, USA</td>
<td>3 years</td>
<td>Body weight at diagnosis and 12.5 years after diagnosis</td>
<td>71% of patients gained weight at first year. Mean = 1.4 kg. Mean weight gain at 2 years = 2.7 kg. Mean weight gain at 3 years = 2.6 kg.</td>
<td>Among women who gained weight, each 5 kg of weight gain was associated with increased risk of all-cause mortality (HR = 1.12, P &lt; 0.05) and breast cancer mortality (HR = 1.13, P &lt; 0.05). Weight gain &gt; 10 kg = 31% increase in all-cause and breast cancer mortality.</td>
<td>Controlled for age, US state, family history of breast cancer, and menopausal status at diagnosis.</td>
</tr>
<tr>
<td>Nichols et al. 2009 (52)</td>
<td>M = 3903, age 25-87 years (mean = 59 years), Invasive non-metastatic disease, New Hampshire, Massachusetts and Wisconsin, USA</td>
<td>6.3 years</td>
<td>Body weight 1-6 years before diagnosis and at study enrollment (mean = 5.6 years from diagnosis)</td>
<td>58% of patients gained 0.5-2.9 kg. 15% of patients gained ≥ 2.9 kg.</td>
<td>Among women who gained weight, each 5 kg of weight gain was associated with increased risk of all-cause mortality (HR = 1.12, P &lt; 0.05) and breast cancer mortality (HR = 1.13, P &lt; 0.05). Weight gain &gt; 10 kg = 31% increase in all-cause and breast cancer mortality.</td>
<td>Controlled for age, family history of breast cancer, and menopausal status at diagnosis.</td>
</tr>
</tbody>
</table>

BMI: body mass index; HRT: hormone replacement therapy; LACE: Life After Cancer Epidemiology; NS: not significant; WHEL: Women's Healthy Eating and Living.
Although the effect of weight gain on DFS is uncertain at this time, it is clear that obesity and weight gain in the post-diagnosis period have a negative effect on overall health and all-cause mortality. An extensive review of non-cancer deaths in adult cancer patients revealed an overall hazard ratio that was 1.37 times the expected age and sex-specific mortality rate for the general population (55). A greater risk of non-cancer related death was attributed to the side effects of cancer treatment and the cumulative effects of comorbid conditions. Excessive weight gain, especially an increase in relative adiposity, predisposes breast cancer survivors to obesity related disorders including cardiovascular disease, diabetes, gallbladder disease and orthopaedic disturbances (20,55). This is concerning because most women diagnosed in the early stages of disease will be cured of breast cancer, but are subsequently exposed to an increased risk of chronic disease after treatment (20,40). Furthermore, weight gain itself, even among women whose BMI remains within the normal range, is associated with an increased risk of morbidity and premature death (56,57).

In addition, weight gain after diagnosis is distressing for many women and may contribute to poor quality of life and loss of self-esteem at a time when vulnerable patients are already under a great deal of stress (15,27,31,58). Moreover, for some women, weight change after diagnosis may serve as a constant reminder of their illness and treatment (19).

Conclusions

Weight gain is a common and persistent problem for many breast cancer survivors. As many as 50–96% of women experience significant weight gain during treatment (6) and many, including some women who remain weight stable during treatment, report progressive weight gain in the months and years after diagnosis. Among those who gain weight, average increases typically range from 2.5–6.2 kg, however significantly higher gains are not uncommon. Weight gain is more common in women receiving adjuvant chemotherapy, especially for women on longer duration treatments and appears to be especially pronounced in premenopausal women. Several studies have reported unfavourable changes in body composition, with or without weight gain, in this population; sarcopenic obesity, characterized by high body fat and low lean body mass is prevalent. This unique pattern of weight gain and/or change in body composition is distressing for most women, poses significant risk for the development of comorbid conditions and may impact on long term disease-free survival.

Given the adverse consequences of weight gain after diagnosis, continued efforts to identify the underlying mechanisms of energy imbalance in the post-diagnosis period are needed. Further insights into the possible inter-related effects of chemotherapy, menopause status and lifestyle on weight gain will help to identify women most at risk and will inform the development of appropriate targeted weight management interventions aimed at promoting overall health and long term survivorship (10,21).

Conflict of Interest Statement

No conflict of interest was declared.

Acknowledgements

V.V is funded by a Doctoral Research Award from the Canadian Institutes of Health Research.

References


Appendix A

Chemotherapy protocols for early stage breast cancer

<table>
<thead>
<tr>
<th>Class</th>
<th>Mode of action</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating Agents</td>
<td>damages the proteins that control growth in the genes of the tumor cell</td>
<td>cyclophosphamide</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>acts as a false building block in the genes of cancer cells, causing cell death</td>
<td>5-fluorouracil, gemcitabine, capcitabine</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>inhibits gene replication</td>
<td>doxorubicin, epirubicin</td>
</tr>
<tr>
<td>Antimotic Agents</td>
<td>prevents genes from reproducing themselves during cell division</td>
<td>vincristine, vinorelbine</td>
</tr>
<tr>
<td>Antimicrotubule</td>
<td>interferes with cell structure and cell division</td>
<td>paclitaxel, docetaxel</td>
</tr>
</tbody>
</table>

Common Chemotherapy Combinations Used to Treat Breast Cancer

AC – doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan, Procytox)
- usually given every 21 days for 4 cycles
- treatment last – 3–4 months

AC + T – doxorubicin, cyclophosphamide + paclitaxel (Taxol) or docetaxel (Taxotere)
- usually given every 21 days – 4 cycles of AC, followed by 4 cycles of paclitaxel or in the case of docetaxel, every 21 days for 6 cycles
- Note: AC with docetaxel often requires colony-stimulating factor drugs (i.e. filgrastim (Neupogen) treatment last – 4–6 months

FAC (or CAF) – cyclophosphamide (orally or IV), doxorubicin and 5-fluorouracil (5-FU, Adrucil)
- usually given every 21 days for 6 cycles
- treatment last – 4–6 months
- Note: when cyclophosphamide is given orally, FAC is usually given every 28 days for 6 cycles

CEF – cyclophosphamide (orally), epirubicin (Ellence) and 5-fluorouracil
- usually given every 28 days for 6 cycles
- treatment lasts – 4–6 months

FEC - 5-fluorouracil, epirubicin and cyclophosphamide (IV)
- usually given every 21 days for 6 cycles
- treatment last – 4–6 months

CMF – cyclophosphamide (orally or IV), methotrexate and 5-fluorouracil
- usually given every 28 days for 6 cycles
- treatment last – 6 months
- Note: this protocol is now used rarely

In some cases, single drugs including vinorelbine (Navelbine), capicabine (Zeloda), paclitaxel (Taxol), docetaxel (Taxotere) or gemcitabine (Gemzar) are used to treat metastatic or recurrent disease

Adapted from Canadian Cancer Society (2009), American Cancer Society (2009), Breastcancer.org (2008)