Post-diagnosis Dietary Intakes, Body Mass Index and Lipid Profiles of Breast Cancer Survivors undergoing Adjuvant Chemotherapy

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Abstract

Background: The number of breast cancer survivors is increasing owing to improved screening, detection and more targeted treatments. With a 5-year survival rate of around 85%, recurrence, mortality and comorbidity are becoming considerable concerns for this population. The role of diet in improving outcomes post-diagnosis is yet to be fully explored. However as weight gain is common both during and after treatment, nutrition and lifestyle interventions aimed at attenuating the risk of weight gain and obesity could be appropriate for reducing the subsequent risk of poor prognosis and associated chronic diseases. Additionally, many women have been found to spontaneously change their diets post-diagnosis The dietary intakes of the New Zealand breast cancer population have yet to be studied.

Objective: This study aimed to describe changes in dietary intakes, BMI and blood lipid profiles of breast cancer survivors undergoing adjuvant chemotherapy.

Design: Data were derived from a longitudinal observational study of 10 women (age 25-65 years) with newly diagnosed breast cancer in Dunedin, New Zealand. Dietary intake assessed by 4-day diet records, BMI and blood lipid profiles were taken at three time-points, before and twice during chemotherapy.

Results: There was no meaningful change in the mean macronutrient intake during the study period. Mean protein intake (% total energy) increased 1.5% from mid-point to final measures. No change in BMI nor cholesterol and triglyceride profiles was observed over study period however there were associations between energy, protein and fat intakes and blood LDL-cholesterol from mid-point to final time-points.

Conclusion: Given previous research shows dietary changes occur post-diagnosis it is interesting that there was generally no change in the macronutrient composition of the diets during the treatment period. However there was a small increase of protein by 1.5% (P=0.017) from the mid-point to final study measures. This lack of change may be the consequence of the short study timeframe, the small sample size or may additionally suggest a lack of nutrition advice being provided in clinical settings. Although there was no change in BMI over the study, 90% of the women were overweight or obese at baseline potentially increasing the risk of poor prognosis from treatment outset. The unfavourable blood lipid profiles observed also highlight a need for lifestyle improvements in this vulnerable group. Continued research is required to fully elucidate the dietary patterns and beliefs regarding nutrition post-diagnosis with a larger sample size and longer follow-up as the study period.

Preface

The Candidate worked with Dr Katherine Black and Dr Lynnette Jones to describe the dietary intakes, BMI and blood lipids of breast cancer survivors in Dunedin, New Zealand. The dataset was derived from a longitudinal, observational study conducted in the School of Physical Education previously analysed by Saskia van den Ende. The candidate was responsible for data entry of dietary analysis into Kai-culator; involved with the statistical analysis along with a biostatistician (Jill Haszard); and was responsible for interpretation and presentation of results, and preparation of the thesis.

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List of Abbreviation

ACS	American Cancer Society
AMDR	acceptable macronutrient distribution ranges
BMI	body mass index
CV	coefficient of variation
CVD	cardiovascular disease
HDL	high-density lipoprotein
i.e	that is
kg	kilogram
kJ	kilojoule
L	litre
LDL	low-density lipoprotein
mmol	millimol
m^2	meters squared
n	number
TAG	triglyceride
TE	total energy
WCRF	World Cancer Research Fund
4-day diet record	four-day diet record
β	beta coefficient from regression analysis

1. Introduction

Breast cancer contributes significantly to the total New Zealand cancer registries and in 2010, was the most commonly diagnosed malignancy in the female population accounting for 27.5% of all new registrations (1). Age-standardised rates parallel those seen overseas however with improved detection and treatment, mortality rates have decreased by 19.4% over this time period resulting in an increased number of breast cancer survivors. Indeed, the current 5-year survival rate in New Zealand is close to 86% (2). Despite the encouraging survival rates, women are still at an increased risk of recurrence, new primary breast cancer, mortality and comorbidity than those without a history of breast cancer (3-5).

Obesity (BMI $\geq$ 30kg/m^2) at diagnosis is a well-recognised risk factor for recurrent cancer, cancer specific death and all-cause mortality in breast cancer survivors (6-11). With the rates of overweight and obesity reaching epidemic proportions, many of the newly diagnosed patients are entering the treatment phase already at risk of poor prognosis (12). Additional weight gain is a common side-effect of adjuvant chemotherapy (13-16), especially with the use of multi-agent regimens therefore having the potential to exacerbate the risk of recurrence and mortality in this already at risk group (17). Moreover, obesity is associated with comorbidity such as cardiovascular disease, diabetes, hypertension and osteoporosis (18). Modifying treatment-related

weight gain through diet and lifestyle measures is therefore a priority for this population (19, 20).

Although research regarding the role of diet in the prevention of recurrence and mortality in the breast cancer survivor population is yet to be fully explained there is some suggestion that a diet high in fruits, vegetables, wholegrains and low in fat may improve non-cancer related outcomes (21, 22). In line with this, the American Cancer Society (ACS) has developed recommendations for both prevention of initial malignancy and for breast cancer survivors based on the 'probable' role of diet in the modification of cancer risk (23). The primary goal for survivors is to achieve and maintain a healthy body weight through a balanced diet and exercise (24).

The post-diagnosis dietary practices of breast cancer survivors has been studied with mixed findings regarding the degree and type of behaviour change adopted (20). This may be partly owing to the variation in study methodologies, such as the time since diagnosis in which diet was investigated and dietary assessment methods used, many choosing food frequency questionnaires (FFQ) that are subject to recall and social desirability bias (20). Despite this, survivors have been found to make spontaneous dietary change (25-27) and more importantly are motivated to improve their lifestyle to aid recovery, reduce the risk of recurrence, and enhance quality of life following diagnosis and treatment (19, 20, 28). Little is yet known about the New Zealand breast cancer population in particular their dietary intakes in relation to body mass index and blood lipids.

2. Literature Review

2.1 Breast cancer

There are multiple risk factors for cancer which can accumulate over time, either acting sequentially or conjunctively to initiate and promote growth of cancerous cells (29). Causal factors are categorised as internal or non-modifiable (increasing age, hormones, genetic susceptibility, mutations secondary to metabolism) or external sometimes referred to as environmental (radiation, chemicals, smoking, infectious pathogens, obesity, alcohol), which by contrast are modifiable (30, 31). There are a number of accepted risk factors for breast cancer, namely increasing age, family history and genetic susceptibility however there is an increasing focus on elucidating the potential role of diet in modifying risk (32, 33).

Despite the wide acceptance that many of the risk factors are modifiable, cancer is now the leading cause of mortality worldwide and in 2008 accounted for 7.6 million deaths (34). Cancer is the generic term for a range of malignant diseases within the body, specifically tumours or neoplasms (35). The cancer cells that comprise these tumours have defining characteristics, namely their ability to proliferate outside of their usual boundaries, indefinitely (36). There are two categories of growth, carcinoma and adenocarcinoma. Carcinoma is the irregular and uninhibited grow of mutated cells, initiated within epithelial tissue whereas adenocarcinoma originates within glandular

tissue (35, 37). The majority of breast cancers are of epithelial origin with a large number of cases derived from ductal or lobular tissue (3).

Improved breast cancer screening, earlier detection and advancing treatment has leant itself to improving survival rates in the breast cancer population, especially for the first five years following treatment (7, 29). Indeed, advancements in treatment modalities (surgery, radiotherapy and chemotherapy) have resulted in greater effectiveness and reduced toxicity thus reducing some of the negative side-effects previously common to patients (38). Additionally adjuvant chemotherapy has been shown to significantly increase disease-free survival and reduce the risk of recurrence and mortality in women with early stage breast cancer (39-41).

The chemotherapy treatment for breast cancer is a systemic one, commonly used in adjuvant to the primary removal of the tumour. The majority of the drugs work by targeting reproducing cells, effectively terminating growth and replication i.e. are cytotoxic (42). The difference in drug regimens administered is determined by the cell type and stage of reproduction, whereby many drugs are given conjunctively to target multiple stages of the cell cycle (40). Most frequently treatments involve the primary use of a multi-agent regimen (usually anthracyclines, antimetabolites and alkylating agents) followed by a single-agent regimen (usually taxanes) (4,7).

2.1.1 Prevalence and prognosis

In the United States, breast cancer mortality rates decreased 2.2% per year between 1990-2007, again the likely result of earlier detection and improved treatment (30). The survival rates after diagnosis are also favourable; 90% survival at 5 years after diagnosis, 82% after ten years and 77% after 15 years (30). However, cancer is the leading cause of death in New Zealand, accounting for around 30% of mortality (43). In 2008, the International Agency for Research on Cancer estimated New Zealand to have an age-standardised incident rate of 89.4 per 100,000, similar to rates in Australia, United States and Europe. Specifically, breast cancer accounts for 13.3% of all cancer cases, making it the second most prevalent disease site (43). Despite the high prevalence, breast cancer survival rates in New Zealand are similar to rates overseas of around 85% at five years post-diagnosis (44).

Although the risk of recurrence is decreasing and survival rates are improving, the rates of mortality are higher amongst cancer survivors compared to the general population. There may also be an increased risk of comorbidities such as cardiovascular disease, especially in light of treatment-related weight gain and sedentary behaviour, possibly secondary to treatment induced fatigue (5, 13, 20). Indeed studies have reported between 20% to 30% of non-cancer deaths in cancer survivors are attributable to cardiovascular disease (CVD) (21, 22). The rate of ischemic heart disease (the most common form of heart disease) in New Zealand women is currently 4.1% (45). This increased risk in the breast cancer survivor population is possibly partly due to a higher prevalence of

overweight and obesity, a lack of physical activity and poor dietary choices (17, 46). The potential role of diet in modifying the risk of primary cancer, prognosis and comorbidities is therefore a relevant and evolving area of research which will be further explored (30).

It is important to note the differential etiologies of pre- and post-menopausal breast cancer and the corresponding risk factors in terms of weight. The 2010 World Cancer Research Fund Report on breast cancer, states that premenopausal women have a probable reduction in risk of breast cancer with increasing body fatness (47). Conversely, there is convincing evidence to support an increased risk of breast cancer in postmenopausal women, in particularly abdominal adiposity. This posses a paradoxical challenge in terms of intervention, as weight loss in premenopausal woman may not confer benefit in terms of survival (47). Additionally, it may be more appropriate to tailor interventions based on menopausal status. However, achieving and maintaining a healthy weight, regardless of menopausal status remains one of the main goals according to the American Cancer Society and the potential benefits in terms reducing the risk of comorbidity and increasing quality of life should not be disregarded (48).

2.2 Obesity and weight gain

Weight gain during the first year of treatment is a common side effect for early stage breast cancer patients, in particular with the use of adjuvant chemotherapy (14-16, 49).

The mechanisms are yet to be fully clarified however it appears that weight gain is multifactorial but probably the result of a combination of fatigue, dietary intake, metabolic and hormonal changes (13, 18, 50). The treatment mode is another factor which influences weight gain whereby women who are prescribed systemic treatment gained significantly more weight than those who received localised treatment (16). Furthermore, multi-agent regimens are associated with greater weight gain compared to single-agent regimens and the dose and duration of treatment can also result in varying weight gain (51, 52).

The amount of weight gain reported throughout the treatment phase varies however early research suggested 50-96% of early stage breast cancer patients gained in the range of 2.5-6.2kg during the treatment period alone, some gaining over 10kg (50, 51, 53, 54). However recent research has supported a pattern of moderate weight gain during the treatment phase and more pronounced and progressive gains after treatment conclusion (15, 50, 51, 55, 56). Indeed weight gain during treatment has been linked to risk of recurrence, all-cause mortality and comorbidity (18, 50). An early study by Camoriano *et al*. revealed that premenopausal woman who gained more than the median amount of weight (5.9kg) at 60 weeks had 1.5 and 1.6 times greater risk of recurrence and death respectively (57). Additional studies support this finding (17, 58) with an American study of 111 women diagnosed with early breast cancer and locally advanced breast cancer undergoing anthracycline-based treatment showed post-diagnosis weight change of more than 5% was associated with an increased risk of both recurrence (RR 2.28; 95% CI: 1.29-4.03) and death (RR 2.11; 95% CI: 1.21-3.66) (59). Similarly, CVD specific mortality has

also been associated with post-diagnosis weight gain (19% increased risk with each 5kg gain) (59).

The composition of weight gained is also important to consider in this population as many studies report a concurrent increase in fat mass and decrease in fat free mass resulting in sarcopenic obesity (56-61). Weight gain is also of clinical relevance in terms of psychosocial outcomes and quality of life in this population with women reporting increased anxiety regarding body image during treatment (62). This having potential follow-on implications surrounding dietary habits whereby women may use food as a coping mechanism. Indeed, Tangney *et al.* found an inverse association between depression and diet quality in breast cancer survivors 0.5-5 years after their diagnosis (63).

When considering the increased prevalence of obesity and CVD amongst breast cancer survivors some consideration of their pre-diagnosis weight is required when reviewing the published literature. Due to increasing rates of overweight and obesity worldwide, it is not surprising that a large proportion of the breast cancer population is overweight or obese at diagnosis (58, 64). Further, obesity pre-diagnosis is associated with poorer prognosis, and any subsequent weight gain during the treatment period can confer additional risk of negative outcomes (17). Specifically, obesity has been linked to recurrence (6, 8) and cancer-specific mortality (7). Indeed, Goodwin *et al.* has reported women in the highest quartile for body mass had a substantially greater risk of distant recurrence 2.1 (95% CI: 1.2-3.6) and death 3.3 (95% CI: 1.5-7.0) (65).

Proposed mechanisms explaining the relationship between weight and body composition change and poor prognosis in the breast cancer population are based on metabolic and hormonal changes secondary to treatment (18). Although the evidence is not yet convincing, studies have suggested obesity related insulin resistance; hyperinsulinaemia, adipokines, cytokines and estrogen are the primary factors associated with poor prognosis in obese breast cancer patients (18).

Estrogen has a well-established role in the risk of breast cancer (66). Adipose tissue through the action of aromatase has the ability to convert androgens to estrogen, making it a major source of estrogen and subsequent tumour growth (67, 68). Research has shown that obese women have 35% and 130% higher concentrations of oesterone and oestradiol respectively compared to women of normal weight (69). Likewise, those who are obese have a higher propensity to be insulin resistant and have hyperinsulinaemia (70). Higher fasting insulin has been linked to greater risk of recurrence and death, again through promotion of tumour cell growth (18, 70, 71).

Differences in study populations including mode and duration of treatments, menopausal status, stage of cancer at diagnosis and post treatment care make it difficult to fully determine the exact mechanisms. Despite this it does appear that controlling weight during treatment could improve both the length and quality of life post-treatment. This is recognised by the American Cancer Society's (ACS) who primarily recommend cancer survivors is to strive for and maintain a healthy weight, in particular if overweight or obese at diagnosis (19).

2.2.2 Post-diagnosis diet in breast cancer survivors

A meta-analysis published by the World Cancer Research Fund (WCRF) looking at causes of cancer noted the 'probable' role that diet has in cancer prevention making this a large area of interest (23). Despite the inconsistent findings, diet is one potentially modifiable risk factor for both initial breast cancer risk but also recurrence. This information has led many breast cancer survivors to include more foods perceived as protective against cancer after a diagnosis (28, 32, 72-74). Alcohol however remains the only dietary consistent conclusively linked to cancer (23).

Unlike that of weight gain and prognosis, the relationship between nutritional factors and subsequent outcomes in breast cancer survivors is less convincing (7). Although research is limited in regards to dietary modification and subsequent risk of comorbidities and recurrence in breast cancer survivors, two studies have shown a reduction in the risk of non-breast cancer related death with increasing compliance to a prudent dietary pattern (high intakes of fruit, vegetables, wholegrains, legumes, low-fat dairy, poultry and fish). Conversely a direct relationship between the intake of a western dietary pattern (high intake of processed and red meat, refined grains, and high-fat foods) and risk of non-breast cancer mortality has been observed (21, 22).

As survivors are at increased risk of developing secondary cancer and comorbid conditions such as cardiovascular disease, diabetes, osteoporosis, obesity and functional

decline, nutrition and lifestyle information and treatments need to target women when they are most receptive (20, 21). Research has suggested this period to be directly following diagnosis and throughout the treatment phase with a survey of cancer survivors showing 52% of breast cancer patients preferring nutrition interventions to be initiated directly or soon after diagnosis (26).

Although a large proportion (30-60%) of the breast cancer survivor population has been shown to independently improve their diet post-diagnosis, a significant number show no dietary changes (20, 25, 26, 28, 75). This may be in light of inconsistent evidence regarding post-diagnosis lifestyle interventions and cancer-specific outcomes and therefore a lack of sound recommendations and guidelines recognised globally. One study has shown that women's diets remain similar to those of the general population for fat and fruit and vegetable intake (both of which were suboptimal) in the 1-3 years post-diagnosis (76). However given the timeframe of this study of one-year post treatment it may be that any dietary changes were missed and it could be short-term dietary changes occur in the immediate post-diagnosis period but that behaviors return to pre-diagnosis in the longer term. Conversely, women have been shown to spontaneously improve their diets with commonly reported changes including increasing fruit and vegetable intake and reducing meat and fat intake (25, 28, 72-74). Whether this is true for the New Zealand breast cancer population however remains unknown.

The lack of uniform findings may be due to a combination of methodological differences such as mode of dietary assessment and sample populations used (20). Although the

majority of studies used FFQ's for data collection, some used diet recalls, records and questionnaires. This giving variable reliability and posing unique challenges regarding the accuracy of the collected data due to social-desirability and recall bias (77). Additionally, many studies have unique interpretations and definitions of breast-cancer survivors as well as having variable follow-up periods. This meaning some studies may capture population when they are more motivated to make healthy dietary changes e.g. just following a diagnosis.

However, studies have shown that a healthy diet and lifestyle is associated with better outcomes in terms of comorbidity and quality of life; both important considerations in a population as long-term survival continues to increase (21, 22, 75). In particular a prudent dietary pattern (diet high in wholegrains, fruits and vegetables, legumes, poultry and fish) is inversely associated with non-cancer specific mortality (21, 22). The second of these studies by Kroenke *et al.* showed that higher compliance or a prudent dietary pattern was associated with reduced risk of all-cause mortality (RR 0.54; 95% CI, 0.31, 0.95; p=0.03).

The ACS has developed nutrition and lifestyle recommendations for both prevention of primary cancer as well as for optimising nutrition and physical activity practices in cancer survivors (19, 24). Due to the inherent increased risk of secondary cancer and chronic disease, these guidelines have been developed in line with other organisations such as the American Heart Association to produce cohesive and non-conflicting messages for patients (19, 48). Additional to weight management, breast cancer survivors are encouraged to consume a healthy, balanced diet with emphasis on plant foods,

wholegrains and limited consumption of processed and red meats as well as alcohol (19, 24).

In regards to suggested macronutrient intakes and in light of lacking evidence to suggest otherwise, percentage of energy from fat is recommended between 20-35% with saturated and trans fats limited to <10% and <3% respectively (19). As adequate protein is integral for maintaining muscle integrity and an important nutrient during all stages of treatment and recovery, survivors are recommended to choose lean, high quality protein including fish, poultry, eggs, low-fat dairy products, nuts, seeds and legumes (24). An intake of 10-35% of energy from protein or 0.8g/kg body weight per day is suggested by the ACS to meet the needs of most adult cancer survivors. Furthermore, patients should aim for 45-65% of energy from suitable carbohydrates including fruits, vegetables and wholegrains rich in micronutrients, fibre, phytochemicals, also being important for weight management. These recommendations are generally in line with the Acceptable Macronutrient Distribution Ranges (AMDR) for macronutrients to reduce chronic disease risk adopted by the Ministry of Health and recommended for the general New Zealand population (78).

2.2.3 Dietary fat and prognosis

Dietary fat is a macronutrient of interest in relation to clinical outcomes in the breast cancer survivor population as it is thought to play an integral role in cancer malignancy etiology with proposed mechanisms including the role fat has in gene expression,

oxidative stress, cell apoptosis, alteration of hormone metabolism and association with higher calorie diets and thus risk of obesity (79). Evidence to date is conflicting regarding time of exposure i.e. whether pre- or post-diagnosis dietary fat intake is of greater importance in terms of survivor outcomes. Indeed the WCRF report states the evidence regarding fats and oils as 'limited' and 'suggestive' of an increased risk of breast cancer and then only in postmenopausal women (23). However a recently published systematic review by Makarem *et al.* has shown some evidence to suggest a positive association between total fat intake both before and after a diagnosis and cancer-specific mortality (79-81). This should be interpreted with caution as most of the studies are epidemiological in nature, thus causality can not be determined. There has however been two randomised controlled trials to date although their findings were not cohesive. Both studies were conducted in the United States investigating dietary fat intakes in cancer survivors and their subsequent prognosis. The Women's Intervention Nutrition Study was the first, showing that women receiving a low-fat diet post-diagnosis had a 24% reduced risk of recurrence compared to the control group who continued with their normal diet (82). The second study, Women's Healthy Eating and Living trial showed that despite significant dietary improvements (decreases in fat intake and increases in fruit and vegetable consumption) in the intervention arm, there was no difference in breast cancer events or mortality during the 7.3-year follow-up period when compared to the control arm (83). This lack of agreement between these studies suggests a possible but by no means convincing effect of reducing fat intake when assessing breast cancer recurrence and mortality.

2.3 Blood lipids and health outcomes

Cardiovascular disease is an inflammatory process that usually occurs in the arteries including those of the heart, brain and peripheries, potentially resulting in infarction and necrosis of surrounding tissue (84, 85). It is characterised by the plaque formation in the wall of these arteries mediated by pro-inflammatory cytokines, primarily interleukin 6 (IL-6) and tumor necrosis factor- α (TNF-α), however it is the blood lipid profiles of patients that are most commonly used in a clinical setting as a risk assessment for heart disease (86). Specifically total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides (TAG) are used as markers of both disease risk as well as being an indicator of diet quality, in particular dietary fat intake (87).

The role of diet in the modification of CVD risk is its potential to mediate inflammation and immune function (75). However it is yet to be established whether the relationship between diet and inflammation is direct i.e. an inverse association with specific foods or dietary patterns; or indirect i.e. a healthier diet helps facilitate the reduction of adiposity and therefore inflammation. Results to date have supported both arguments; some showing a higher diet quality or healthy eating index is inversely associated with inflammation (88, 89). Other studies have shown similar findings with diet and inflammation however when adjusted for BMI or physical activity, this association is attenuated or disappears, demonstrating that body mass moderates the relationship between diet and inflammation (75, 90). Indeed, in an intervention trial aimed at reducing

adiposity, Thompson *et al.* found that irrespective of the prescribed diet arm (either high fat-low carbohydrate or high carbohydrate-low fat), beneficial changes in blood lipid profiles were seen after 6 months compared to the control arm (91). Thus showing the importance of weight management in the control of blood lipids.

As the incidence of cancer increases with age, so too does the risk of cardiac disease. This along with the cardiotoxic potential of many chemotherapy agents (in particular anthracyclines) commonly used for the treatment of breast cancer results in an increased risk of CVD and related adverse outcomes (21, 22, 92). Diet and lifestyle therefore have an important role in helping to potentially mitigate this increased risk among this patient group.

2.4 Quantitative vs qualitative dietary assessment measures

The wealth of studies on dietary intake and breast cancer outcomes has lent itself to a large variation in the dietary assessment methods used, with many studies using assessment tools that had not been validated (20). This may explain some of the variability in the findings of published studies. The majority of studies assessing post-diagnosis intakes use food frequency questionnaire (FFQ) which provide descriptive information on usual intake and if semi-quantitative can also account for portion sizes (93). The advantage of using this method of assessment is it has a low respondent burden, its relatively cheap, easily disseminated, results are simple to collect and process (93). Although this method of dietary analysis is appropriate for studies with large sample sizes,

it may be subject to recall bias (94). This technique also relies on self-reported data and should therefore be interpreted as estimates rather than absolute values of intake (7). Given the high use of FFQs that were not validated in the published literature, some of the inconsistent findings may due to measurement error (95).

The gold standard of dietary assessment is the weighed food record, due to its precision and reliability. Respondents are asked to record and weigh all foods and beverages during a specific time period, usually three days (93). This measure of actual intake requires motivated, numerate and literate participants and due to its high respondent burden and large cost, may only be suitable for small groups (93). However limitations of this technique include its potential under-reporting, social desirability bias and respondents changing their intake for the sake of convenience (93). Additionally, its high respondent burden and relative expense has meant few studies have used this technique due to its limited feasibility in large sample sizes.

2.5 Conclusion of literature review

The inconsistency of findings relating to post-diagnosis diet and breast cancer outcomes could be explained by the variation in the timing of the studies post treatment as well as length of follow-up. Even when studies report participants as having 'early-stage' breast cancer they use different time-spans since diagnosis making it hard to compare studies. The difference in the stage of breast cancer in participants of studies is a further limitation in terms of generalising and comparing findings as the later the stage of cancer the more at

risk participants may be for poorer prognosis, recurrence, mortality and development of comorbidities (96). This may therefore reduce the potential effect of modifiable risk factors such as diet.

Additionally, the time in which dietary intake data is collected is of significance to the results as the stage of cancer treatment or survival may be indicative of specific dietary patterns. Further, time since diagnosis has not been adjusted for in many of the studies and (7) differences in screening, treatment and intervention protocols between countries may have contributed to variable findings. To date there have been no studies conducted in New Zealand and given differences in health care and dietetic support between countries, published results may not be generalisable to this population.

3. Objective Statement

To date there is no research on the dietary intake and relevant clinical indicators (BMI kg/m^2 and blood lipids) post-diagnosis in the New Zealand breast cancer population. Therefore, this study will:

1) Describe the macronutrient intakes of breast cancer survivors in Otago, New Zealand over the course of their adjuvant chemotherapy treatment.

2) Investigate the association between blood lipids and macronutrient intake in breast cancer survivors.

3) Examine change in body mass index (BMI) and in relation to dietary intake over the course of treatment in breast cancer survivors.

4. Subjects and Methods

4.1 Study design

This was an observational study, descriptive in design. It aims to assess the macronutrient intake of breast cancer patients over the course of their adjuvant chemotherapy treatment. This type of descriptive study is used to determine relationships and associations between variables namely dietary intake in relation to BMI (kg/m^2) and blood lipids.

The presented data is from a sub analysis of an observational, longitudinal study, which aimed to investigate the physiological and psychological impact of adjuvant chemotherapy treatment in women with primary breast cancer who are part of an exercise treatment (EXPINKT^{TM}). The EXPINKT^{TM} study was conducted in the School of Physical Education, University of Otago whereby women were invited to participate in supervised low intensity exercise centered on functional and stretching exercises throughout the study period. The results generated from this study are designed to serve as a pilot to guide further research with a larger sample size and are therefore exploratory in nature.

4.2 Participants

Ten women between the age of 25 and 65 years with newly diagnosed breast cancer volunteered to participate in the study. To be included, women had to be undergoing a chemotherapy regimen that included both a multi-agent and single agent treatment. Participants were recruited through the Dunedin Hospital via their Oncologist who provided potential participants with an information sheet detailing the study background and inclusion criteria. Women were then referred to the University of Otago for additional information.

Participants were excluded from the study if they had recurrent breast cancer, distant metastases, were planning to participate in exercise/dietary programs for weight loss during the study period, had thyroid problems or diagnosed with diabetes mellitus.

4.3 Outcome Measures

Dietary intake, body mass index and blood lipids (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides) were measured at the three study time-points. Baseline measures were taken before the commencement of the first chemotherapy treatment, the mid-point measure was taken within 10 days of a participant's final multi-agent treatment and the final time-point was taken within 10 days of the single agent regimen.

4.4 Dietary Assessment

Participants were asked to complete a 4-day, weighed food diaries (**Appendix A**) over three consecutive weekdays and one weekend day at the three time-points. Participants were instructed to record a description of all food and beverages consumed, amounts in household measures or weights, the time of consumption as well as additional foods such as sauces, dressings, gravy, sugar, margarine. Additionally, cooking methods and brand names where applicable were asked to be documented. Participants were instructed to maintain a normal eating pattern during the four days to ensure accuracy.

Dietary analysis was completed using Kai-culator dietary assessment programme (dietary assessment method v1.08p) developed by the Department of Human Nutrition, University of Otago. This program uses food composition databases which include current and previous versions of FOODfiles (FOODfiles 2010v2) from Plant and Food Research Ltd and selected recipes calculated for the 2008/09 New Zealand Adult Nutrition Survey (97). If recorded foods were not present in the database, suitable substitutions were made and recorded. All diets were entered by one person to account for inter-individual variation in interpretation of records.

4.5 Body Mass Index

Participant BMI was calculated at each of the three time-points from weight and height using (weight (kg)/height (m^2)). Height was measured using a free standing stadiometer (School of Physical Education, University of Otago) and was recorded to the nearest centimeter. Weight was measured using Biospace scales (Biospace InBody230, Seoul, Korea) and was recorded to one decimal place. Both were taken without footwear and in light clothing. Duplicate measures were taken and repeated if they differed by greater than 0.1kg for weight and 1cm for height.

4.6 Blood Lipids

The Diabetes and Lipids Laboratory in the Department of Human Nutrition, University of Otago, performed laboratory analyses using the Cobas C311 (Roche Diagnostics, Manheim, Germany). All samples were collected at each study time-point and the plasma was collected in EDTA containing tubes (1mg/mL). All samples were taken to the laboratory within two hours of collection and centrifuged at 1500G for 15 minutes at 4^{o}C. Once plasma was separated from the red blood cells, aliquots were stored at -80^{o}C until analysis. All samples were analysed using a standardised automated methods.

4.6.1 Total cholesterol

Total cholesterol was determined enzymatically using colorimetric methodology using Roche/Boehringer-Mannhein Diagnostics reagents. Cholesterol esters were first cleaved by the action of cholesterol esterase to yield free cholesterol and fatty acids. Hydrogen peroxidase is a byproduct of the reaction, which in the presence of peroxidase, effects the oxidative coupling of phenol and 4 aminophenazone to form a red quinone-amine dye. This dye is proportional to the concentration of cholesterol. Absorbance is measured at 500nm. Intra run CV% for cholesterol was 0.91%.

4.6.2 HDL-cholesterol

HDL-cholesterol was determined using a precipitation based method using phosphotungstic acid/$MgCl_2$ whereby apolipoprotein B-containing lipoproteins are separated from very-low-density lipoproteins (VLDL), LDL and apolipoprotein (a). This was then followed by ultracentrifugation of the supernate to isolate the HDL. The clear residue remaining was analysed within 2 hours.

4.6.3 Triglycerides

Triglyceride (TAG) concentration was determined again using enzymatic, colorimetric

test principles (Roche Diagnostics, Manheim, Germany). This method firstly hydrolyses triglycerides to glycerol and three fatty acids through a series of coupled reactions. Glycerol-3-phosphate is then oxidised to dihydroxyacetone phosphate and hydrogen peroxide. Hydrogen peroxide then reacts with 4-aminophenazone and 4-chlorophenol in the presence of peroxidase to form a red dyestuff (tinder endpoint reaction), which is proportional to TAG concentration and is measured photometrically. Absorbance was measured at 500nm. The intra run CV% for triglycerides was 1.38%.

4.6.4 LDL-cholesterol

Plasma LDL cholesterol in mmol/L was calculated using the Friedewald formula:

LDL cholesterol = Total cholesterol – HDL - (TAG/5) (98).

4.7 Statistical Analysis

All statistical analyses were done using STATA 12.0 (STATA Inc., College Station, Texas). A Shapiro-Wilk test was used to check for normal distribution. Two sided, paired t-tests were used in the primary analysis to assess any change in dietary intake, lipids and BMI across time-points. Additional t-tests were used to look at change in macronutrients in relation to BMI. Change was significant if $p<0.05$. Correlation analyses between blood lipids and macronutrients were additionally run to look the strength and direction of

relationships between these variables. Furthermore, change dietary intake and blood lipids was determined by regressions analyses using absolute macronutrient values.

5. Results

5.1 Macronutrients

As shown in **Table 5.1**, the mean (range) energy intake at baseline was 7602.1 (5415-10,512) kJ. There were no significant differences between the baseline and mid-point dietary measures (p=0.849) nor between baseline and final time-points (p=0.239) for energy intake, however there was a trend for an increase in energy intake between the mid-point and end measures although this was not statitically significant (p=0.082) (**Table 5.2**).

The majority of the energy intake came from carbohydrate which contributed 44.7 to 47.1% of total energy intake. Protein contributed the least to energy of all the macronutrients with a group mean intake of 15.8% TE over the study duration. Lastly, fat as a percentage of total energy ranged from 35.6% to 37.0% during the study period.

The absolute amount of fat ingested ranged from 32.1g to 124.6g/day across all time-points. Saturated fat intake ranged from 12.4g to 52.3g/day across time-points with mean intakes of 14.8%, 15.2% and 13.6% total energy intake at baseline, mid-point and final. Major food sources of saturated fat included meat, poultry, processed meats; pasta and potatoes e.g. chips, fries, stuffed potatoes; cheese; cakes, biscuits, desserts and confectionary; fats and oils e.g. butter, margarine, oil, cream.

There was a correlation between protein and fat intake at baseline (r=0.777, p=0.008), mid-point (r=0.695, p=0.038) and final time-points (r=0.854, p=0.002). However no other macronutrients showed correlations aside from energy which not surprisingly was positively correlated with fat, protein and carbohydrate at all three time-points.

Mean (range) intake of protein was 64.3g (38.8-94.3g), 66.9g (32.7-90.2g) and 67.71g (26.7-103.1g) at baseline, mid-point and final time-points respectively. As shown in **Table 2** there was no significant change in protein intake from baseline to mid-point (p=0.475) or to the end of the study duration (p=0.491). However percentage of TE from protein significantly increased by 1.5% from mid-point to final measures (p=0.017). The study population however, showed mostly inadequate protein intakes at the mid-point measure with only three of the nine participants meeting the Ministry of Health guidelines of 15-25% total energy. Conversly the majority of participants (70%) met the guidelines at both baseline and final time-points.

The mean (range) intake of carbohydrate was 198.9g (126.7g to 337.1g) over the three time points. There was no significant difference in carbohydrate intake as a percentage of total energy across all time-points however 5/10, 3/9 and 6/10 participants did not manage to meet the Ministry of Health guidelines of 45-65% total energy at baseline, mid-point and final time-points respectively.

Table 5.1. Group mean ± standard deviation (range) for macronutrient intakes at study time-points

	Baseline (n=10)	Mid-point (n=9)	Final (n=10)
Total Energy (kJ)	7602.1 ± 2095.3 (5415 - 10512)	7772.6 ± 2287.9 (3944 - 11360)	6821.8 ± 1713.5 (2697 - 9152)
Protein (% of total energy)	15.8 ± 2.8 (11.7 - 20.2)	14.6 ± 3.7 (10.5 - 23.1)	16.9 ± 3.6 (10.7 - 22.9)
Total Fat (% of total energy)	35.6 ± 6.1 (27.9 - 46.0)	37.0 ± 5.4 (28.2 - 46.1)	36.4 ± 5.4 (28.8 - 44.0)
Carbohydrate (% of total energy)	45.2 ± 9.5 (36.2 - 60.8)	47.1 ± 9.0 (31.0 - 62.6)	44.7 ± 8.5 (30.5 - 59.3)

5.2 Body Mass Index

The mean (range) BMI of the group across time-points was 30.8 (24.6 to 38.3) kg/m^2, obese according to the World Health Organisation cut-points (99). Additionally, 90% of participants were either overweight or obese at baseline with mean BMI of 30.5 ± 4.2kg/m^2, with half (5/10) obese at this time-point. This number stayed the same however the proportion increase to 5/9 women at both the mid-point and final study measures due to one participant declining to have her measures taken. There was no change in BMI over study time-points; baseline to mid-point (mean increase of 0.10, p=0.748), mid-point to final (mean difference 0.16, p=0.795) and baseline to final (mean difference 0.16, p=0.721) as shown in **Table 5.2**.

5.3 Blood Lipids

There was no significant change in total cholesterol nor triglycerides between all study time-points i.e. baseline to mid-point, mid-point to final and baseline to final as shown in **Table 5.3**.

Similarly, LDL and HDL cholesterol did not change from baseline to mid-point or from mid-point to final however there was a tendency of a change from baseline to final, with an increase in LDL cholesterol of 0.61mmol/L (p=0.083). In contrast, HDL tended to decrease from baseline to final measures (p=0.091).

Table 5.2. Change in macronutrient intake and body mass index across study time-points[1]

	Baseline-Mid-point	p-value	Mid-point-Final	p-value	Baseline-Final	p-value
Total Energy (kJ)	147.8 ± 2251.8	0.849	-1061.2 ± 1603.3	0.082	-780 ± 1955.1	0.329
Protein (% of TE)	-1 ± 3.9	0.475	1.5 ± 1.4	0.017*	0.7 ± 3.3	0.383
Total Fat (% of TE)	2.5 ± 8.1	0.385	-0.3 ± 8.2	0.921	1.4 ± 8.5	0.383
Carbohydrates (% of TE)	0.8 ± 8.3	0.780	-2.6 ± 8.7	0.392	-1.2 ± 5.0	0.476
BMI (kg/m^2)	0.10 ± 0.90	0.748	0.16 ± 1.74	0.795	0.16 ± 1.24	0.721

[1]Paired t-test (two-sided)
*$p<0.05$

Table 5.3. Change in blood lipids (mmol/L) across study time-points

	Baseline - Mid-point	p-value	Mid-point – Final	p-value	Baseline – Final	p-value
Total cholesterol (mmol/L)	0.51 ± 1.00	0.196	0.008 ± 1.24	0.987	0.18 ± 1.11	0.660
LDL cholesterol (mmol/L)	0.42 ± 1.15	0.335	0.37 ± 1.31	0.449	0.61 ± 0.86	0.083
HDL cholesterol (mmol/L)	-0.20 ± 0.34	0.146	-0.008 ± 0.360	0.955	-0.38 ± 0.55	0.091
Triglycerides (mmol/L)	0.61 ± 1.18	0.187	-0.78 ± 1.20	0.12	-0.12 ± 0.58	0.582

Of interest, 3/9, 2/9 and 3/9 women had elevated total cholesterol levels outside the normal reference range at baseline, mid-point and final respectively as shown in **Figure 5.1**.

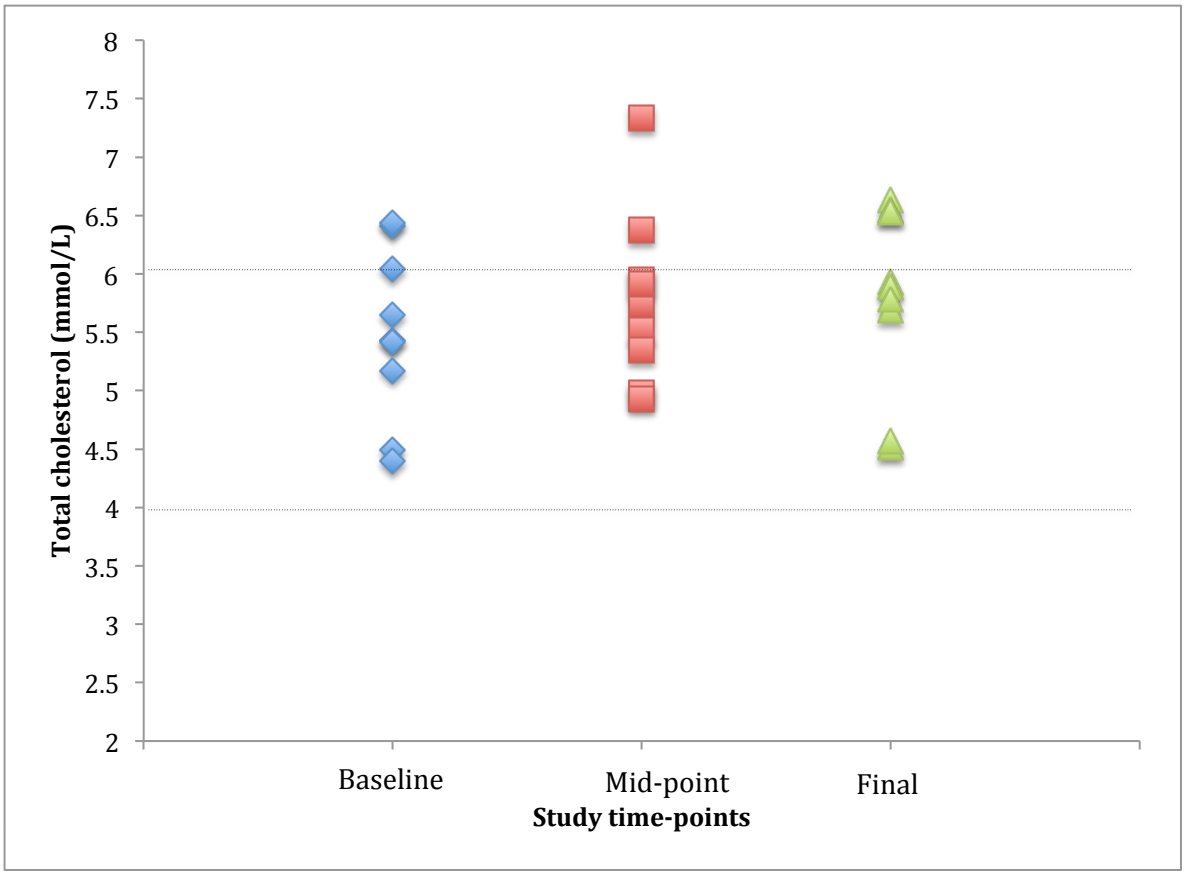

Figure 5.1. Total cholesterol (mmol/L) for baseline, mid-point and final time-points

Furthermore, five of the nine participants had triglycerides outside of the normal reference range at baseline, four of which were elevated and one participant had a TAG concentration below the lower range of 0.8mmol/L. Furthermore, there was an astounding 7/9 women with elevated TAGs at mid-point, however this decreased to three at the final time-point (**Figure 5.3**).

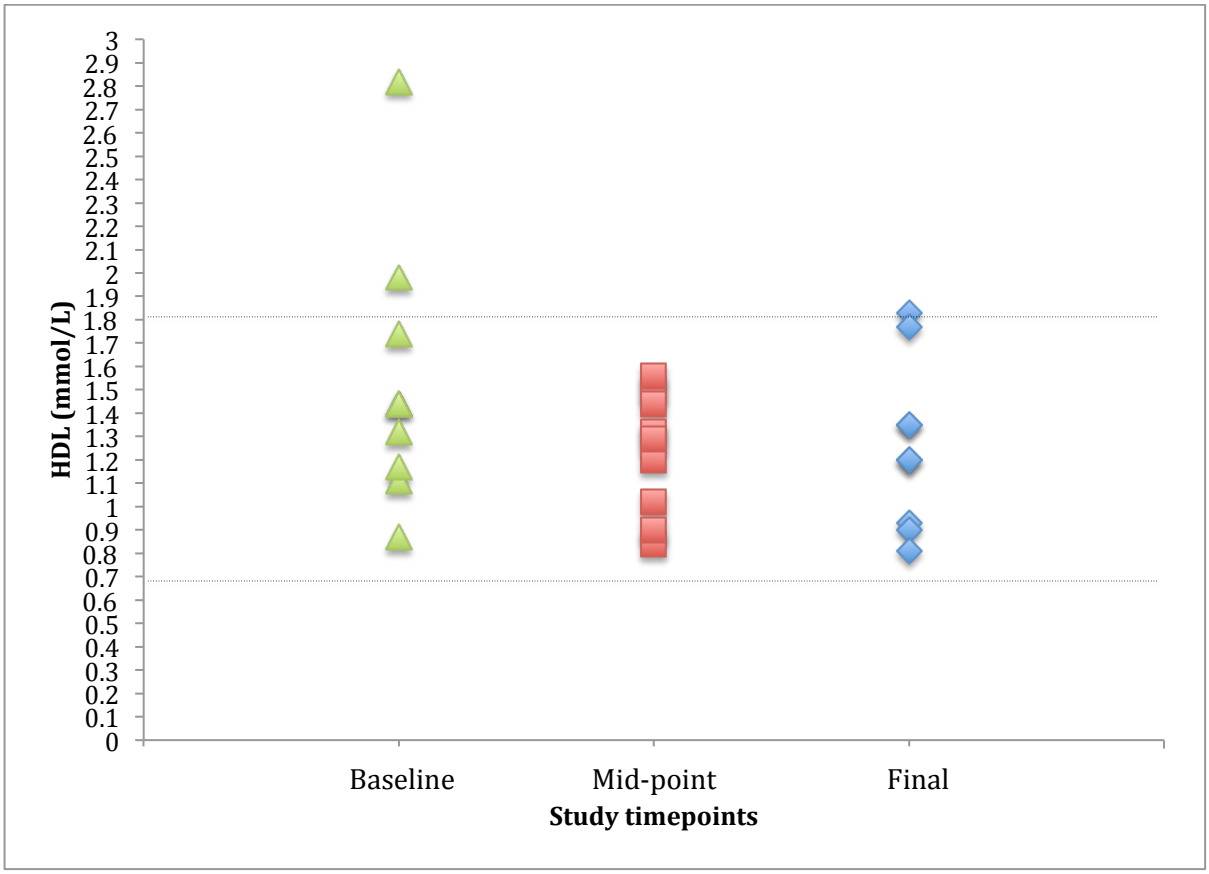

Figure 5.2. Absolute HDL-cholesterol (mmol/L) at baseline, mid-point and final study time-points

5.3 Blood lipids in relation to macronutrient intake

LDL cholesterol was positively correlated with energy at baseline (r=0.7401, p=0.023) however this relationship disappeared at the following time-points. There was no evidence of a relationship between total cholesterol or HDL cholesterol with either energy or protein. No correlation between LDL and protein at any of the study time-points was seen either.

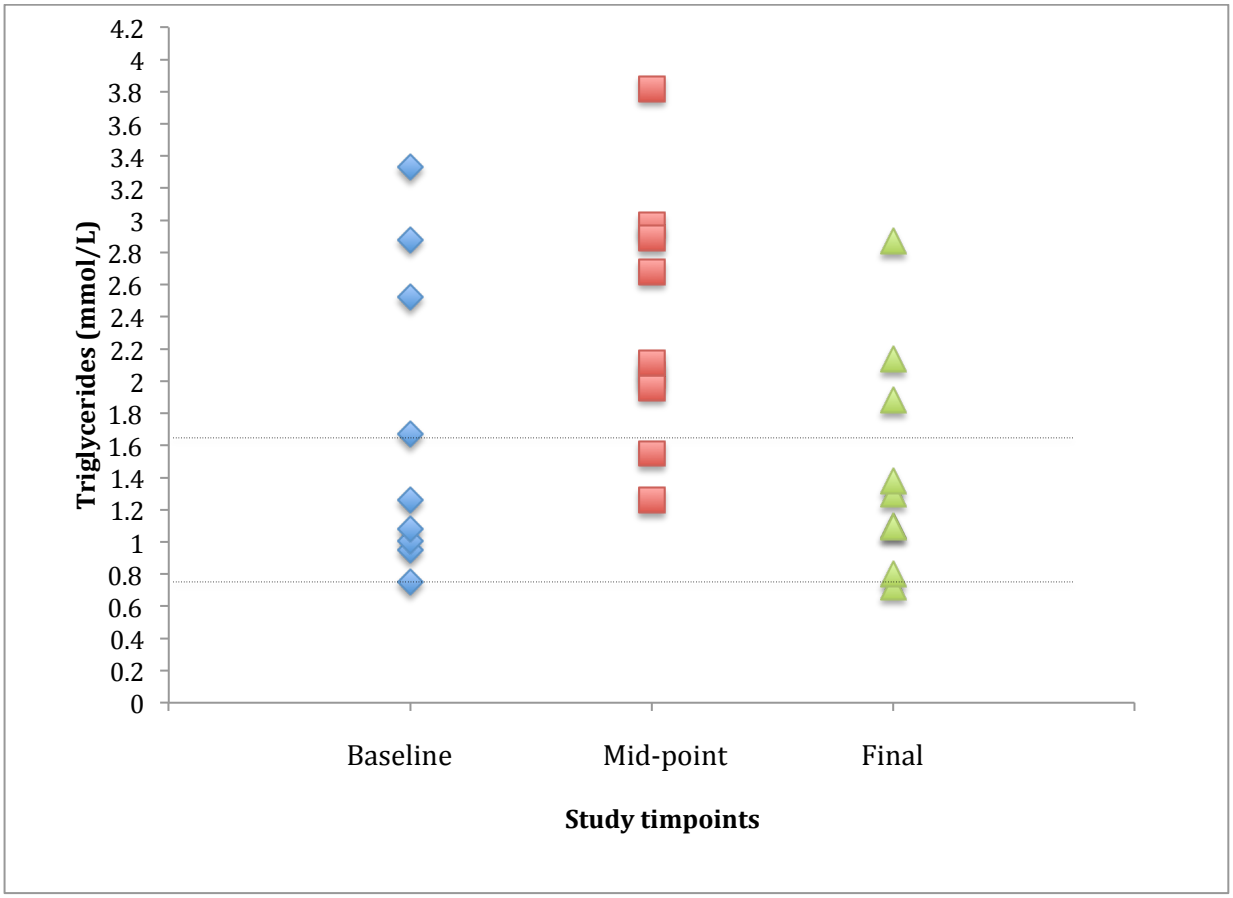

Figure 5.3. Triglyceride levels (mmol/L) at baseline, mid-point and final study time-points

Additionally, **Table 4** shows a statistically significant but weak negative association between LDL cholesterol and total energy intake from mid-point to final (B=-0.0004, p=0.012). This translating to a decrease in LDL cholesterol of 0.0004mmol/L in relation to a 1kJ increase in energy between these time-points. There was no relationship detected from baseline to mid-point (B=0.0002 , p=0.146) nor baseline to final (B=-2.95x10^{-6}, p=0.987) between LDL and energy.

Table 5.1. Regression analysis for change in LDL and HDL-cholesterol by change in macronutrient intakes between study time-points[1] (n=10)

	LDL cholesterol			HDL cholesterol		
	B	95% CI	p-value	B	95% CI	p-value
Total Energy (kJ)						
Baseline - Mid-point	0.0002	-0.0001, 0.0006	0.146	0.00008	-0.00005, 0.002	0.905
Mid-point - Final	-0.0004	-0.0007, -0.0001	0.012*	0.00005	-0.0002, 0.0002	0.673
Baseline - Final	-2.95×10^{-6}	-0.0004, 0.0004	0.987	-0.003	-0.0002, 0.0003	0.771
Total Fat (g)						
Baseline - Mid-point	0.014	-0.014, 0.042	0.266	0.004	-0.007, 0.015	0.378
Mid-point - Final	-0.029	-0.052, -0.005	0.025*	0.002	-0.014, 0.017	0.799
Baseline - Final	-0.008	-0.046, 0.029	0.604	0.011	-0.011, 0.033	0.277
Protein (g)						
Baseline - Mid-point	0.029	-0.049, 0.107	0.386	0.015	0.012, 0.042	0.216
Mid-point - Final	-0.064	-0.097, -0.032	0.004*	-0.008	-0.037, 0.022	0.532
Baseline - Final	-0.028	-0.083, 0.027	0.259	-0.013	-0.050, 0.024	0.429
Carbohydrate (g)						
Baseline - Mid-point	0.004	-0.010, 0.019	0.439	0.002	-0.002, 0.007	0.201
Mid-point - Final	-0.006	-0.022, 0.009	0.342	-0.0005	-0.007, 0.006	0.856
Baseline – Final	-0.0001	-0.012, 0.009	0.977	0.0003	-0.007, 0.008	0.937

[1] Paired t-test (2 sided); *P<0.05

Note: Abbreviations; low-density lipoprotein (LDL); high-density lipoprotein (HDL); coefficient (B).

Change in LDL cholesterol was also negatively associated with change in fat (B= -0.029, p=0.025) and protein (B=-0.064, p=0.004) respectively. Therefore for each 1g increase of fat or protein, LDL increased by 0.029 and 0.025mmol/L respectively. However there was no association seen at any other time-points nor with LDL and carbohydrates or between HDL cholesterol and energy, fat, protein or carbohydrates at any of the study time-points.

Although not shown, the same regression analysis found there was a tendency for total cholesterol (mmol/L) to be positively associated with energy from baseline to mid-point (B=0.0003, p=0.061). This reached statistical significance at mid-point however the relationship became negative (B=-0.0005, p=0.021). The association was lost again at the final time-point.

Furthermore, there was a tendency for carbohydrates (g) to be associated with change in triglycerides from mid-point to final time-points (B=-0.007, p=0.081) (data not shown). No other associations between the changes in TAGs and any other macronutrient were detected.

6. Discussion

The results of this study show that the carbohydrate and protein intake was lower than the Ministry of Health AMDRs for optimal macronutrient balance. Conversely consumption of fat, particularly saturated fat intakes were higher than recommended, this suggesting that the dietary intakes of Dunedin breast cancer patients during chemotherapy is sub-optimal. Further work can therefore be done to improve their diets and with this, potentially long-term prognosis. Especially in light of the blood lipid profiles and BMI, both of which were unfavourable for the majority of the group. The need for more education regarding the risk of comorbidity and the role of diet in attenuating this risk is warranted.

The current recommendations for total fat intake in the breast cancer survivor population by the American Cancer Society is 20 to 35%, with saturated fat limited to <10% and trans fat <3% (19). Relative to TE, this study found total fat intake to be higher than the ACS recommendations ranging from 35.6 to 37.0% from baseline to final time-points and was therefore a substantial contribution of total energy. This range was slightly higher than the national average reported by the New Zealand Adult Nutrition Survey 2008/09 for all females who were shown to have mean intakes of 33.8% (95% CI: 33.2-34.3) total energy (100). Several published studies investigating dietary intakes in breast cancer survivors without dietary intervention have also reported high fat intakes similar to those reported in this study (28, 101-103). In line with the presented results, these studies have shown little change in fat

intake during follow-up suggesting dietary intakes pre-treatment are maintained throughout survivorship and the "teachable moment" (20) in which to best motivate and elicit behaviour change is missed for a large proportion. Indeed intervention studies who have provided dietary counseling post treatment have shown improved nutritional intakes at follow up (104-106). In New Zealand, nutritional support is limited with hospital dietitians providing acute advice/support to inpatients with little follow up in an outpatient setting. This leaves most women in Otago lacking the knowledge to change their diets to meet the guidelines and improve health (unpublished data).

Poor dietary choices are further highlighted by the saturated fat intakes seen among this group, which were high ranging from 13.6 to 15.2% over the study period. Again, this was greater than that of the general population, with New Zealand females having an average intake of 13.1% (100). With this population's inherent increased risk of comorbidity, in particular CVD, a high intake of saturated fat is likely to confer additional risk and should be a targeted dietary component in any nutrition counseling for this vulnerable group.

Given that adequate intakes of protein are important during the treatment phase to help mitigate the effects of chemotherapy by improving muscle integrity and attenuate lean mass losses, it would seem to be encouraging that an increase of 1.5% in relative protein intake from baseline to final time-points was seen. Although this increase in protein could be seen as positive, the observed association between protein and fat intake during this study could alternately mean that inappropriate protein sources are being chosen. Indeed the major protein sources were processed meats such as

sausages, mince, hamburgers as well as high intake of red meat including roast beef and lamb.

Additionally most of the group (6/9) had inadequate intakes of protein at the mid-point measure. This suggesting that treatment may have impacted on protein intakes, as it is known to effect appetite and food preferences (107). Therefore the increase in protein intake at the end of the study may be the result of improved management of chemotherapy treatment and side-effects such as nausea, anorexia, fatigue.

Overall, the group mean protein consumption contributed to 14.6 to 16.9% of total energy, which is at the lower end of the Ministry of Health recommendations (15-25% TE for an optimal diet that reduces the risk of chronic disease) (78). This is comparable to that seen in the general New Zealand female population, with a mean contribution to energy intake of 16.5% (100). Wayne *et al*. similarly showed in 240 newly diagnosed early stage breast cancer patients a clinically insignificant increase of protein by 0.6 ± 3.4 (mean ± standard deviation) over a 2 year follow-up period (28). However there is limited published research comparing pre-and post-diagnosis protein intake to allow a full interpretation and understanding of the results.

Previous research has suggested that breast cancer treatment results in changes in appetite; taste and can induce nausea and vomiting (62). It was therefore interesting to see that there were no other significant changes in macronutrient intake during the study period including carbohydrate and energy intake. A potential explanation for this may be that the treatment had a short-term impact on the groups' self-efficacy and ability to make positive dietary change. It could also be reflective of the lack of

breast cancer specific nutrition advice being provided to patients in clinical settings that addresses the unique requirements of this group both acutely during the treatment phase as well as long-term. Patients may therefore be receiving nutrition advice indicated for other cancer sites, potentially overcompensating for predicted gastrointestinal and appetite changes. Furthermore, this group may have changed their intake from that pre-diagnosis but because the baseline dietary measure was post-diagnosis any changes in intake or food choices may have been missed. However when the macronutrient composition of group was compared to that of the general population, the similarity suggests that the lack of change is genuine.

Body mass index did not change throughout the study period, with the majority (90%) of the group classed overweight or obese, at baseline. Similar rates of overweight and obesity have been paralleled in other studies (20, 108, 109). Such high rates of obesity are not surprising as a high BMI is one of the risk factors for breast cancer as well as 64% of the New Zealand adult population being overweight or obese, with 29% obese (45). However the mean BMI (30.5 ± 4.2) kg/m^2 of the group was higher than the national average of 27.7kg/m^2 (45). With overweight and obesity at the time of diagnosis being linked to poorer prognosis and survival compared to those of a healthy weight, lifestyle interventions addressing both diet and exercise is warranted for this population group (6, 11, 80, 110-112). Additionally, strategies targeting prevention through diet and exercise in the general population would likely be beneficial for reducing the rates of initial cancer in post-menopausal women. This is not to say that weight management post-diagnosis does not impact on future health as observational studies have shown that weight management post-diagnosis can impact on the rates of recurrence and the risk of comorbidity (50).

A positive can be taken from the fact that the women in the present study did not gain weight over the course of treatment this needs to be interpreted with caution as it may be that the study period was too short and weight gain may be more pronounced after treatment when nutrition related side-effects such as nausea and fatigue ease. This is supported by previous studies, which have shown there is only minimal if any weight gain during the treatment period, (13, 53, 60) with more progressive weight gain post treatment (50, 51, 55, 113).

Despite this study duration not being sufficient to assess changes from pre-diagnosis to long term post treatment outcomes, it exhibits relatively static dietary intake throughout chemotherapy treatment that is suboptimal in nature. It appears that the mid-point to final study period is where most change in macronutrient intake occurs i.e. towards the end of the treatment. Additionally, LDL-cholesterol was associated with all the macronutrients except carbohydrates between these two time-points suggesting this to be an important treatment period for nutrition counseling. Indeed, intervention studies have shown that this population is motivated to make change and with education and support regarding diet and lifestyle can improve diet quality significantly (20, 82, 83, 105, 114).

The need for lifestyle and dietary intervention for this population is further highlighted by their blood chemistry. With the majority having cholesterol concentrations outside levels recommended for the prevention of CVD set by the New Zealand National Heart Foundation (86). Of most relevance, all participants had total cholesterol levels above 4.0mmol/L across study measures and 7/9 had LDL levels

higher than 2.0mmol/L at baseline, this increasing to 100% of the group at mid-point and final. Although high-density lipoprotein and TAG levels among the group were not as unfavourable with 3/9 women having HDL levels lower than 1.0mmol/L and elevated TAGs above 1.7mmol/L by the end of the study. The mean total cholesterol (5.69mmol/L) of the group however was comparable to that of the general female population (5.17mmol/L) although slightly higher. This having potential implication in terms of increasing inflammation in a population where inflammation secondary to treatment and weight gain is already likely evident.

There was a tendency for LDL cholesterol to increase from baseline to final measures by 0.61 ± 0.86mmol/L, (p=0.083) suggesting that although there was no significant change in dietary intakes particularly fat, diet may still be having an effect on clinical measures and with a greater sample size the association may strengthen or become clear. Additionally between these same time-points (baseline to final), HDL appeared to decrease by 0.38 ± 0.55mmol/L, (p=0.091). Although these results were not statistically significant, they are both moving in unfavourable directions reinforcing the potential risks of comorbidity in this group.

Interestingly blood lipids were associated with macronutrients. This is evident from the mid-point to final study period. Low-density lipoprotein was negatively associated with total energy, absolute fat and protein i.e. as intake increased, LDL-cholesterol decreased and although these findings are statistically significant, they are unlikely to be clinically significant. This change is not in the expected direction and a possible explanation for this inverse association may be underreporting of dietary intake. Indeed, it has been shown that women participating in studies significantly under

report foods they perceive to be 'unhealthy' i.e. are bias to socially desirable behaviour in particular with the use of diet records with a high respondent burden (77).

Some of the lipid results were inconsistent whereby LDL was positively correlated with energy from baseline to mid-point but negatively associated with energy from mid-point to final in the regression analysis. This potentially highlighting the issue of small sample sizes whereby results may be in fact change findings. Furthermore, participants were instructed to keep a record of 3 consecutive days and 1 weekend day instead of the standardised protocol of 3 non-consecutive days and 1 weekend day making comparability of these results difficult. Despite this, they are still a relatively accurate and reliable method of dietary assessment making this a strength of the study especially in light of many studies using FFQ's that were not validated or other methods of self reported intake (20).

6.1 Conclusion

In light of the study limitations, these results should be interpreted as exploratory, offering insight into relevant areas for further research in this population. Being a descriptive study, only changes and associations can be determined meaning the results can only guide further areas of research. The modest sample size may have also limited the ability to detect any change in the outcome measures. Despite this, the results have highlighted areas of interest for further study. More research is clearly needed to further elucidate the eating habits and dietary intakes of this population

using a more powered sample, in particular dietary change both pre- and post-diagnosis with longer follow up. Addressing the issue of where nutrition information is sought by this group would also be of interest and add valuable information as to why this group makes certain decisions regarding food choices. Additionally, comparing perceived changes in diet intake and quality verse actual intakes would strengthen this knowledge about food decision and beliefs in this group. Ultimately, the lack of dietary change suggests a need for a greater nutrition based focus in this population following a diagnosis to help mitigate the negative impacts of treatment and potentially help improve prognosis.

7. Application to Practice

As obesity is an established risk factor for poor prognosis in breast cancer survivors and with the majority of the study population overweight or obese at baseline, women need to be targeted early when motivation to make sustainable behaviour change is high. Especially in light of evidence suggesting that little change in line with cancer preventative recommendations is occurring in breast cancer survivors (115). Although this study did not address where these women were obtaining their nutrition information, research has shown dietitians are not a primary source of nutrition education. Indeed a Finnish study showed that out of 97 breast cancer patients, only 11.1% received information from a dietitian, the majority (33.3%) sourced information from the mass media (74).

Though diet and dietary components such as fruits and vegetables, fibre or fat have not been clearly linked to cancer outcomes; the role of diet in preventing and reducing the risk of obesity is undeniable. Dietary counseling and interventions, through this indirect relationship in modifying overweight and obesity are therefore justifiable. Modifying the risk of comorbidity is also an important clinical consideration in this population. Again, many of the women had elevated cholesterol and would therefore benefit from healthy eating advice in line with cardioprotective dietary advice.

This study has been a useful exploratory analysis looking into the dietary habits of the breast cancer population in New Zealand however more information needs to be

collected on a larger number women to fully elucidate where issues lie in terms of their dietary habits and nutrition beliefs. It would be useful to gain more information regarding misconceptions of treatment side effects and risk of comorbidity within health professions in particular dietetics as well as patients. Additionally long-term information post-treatment would show whether this population has increased self-efficacy and a greater ability to elicit dietary behaviour change after chemotherapy compared to during. This would help to inform the professions when the most effective time to provide counseling is. From the lack of dietary change it is possible that the dietetic profession needs to both improve the awareness of this vulnerable groups health concerns and provide more proactive nutrition support for the long-term benefit of this population.

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