Quality of Life, Exercise Behaviour and Baseline Dietary Intake of Women Undergoing Neoadjuvant Chemotherapy in the DHA WIN Randomized Controlled Trial

by

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

Master of Science

in

Nutrition and Metabolism

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ABSTRACT

Breast cancer is the second most common cancer in Canada. It is estimated that one in eight Canadian women will be diagnosed with the disease in their lifetime. Neoadjuvant chemotherapy is often prescribed to improve surgical resection outcomes and reduce micrometastases. Achieving a pathological complete response (pCR) after neoadjuvant chemotherapy is associated with an improved prognosis. However, chemotherapy has been associated with side effects that undermine quality of life (QoL) and inhibit physical activity. Both exercise and supplementation of omega-3 polyunsaturated fatty acids during chemotherapy have been associated with reduced side effects and improved QoL in breast cancer patients. There are mixed findings regarding the relationship between exercise and pCR in patients with breast cancer.

The current study analyzes secondary outcomes from the DHA WIN phase II randomized controlled trial which was designed to evaluate docosahexaenoic acid (DHA) supplementation (4.4 g/day) on tumour growth and metabolism in women with breast cancer undergoing six cycles of neoadjuvant chemotherapy (3 weeks/cycle) (n = 49). QoL questionnaires were completed at baseline and at the end of chemotherapy treatment (n = 47). Exercise questionnaires were completed at baseline, the start of cycles 2 to 6 and the end of cycle 6 (n = 42). A food frequency questionnaire was completed at baseline (n = 46) and pCR was assessed after surgery (n = 49).

Estimated daily dietary intake of macronutrients, cholesterol, sodium, sugar and dietary fiber were not statistically significantly different between the DHA and placebo groups. Compared to Albertan women that completed the 2015 Canadian Community Health Survey (CCHS), the estimated daily intake of the DHA WIN cohort was greater for protein, total fat, total monounsaturated fatty acids, sodium and dietary fiber (all $p \le 0.05$). Compared to the CCHS cohort, a greater percentage of the DHA WIN cohort was above the acceptable macronutrient

distribution range for fat (52.2% versus 32.9%, p = 0.008) and carbohydrate (8.7% versus < 3%, p = 0.008).

All subscales of the Functional Assessment of Cancer Therapy (FACT) questionnaire (except emotional well-being), the fatigue subscale and the State-Trait Anxiety Inventory (STAI) score decreased over time in both the DHA and control groups (p-time \leq 0.03). Emotional well-being and the Fordyce Emotions Combination score increased over time in both groups (p-time \leq 0.03). DHA supplementation did not significantly mitigate the change in any QoL indicator over time.

A change over time was observed for mean weekly aerobic exercise (p-time < 0.001) and resistance training frequency (p-time = 0.01). However, the DHA treatment did not significantly affect mean weekly aerobic exercise (p-interaction = 0.56) or resistance training frequency (p-interaction = 0.28) over time.

Participants that met WHO's aerobic exercise recommendation at baseline experienced a smaller decline in their FACT-General (FACT-G) total score, a greater decline in their Perceived Stress Scale and STAI scores, as well as a greater increase in their emotional well-being score over time (p-interactions ≤ 0.05). Similarly, participants that met WHO's aerobic exercise recommendation at the end of cycle 6 experienced a smaller decline over time in their FACT-G total score and functional well-being (p-interactions = 0.01).

Participants that met WHO's resistance training recommendation at baseline experienced a smaller decline in their FACT-G total score and FACT-Breast (FACT-B) total score over time (p-interactions ≤ 0.06). Similarly, participants that met WHO's resistance training exercise recommendation at the end of cycle 6 experienced a smaller decline in their functional well-being and FACT-B trial outcome indices (p-interactions ≤ 0.07). Meeting WHO's aerobic or resistance

training exercise recommendation at baseline or the end of cycle 6 was not associated with achieving a pCR.

These findings suggest that aerobic and resistance training exercise before and during treatment have the potential to mitigate the negative effect of chemotherapy on various QoL indicators in patients with breast cancer. DHA did not appear to mitigate the change in participants' QoL over time. Further research is needed to determine the role of exercise in achieving a pCR in this population.

PREFACE

This thesis is an original work by Claire Douglas. The clinical trial titled "Docosahexaenoic Acid (DHA) for Women with Breast Cancer in the Neoadjuvant Setting (DHA-WIN)" that produced the data that was analyzed in the thesis research received Health Canada approval (#HC6-24-c220167) and full ethical approval by the Health Research Ethics Board of Alberta-Cancer Committee (HREBA.CC-18-0381). The trial is registered at ClinicalTrials.gov (NCT03831178).

DEDICATION

To my mom, dad, brother and partner. Thank you for your continuous support and encouragement. I owe my participation in this program to all of you.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my supervisor, Dr. Catherine Field. Dr. Field, your kindness and enthusiasm for research is inspiring to myself and so many others. I consider myself remarkably fortunate to have been the benefactor of your supervision and mentoring.

Thanks to my committee member, Dr. Kerry Courneya. Your input and expertise have greatly benefited this project. I would also like to thank my third examiner, Dr. Catherine Chan, and the chairperson for my thesis examination, Dr. Gurcharn Brar.

Thank you to Dr. Sunita Ghosh for your assistance with statistical analysis.

I would also like to acknowledge the past and present members of the Field lab that have offered invaluable support and assistance throughout my time at the University of Alberta. A special thank you to Sue Goruk, Jaqueline Munhoz, Ren Wang, Jenna Evanchuk, Sydney Peskett and Amera Hollingsworth-Harris.

Thank you also to Dr. Marnie Newell and the numerous individuals that comprised the DHA WIN study team and contributed to the trial design and data collection. I acknowledge and appreciate the funding provided by the Canadian Institutes of Health Research, the Cross Cancer Institute Investigator Initiated Trials and the Butler Family Foundation for the DHA WIN clinical trial.

Finally, and most importantly, thank you to the women that participated in the DHA WIN clinical trial. The data collected through voluntary participation has been the foundation of this research, and I greatly appreciate you taking the time to participate in this trial during a difficult time in your lives.

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LIST OF ABBREVIATIONS

ACSM, American College of Sports Medicine

AI, adequate intake

ALA, alpha-linolenic acid

AMDR, acceptable macronutrient distribution range

ASCO, American Society of Clinical Oncology

BC, breast cancer

BMI, body mass index

BPI, brief pain inventory

CCHS, Canadian Community Health Survey

CDRR, chronic disease risk reduction intake

CCI, Cross Cancer Institute

C-DHQ II, Canadian-Diet History Questionnaire II

CES-D, Center for Epidemiologic Studies-Depression

CRF, cancer-related fatigue

DHA, docosahexaenoic acid

DHA WIN, Docosahexaenoic acid for Women with Breast Cancer in the Neoadjuvant Setting

DRI, dietary reference intake

EAR, estimated average requirement

ECOG, Eastern Cooperative Oncology Group

EPA, eicosapentaenoic acid

ER, estrogen receptor

ES, endocrine symptoms

FACIT, Functional Assessment of Chronic Illness Therapy

FACT, Functional Assessment of Cancer Therapy

FACT-B, FACT – Breast

FACT-ES, FACT – Endocrine Symptoms

FACT-G, FACT – General

FFQ, food frequency questionnaire

GEE, generalized estimating equations

HER2, human epidermal growth factor receptor 2

HRQoL, health-related quality of life

MCID, minimal clinically important difference

n-3, omega-3

pCR, pathological complete response

PR, progesterone receptor

PSS, Perceived Stress Scale

PUFA, polyunsaturated fatty acid

QoL, quality of life

RCT, randomized controlled trial

RDA, recommended dietary allowance

RDI, relative dose intensity

STAI, State-Trait Anxiety Inventory

TNBC, triple-negative breast cancer

TOI, trial outcome index

UL, tolerable upper intake level

WB, well-being

WHO, World Health Organization

CHAPTER 1: INTRODUCTION

Chemotherapy has been associated with several side effects that undermine the quality of life (QoL) and inhibit physical activity in patients with breast cancer [1, 2]. Both exercise [2-5] and supplementation of omega-3 polyunsaturated fatty acids (n-3 PUFAs) [6, 7] during chemotherapy have been associated with reduced side effects and improved QoL in breast cancer patients. This paper will describe QoL, exercise behaviour and dietary habits in women with breast cancer undergoing neoadjuvant chemotherapy and investigate relationships between the aforementioned variables. This chapter will provide a background on the relevant topics and review the current literature.

1.1 Breast Cancer

Breast cancer is the second most common cancer in Canada, and the most common cancer among Canadian women [8]. It is estimated that one in eight Canadian women will be diagnosed with the disease sometime in their lifetime. It was estimated in 2023 that 29,400 Canadian women would be diagnosed with breast cancer that year [9], of which approximately 82% would have been diagnosed at stage I or II [8]. Early detection and advances in treatment have made the likelihood of surviving the disease for at least five years following a diagnosis approximately 89% in Canada [8]. Several factors contribute to one's risk of developing the disease. These include non-modifiable risk factors such as age, genetic predisposition, early menarche and late menopause, as well as a number of modifiable risk factors including diet, being overweight or obese, and physical activity [10, 11].

Treatment choices for breast cancer depend on the molecular subtype, grade and stage of the tumour [12]. Invasive breast cancer can be categorized by molecular subtype, which is determined by the expression of the estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) [12]. Luminal A breast cancer (ER+ and/or PR+, and HER2-) comprises approximately 60% of cases and is associated with a good prognosis [12]. Luminal B breast cancer (ER+ and/or PR+, and HER2+) and HER2+ breast cancer (ER-, PR- and HER2+) make up about 30% and 10% of cases, respectively [12]. Both subtypes are associated with a poor prognosis. Triple-negative breast cancer (TNBC) represents 15-20% of cases [12]. It is more aggressive than other subtypes and is associated with the worst prognosis.

The tumour grade is based on the appearance of tumour cells compared to nontumour cells, and is one index used to determine the aggressiveness of the tumour [12, 13]. Breast cancer is graded from one to three, with higher grades indicating more abnormal cells which tend to proliferate faster and are more likely to metastasize [14]. The tumour stage describes the extent of cancer in the body, and is based on tumour size, lymph node invasion and the presence of metastases [12]. There are five stages for breast cancer ranging from zero to four, with higher numbers indicating larger tumours and cancer that has spread more [15]. Some stages are subdivided using the letters A, B and C, with earlier letters indicating a lower stage [15, 16]. Both tumour stage and grade provide prognostic information for breast cancer tumours, with higher stages and grades typically having a poorer prognosis [13, 17].

Treatment for non-metastatic breast cancer often involves surgically removing the tumour with preoperative (neoadjuvant) or postoperative (adjuvant) radiotherapy or systemic therapy, including chemotherapy [12]. Neoadjuvant chemotherapy was originally used in patients with inoperable tumours in an attempt to make them operable [18]. However, it is now commonly used for earlier, operable breast cancer and locally advanced breast cancer to allow for breast conservation therapy, reduce micrometastases, and improve surgical resection outcomes and

prognoses [1, 19-22]. Approximately 20% of newly diagnosed patients with breast cancer receive neoadjuvant chemotherapy, which is more frequently prescribed to patients with TNBC or HER2+ subtypes [19, 23, 24]. Its efficacy is determined, in part, by achieving a pathological complete response (pCR), which has been defined as the absence of any residual invasive tumours in the breast and axillary lymph nodes [25]. For example, a recent meta-analysis concluded that achieving a pCR after neoadjuvant chemotherapy was associated with overall survival and event-free survival in breast cancer patients, particularly for TNBC and HER2+ breast cancer [26]. Approximately 20% of breast cancer patients that receive neoadjuvant chemotherapy achieve a pCR [27]. Ki-67, a marker of tumour proliferation, has been shown to be an independent predictor of pCR in breast cancer patients, and is another common endpoint to measure efficacy of neoadjuvant chemotherapy in clinical trials [19, 28, 29].

Chemotherapy has consistently been proven to improve survival among breast cancer patients [30]. Relative dose intensity (RDI) is defined as the ratio of delivered dose intensity to planned dose intensity for a chemotherapy regimen [31]. It is recommended that an RDI ≥ 85% be achieved in ER+/PR+ and HER2- patients, and an RDI ≥ 75% in TNBC in order to optimize survival benefits [30]. However, there are numerous toxic side effects associated with chemotherapy that may contribute to poorer treatment outcomes including fewer courses of chemotherapy delivered, dose reductions, treatment delays and decreases in overall treatment time [32]. For example, a retrospective review that included 20,799 patients with early-stage breast cancer treated with adjuvant chemotherapy reported that 55.5% of patients received an RDI of <85% [33]. Side effects of chemotherapy include fatigue, dizziness, constipation, loss of appetite, nausea, vomiting, reduced exercise capacity and weight gain which ultimately affects individuals' QoL [6, 21, 34, 35]. Co-adjuvant therapies have the potential to reduce side effects and maintain

patients' QoL, which may contribute to improved chemotherapy tolerability and increased RDIs of chemotherapy [6, 32].

1.2 Docosahexaenoic acid for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN) Randomized Controlled Trial

Not all patients that receive neoadjuvant chemotherapy achieve a pCR, and it is therefore important to identify agents that increase the efficacy of this treatment without causing additional side effects [19]. Previous preclinical studies have demonstrated the ability of DHA to reduce tumour growth when combined with chemotherapy [19, 36-39]. DHA supplementation has also been shown to increase chemotherapy efficacy in animal models of breast cancer [40]. Increased dietary intake of n-3 long-chain PUFAs, including DHA, increases incorporation of DHA into breast adipose tissue [19, 41], which has been correlated with the tumour response to chemotherapy in patients with breast cancer [42]. For example, in a single-arm phase II study, Bougnoux et al. (2009) found that DHA supplementation (1.8 g/day) during chemotherapy in women with advanced metastatic breast cancer was associated with improved outcomes [43]. The objective of the DHA WIN phase II clinical trial was to investigate the effect of DHA supplementation (4.4 g/day) during neoadjuvant chemotherapy on treatment efficacy in women with non-metastatic breast cancer. In addition to the primary outcome (Ki67 index), several secondary outcomes were measured during the trial, including QoL, exercise, food frequency questionnaires and rate of pCR.

1.3 Quality of Life

Although the ultimate goal of cancer treatment is curing patients of their disease, QoL during and after treatment is also a priority to many patients [44]. The World Health Organization

(WHO) describes QoL as one's perception of their reality in the context of their culture and values [45]. Health-related QoL (HRQoL) considers how disease and treatment affect an individual's sense of overall function and well-being [44]. QoL has become an important outcome measure and factor in treatment decisions [1]. Therefore, it is critical to better understand how neoadjuvant chemotherapy affects patients' QoL.

1.3.1 Quality of Life During Cancer Treatment

Neoadjuvant chemotherapy is associated with a number of physical and psychosocial side effects including cancer-related fatigue (CRF) and impaired HRQoL [21]. Zhao et al. (2022) found that among ten studies that investigated physical aspects of QoL, 80% of breast cancer patients receiving neoadjuvant chemotherapy experienced some physical symptoms, including nausea, vomiting, fatigue, impaired cognitive function and pain [1]. One observational study with 134 breast cancer patients found that 48.5% of participants experienced chemotherapy-induced nausea and vomiting [46]. A number of studies have reported increased fatigue among patients with breast cancer subject to neoadjuvant chemotherapy [47, 48]. One study found that QoL significantly decreased after preoperative chemotherapy [49]. This finding stayed consistent for the physical symptoms and pain subscale, as well as the side-effects of treatment subscale, but the authors found that the subscale titled "Dress, sexual aspect, other" significantly increased after preoperative therapy. Specifically, the latter subscale asked respondents, among other things, if they found it difficult to wear the clothes they wanted to wear, if they were satisfied with their sex life and whether they worried about their family getting the same disease. Hermelink et al. (2007) conducted a prospective longitudinal study and found that cognitive function remained stable in

most patients undergoing neoadjuvant chemotherapy, but that 27% of patients experienced cognitive decline [50].

Zhao *et al.* (2022) reported that among eight studies that examined neoadjuvant chemotherapy's psychological effects, 52% of breast cancer patients experienced negative psychological effects related to emotional well-being, anxiety/depression and role function. Lee *et al.* (2022) found that patients with breast cancer experienced the most severe depression during neoadjuvant chemotherapy, compared to before and after chemotherapy [51]. In contrast, patients experienced the highest level of anxiety before chemotherapy, which gradually improved during treatment. Another study found that chemotherapy-induced nausea and vomiting was significantly associated with anxiety, highlighting the interrelatedness of the discussed symptoms [46].

Zhao *et al.* (2022) found that among five studies, 55% of breast cancer patients receiving neoadjuvant chemotherapy did not receive adequate family or societal support [1]. The authors found that family social support was positively correlated with patient self-esteem, which further emphasizes the importance of social support for these individuals. It is imperative to identify ways to reduce the side effects of neoadjuvant chemotherapy in order to prevent a reduction in patients' OoL.

1.3.2 DHA and QoL

1.3.2.1 Omega-3 Fatty Acids

Omega-3 PUFAs are involved in many physiological and metabolic processes, and contribute to cell membrane structure, fluidity and cell signaling [52, 53]. The most abundant n-3 PUFA in the diet is the short-chain alpha-linolenic acid (ALA, 18:3n-3), which is a dietary essential fatty acid that serves as a precursor for a number of n-3 long-chain PUFAs, including

eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3). However, it is estimated that less than 1% of ALA is converted to DHA [52]. Therefore, one must directly consume DHA in order to significantly increase tissue levels [19].

Supplementation of EPA and DHA during chemotherapy has been shown to reduce toxicity and improve disease outcomes in cancer patients [6, 32]. This was reported to be due to modulation of inflammatory profiles, maintenance of nutritional status by reducing gastrointestinal side effects, maintenance of skeletal muscle and improved neuronal recovery following chemotherapy-related toxicities [32].

1.3.2.2 The Role of DHA in QoL of Breast Cancer Patients

A recent systematic review examined randomized controlled trials (RCTs), quasi and semiexperimental studies that investigated the effects of supplementation or consumption of foods
enriched in n-3 fatty acids (300 – 6000 mg/day) in breast cancer patients that were receiving
treatment or were in the follow-up period [6]. The authors found that n-3 fatty acid
supplementation led to a significant decrease in perceived stress, sleep disturbance, depression,
pain, joint stiffness and fatigue. Among the studies reviewed, only one considered QoL among
breast cancer patients that were supplemented with n-3 fatty acids *during* neoadjuvant
chemotherapy [54]. It consisted of an RCT in which the treatment group received 2.4 g/day of n3 PUFA (1.6 g EPA and 0.8 g DHA) during the six months of chemotherapy. Both groups
experienced an increase at three and six months in fatigue, nausea, drowsiness, appetite and
dyspnea and there were no significant differences between groups [54].

A review done by Newell *et al.* (2021) concluded that supplementation of EPA and DHA in clinical cancer therapy improved overall QoL among patients with various types of cancer [7].

Focusing on breast cancer patients, Martinez *et al.* (2019) carried out a single-arm clinical trial in which patients were supplemented with n-3 fatty acids, hydroxytyrosol and curcumin for one month during hormonal therapy [55]. The authors observed a 21.5% decrease in patients' worst pain score obtained from the brief pain inventory (BPI) after 30 days of treatment. However, Shen *et al.* (2018) found that in an RCT with women also undergoing hormonal therapy for breast cancer, supplementation of 3.3 g/day of EPA + DHA for 24 weeks significantly decreased the BPI worst pain scores among obese patients, but there were no differences in treatment arms among nonobese patients [56]. Another RCT supplemented breast cancer patients with 0.2 g EPA and 1.0 g DHA per day for 16 weeks during treatment and one month following treatment, and the authors observed a significant reduction in peripheral neuropathy in the treatment group compared to the control group [57]. Taken together, these findings suggest that n-3 supplementation during chemotherapy may improve the QoL of breast cancer patients, but further investigation is needed to understand its effect on patients receiving neoadjuvant chemotherapy.

1.4 Exercise

Physical activity has been shown to reduce risk, recurrence and mortality from breast cancer [11]. One study demonstrated that meeting WHO's recommendation for aerobic exercise was associated with a 12% risk reduction for breast cancer [58]. Similarly, a meta-analysis investigating 38 cohort studies reported that the most physically active women had a 12-21% reduced risk of breast cancer than the least physically active women [59].

Several biological mechanisms underlying the role of physical activity in breast cancer outcomes have been proposed. These include changes in body composition, improvements in metabolic function, a reduction in estrogen availability, changes in inflammatory and immune

mediators and alterations in tumour gene expression [11, 60]. Physical activity has also been shown to alter the phenotype of tumour vasculature, which may improve chemotherapy efficacy and enhance tumour regression [25, 61, 62]. Specifically, preclinical studies have demonstrated that moderate aerobic exercise is able to remodel breast tumour vasculature and improve blood flow and drug delivery to tumours [63, 64]. It is also important to highlight that a combination of aerobic and resistance training has been shown to improve chemotherapy completion rates in women with breast cancer undergoing adjuvant chemotherapy [65]. Chemotherapy completion rates have been strongly associated with an improved prognosis [25], and therefore the association between exercise and treatment completion may help explain the beneficial role of exercise on patient outcomes.

WHO recommends that adults aged 18 to 64 perform at least 150-300 minutes of moderate-intensity aerobic physical activity, 75-150 minutes of vigorous-intensity aerobic physical activity, or an equivalent combination of both, per week [66]. WHO also recommends that this population do muscle-strengthening activities at moderate or greater intensity on two or more days per week. It is worth noting that WHO has also released guidelines for people living with chronic conditions, including cancer survivors [66]. These guidelines are consistent with those previously described for healthy individuals, but also include the recommendation for older adults to do multicomponent physical activity that emphasizes functional balance and strength training at least three days per week. The American College of Sports Medicine (ACSM) has also developed exercise guidelines for cancer survivors, including both patients actively receiving treatment and those that have finished treatment [67]. The ACSM produced a roundtable report in 2018 that detailed the type and duration of exercise shown to improve specific cancer-related side effects [67]. Generally, they reported that moderate-intensity aerobic training for a minimum of 30 minutes at least three times

per week, for a minimum of 8-12 weeks positively effects health-related outcomes including anxiety, depression, fatigue, QoL and physical function. They also found that resistance training at least twice weekly in addition to the aerobic exercise recommendation demonstrated similar benefits to aerobic exercise alone. Lastly, the American Society of Clinical Oncology (ASCO) recommends regular aerobic and resistance exercise during active treatment with curative intent [68]. Previously established guidelines can serve as cutoff points to help assess whether meeting the recommendations leads to better clinical outcomes. Physical activity is recommended for individuals with any cancer type, but the kind, intensity and duration may need to be tailored to the specific individuals' condition [2]. This highlights the need to understand the role of different types of exercise in different clinical scenarios.

1.4.1 Exercise During Cancer Treatment

Physical activity of patients with cancer is often inhibited by side effects of chemotherapy, including severe fatigue, lack of energy and negative effects on individuals' mental health [2]. However, physical activity has been shown to reduce the severity of side effects, decrease fatigue and positively impact patients' QoL [2]. Therefore, it is critical to provide appropriate and evidence-based recommendations to patients with cancer because this may help encourage individuals to take part in physical activity despite treatment side effects.

Physical activity has been shown to alleviate fatigue and improve HRQoL in patients with breast cancer [3]. A recent meta-analysis of RCTs examined the effects of exercise interventions on CRF and QoL in cancer patients [4]. The authors concluded that exercise interventions reduced CRF and improved QoL, with greater effects observed for aerobic exercise. Consistent with these findings, Carayol *et al.* (2019) found that a combined diet and exercise intervention in patients

with early breast cancer undergoing chemotherapy and radiotherapy significantly improved fatigue and QoL at the end of treatment and 12 months post-intervention [5]. Another study investigated the effect of a 12-week self-managed home-based moderate intensity walking intervention on psychosocial health of patients with breast cancer undergoing chemotherapy [69]. The walking intervention significantly reduced fatigue, and increased self-esteem and mood compared to the control group. Several studies have demonstrated that the beneficial effects of exercise on fatigue and QoL persist for months after treatment [70-72].

1.4.2 Association Between Exercise and Achieving a Pathological Complete Response

As previously mentioned, exercise may act through several physiological mechanisms to exert beneficial effects on breast cancer outcomes, including chemotherapy efficacy and treatment completion rates. As a result, it has been hypothesized that physical exercise could improve pCR rates after neoadjuvant chemotherapy [25]. However, there are few studies investigating this association in breast cancer patients. One prospective study found that there was no relationship between pre-treatment levels of physical activity classification and pCR [73]. However, this study did not consider exercise levels *during* treatment. In contrast, results from a recent RCT that randomized breast cancer patients to usual care or a home-based exercise and nutrition counselling intervention found that among women receiving neoadjuvant chemotherapy, those assigned to the exercise and nutrition intervention were more likely to achieve a pCR than the control group [74].

Two clinical trials are currently underway that aim to investigate the effect of exercise on achieving a pCR in patients with breast cancer. One study is a prospective clinical trial in which patients are randomized to a home-based physical exercise intervention or routine care during neoadjuvant chemotherapy [25]. The primary endpoint of the trial is pCR. A similar RCT is

investigating the effects of supervised exercise training compared to usual care on tumour size, with pCR serving as a secondary outcome [21].

1.5 Dietary Intake

1.5.1 Dietary Intake and Breast Cancer Risk

Nutritional status and different dietary patterns have been associated with breast cancer risk, treatment outcomes and QoL in survivors [75]. Previous studies have investigated the role of nutrition, dietary patterns and individual foods in the risk of breast cancer. For example, increased consumption of alcohol, processed meats and animal fats as well as lower consumption of dietary fiber, fruits and vegetables may increase one's risk of breast cancer [76]. Previous studies have also demonstrated that healthy eating patterns reduce the risk of breast cancer, whereas unhealthy eating patterns increase the risk [75].

There are mixed findings regarding macronutrient intake and risk of breast cancer. A recent systemic review reported a significant association between dietary fat intake and breast cancer risk, which may be due to increased oxidative stress and obesity [76]. However, other studies have shown a negative association with breast cancer risk and dietary fat [77, 78]. Different types of fat may help explain these inconsistencies. For example, one study found that intake of saturated fatty acids was not associated with breast cancer risk, but polyunsaturated and total unsaturated fatty acid intake were associated with a decreased risk of breast cancer [77]. Similarly, multiple studies have demonstrated a positive association between dietary carbohydrate consumption and breast cancer risk, which may in part be due to insulin resistance [77-79]. Other studies, including a recent meta-analysis, found no significant association between dietary carbohydrate intake and breast cancer risk [79]. It is important to note that different types of dietary carbohydrates, including

sugars, starches and fiber may affect one's health in different ways. For example, dietary fiber has been associated with reduced breast cancer incidence, whereas sugar intake has been positively associated with breast cancer risk [80]. Lastly, several studies have found no significant association between total protein intake and breast cancer risk [81, 82]. However, when separated into vegetable protein and animal protein, they were associated with lower and higher breast cancer incidence, respectively [82]. Overall, inconsistent findings between breast cancer risk and macronutrient intake highlight the need for further investigation regarding nutrient intake and breast cancer risk.

1.5.2 Dietary Recommendations

1.5.2.1 Dietary Reference Intakes

Health Canada has provided healthy eating guidelines for the general population. It is recommended that individuals regularly consume fruits and vegetables, whole grain foods and protein, particularly plant protein, while limiting their intake of highly processed foods, added sodium, sugars and saturated fat [83]. Dietary reference intakes (DRIs) have been established to serve as nutrient recommendations for healthy Canadians [84]. DRIs include four types of nutrient reference values, including the estimated average requirement (EAR), recommended dietary allowance (RDA), adequate intake (AI) and the tolerable upper intake level (UL) [84]. The EAR of a nutrient is developed based on scientific evidence and is the estimated amount to meet the requirement of half of all healthy individuals in a population of a given age and gender. The RDA serves as the goal for individuals as it ensures a low risk of insufficiency. It is calculated from the EAR plus twice the standard deviation and is the daily dietary intake of a nutrient that is sufficient to meet the requirement of 97-98% of healthy persons. When data is not sufficient to develop an

EAR and RDA, an AI value is established based on population data or by estimating how much of a given nutrient is consumed by a group of healthy people which is assumed to be adequate to promote health. The UL is the highest average daily intake level of a nutrient that is unlikely to induce any adverse health effects. In addition, the acceptable macronutrient distribution ranges (AMDRs) for carbohydrate, fat and protein are calculated based on population intake and considerable research studies. Expressed as a percentage of total energy, these ranges are updated on a regular basis with new information to reflect ranges associated with reduced risk of chronic disease [84]. Lastly, the chronic disease risk reduction intake (CDRR) is the level of a nutrient expected to reduce the risk of chronic disease development [85, 86].

These DRIs serve as a benchmark to determine how well Canadians are eating and can be used to assess nutritional intake of different groups or individuals [87]. It is important to note that it is not appropriate to simply compare the mean intake of a group to the EAR or RDA [87]. Instead, the EAR for a nutrient is used to estimate the prevalence of inadequacy within a group. In contrast, the prevalence of inadequacy cannot be determined for nutrients with an AI [87]. Instead, the average intake of the group can be compared to the AI, and if the group's average intake is greater than the AI, the prevalence of inadequacy is likely to be low. However, if the average intake is less than the AI, it cannot be concluded that the prevalence of inadequacy is high because it is possible that the AI exceeds the true RDA, and therefore the prevalence cannot be estimated [87]. Lastly, the UL is used to estimate the prevalence of intakes that are at risk of being excessive. Available DRIs will be used to assess the intake of the DHA WIN cohort.

1.5.2.2 Recommendations for Women with Breast Cancer

Consistent with dietary recommendations for the general population, a healthy dietary pattern, characterized by a high intake of fruits, vegetables, whole grains, poultry and fish, and a

low intake of red meat, refined foods, sweets and high-fat dairy products may positively impact the prognosis and survival of women with breast cancer [10]. The World Cancer Research Fund/American Institute for Cancer Research has provided evidence-based lifestyle recommendations for patients with breast cancer with the goal to increase overall survival. Along with being physically active and maintaining a healthy body weight, it is recommended that individuals follow a fiber- and soy-rich diet and limit the intake of fats (in particular, saturated fatty acids). In addition, nutritional interventions during chemotherapy may help ensure adequate energy and nutrient intake, which may in turn improve treatment efficacy and reduce toxicity during cancer treatment [10]. For example, Souza et al. (2021) conducted an RCT in breast cancer patients undergoing neoadjuvant chemotherapy. The intervention group received an individualized diet plan created by a dietician that was consistent with guidelines set by the European Society for Clinical Nutrition and Metabolism for patients with cancer [22, 88]. The authors found that nausea and vomiting increased in the control group, but decreased in the intervention group. The nutritional intervention also contributed to improved role function, grip strength and reduction in leucopenia and abdominal pain [22].

1.5.3 Canadian Community Health Survey

The Canadian Community Health Survey (CCHS) is a cross-sectional survey that gathers information on health status, health care utilization and health determinants of Canadians [89]. The CCHS-Nutrition collects information about individuals' dietary intake through a 24-hour recall [90, 91]. To date, the most recent nutritional intake data released by Health Canada is from the 2015 CCHS-Nutrition survey. This publicly available data serves as a useful reference tool to

compare how the dietary intake of women in the DHA WIN sample compares to that of Albertan women above the age of 19.

1.5.4 Food Frequency Questionnaires

Food frequency questionnaires (FFQs) are dietary assessment tools used to asses habitual intake by asking about the frequency of consumption and portion sizes of specific foods or food groups [92, 93]. FFQs reflect intake over a longer period of time, usually ranging from the previous month(s) to one year. This avoids the issue of day-to-day variability seen in other dietary assessment tools, such as a 24-hour dietary recall [93]. The Canadian-Diet History Questionnaire II (C-DHQ II) is an FFQ comprised of 165 questions that queries about intake in the past year or month and includes questions about portion sizes [94]. It is available in paper and electronic formats. The C-DHQ II food list was created based on analyses of 24-hour dietary recall data from the CCHS. Each question on the C-DHQ II is linked to a nutrient profile generated from the CCHS nutrient database that consists of 33 nutrients and can be used to estimate participants' daily nutrient intake [95]. The questionnaire can be self-administered and the respondents' burden is small, with an estimated completion time of about 30 minutes [92, 93]. FFQs are a simple, cost-effective method that permits the assessment of long-term dietary intake [92].

CHAPTER 2: RATIONALE, OBJECTIVES AND HYPOTHESES

2.1 Rationale for Thesis Research

Chemotherapy has been associated with a number of side effects that undermine QoL and inhibit physical activity in patients with breast cancer, and these effects may differ between different chemotherapy regimens [1, 2]. This may ultimately contribute to reduced treatment tolerability and poorer clinical outcomes [32]. Current literature suggests that n-3 PUFA supplementation [6, 7] as well as exercise [2-5, 69] during chemotherapy may mitigate side effects and help maintain patients' QoL, but research on these associations is limited in patients with breast cancer receiving neoadjuvant chemotherapy. In order for n-3 PUFA supplementation and exercise to be utilized in clinical oncology, it is imperative to demonstrate their benefits in specific clinical settings (i.e. with a specific cancer type and treatment protocol) [96]. Therefore, further research is warranted to investigate the role of n-3 PUFA supplementation and exercise on QoL in women with stage I-III non-metastatic breast cancer undergoing neoadjuvant chemotherapy.

The current study is an analysis of secondary outcomes from the DHA WIN study, a phase II RCT evaluating DHA supplementation (4.4 g/day) on tumour growth and metabolism in women with breast cancer undergoing six cycles of neoadjuvant chemotherapy (3 weeks/cycle) [19]. QoL questionnaires were completed at baseline and at the end of chemotherapy treatment. Exercise questionnaires were completed at the start of each 3-week cycle, and the end of cycle 6. Classification of pCR was assessed at surgery by a pathologist. The current thesis will utilize the aforementioned outcomes to help determine the relationships between chemotherapy, QoL, exercise levels and pCR in patients with breast cancer.

2.2 Research Objectives and Hypotheses

The overall aim, objectives and hypotheses of the current thesis research are outlined below.

Overall aim:

The overall aim is to describe QoL, exercise behaviour and dietary habits in women with breast cancer undergoing neoadjuvant chemotherapy, and identify potential relationships between DHA, exercise, QoL and achieving a pCR.

Research objectives and hypotheses:

- Determine how QoL changes from baseline to the end of neoadjuvant chemotherapy among breast cancer patients in the DHA WIN cohort and determine the role of DHA and exercise in mitigating potential changes.
 - a. It is hypothesized that QoL will decrease from baseline to end of chemotherapy and that this decrease will be less in the DHA group and among participants that meet WHO's aerobic or resistance training exercise recommendations at baseline or the end of cycle 6. Timepoints for exercise categorization (i.e. baseline and the end of cycle 6) were chosen to allow for analysis of both pre-treatment exercise levels and levels at the end of chemotherapy treatment (when patients may be experiencing side effects from chemotherapy).
- 2. Describe participants' aerobic and resistance training exercise levels throughout the trial and compare them between treatment groups, and determine whether meeting exercise recommendations predicted achieving a pCR.

- a. It is hypothesized that a greater proportion of the DHA group will meet exercise guidelines compared to the placebo group at the end of chemotherapy.
- b. It is hypothesized that meeting WHO's aerobic or resistance training exercise recommendations will increase the likelihood of achieving a pCR.
- Describe the estimated daily dietary intake of DHA WIN participants at study entry with the CCHS and Canadian DRIs and compare daily intake between the DHA and placebo groups.

2.3 Thesis Outline

Chapter 1 introduced topics relevant to the thesis and provided a review of the current literature. Chapter 2 provides the rationale, objectives and outline of the current paper. Chapter 3 will provide an overview of the DHA WIN RCT and highlight components of the trial that are relevant to the current thesis research. It will also provide baseline characteristics of participants, and briefly describe the methods employed to analyze the QoL, exercise levels and dietary intake of the trial's participants.

Chapter 4 will describe the baseline estimated daily dietary intake of participants and compare it to current DRIs and the CCHS. It will also compare participants' aerobic and resistant training exercise levels to the WHO's exercise recommendations. Chapter 5 will discuss how QoL and exercise changed during chemotherapy, as well as their relationships with each other and the DHA intervention. It will also investigate whether meeting WHO's exercise guidelines predicted achieving a pCR. Chapter 6 will discuss the results as they relate to the project's objectives and summarize the key findings. It will also describe limitations of the current research and provide recommendations for future directions.

CHAPTER 3: METHODS

3.1 Docosahexaenoic Acid for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN) Randomized Controlled Trial

The DHA WIN trial is the first two-arm, double-blind, phase II RCT to investigate the effects of DHA supplementation concomitant with neoadjuvant chemotherapy in women with non-metastatic breast cancer [19]. The primary outcome of the trial is the Ki67 index, which is a common endpoint to measure efficacy of neoadjuvant chemotherapy in clinical trials [19].

3.1.1 DHA WIN RCT Protocol

The protocol for the DHA WIN RCT has previously been published [19]. Briefly, the RCT involved women with stage I-III non-metastatic breast cancer that were prescribed neoadjuvant chemotherapy. Participants were randomized to receive 4.4 g/day of DHA or a placebo supplement (Figure 1). All women received standard-of-care chemotherapy, which was one of two docetaxelbased neoadjuvant chemotherapy regimens that were used in this population. Each regimen consisted of six cycles of chemotherapy that were administered in 3-week intervals. The DHA group received 11-1 g DHA-enriched, algae-sourced triglyceride oil capsules (life'sDHA S40-O400), while the placebo group received 11 g of a corn/soy oil blend per day (DSM Nutritional Products, Columbia, Maryland). It is worth noting that the placebo supplements contained equal amounts of polyunsaturated fatty acids as the DHA supplement, in the form of linoleic acid. Participants were instructed to orally consume the capsules at any time throughout the day, with or without food. The intervention began at the start of the first cycle of chemotherapy and continued throughout chemotherapy treatment. It is important to note that for patients unable to complete the full six cycles of chemotherapy, local guidelines mandated surgery between three to five weeks after the last cycle of chemotherapy was administered, and therefore supplementation

of the intervention was continued until surgery [19]. Compliance was determined by a review of the patient dosing diary and the recorded number of any remaining capsules returned at the end of the study.

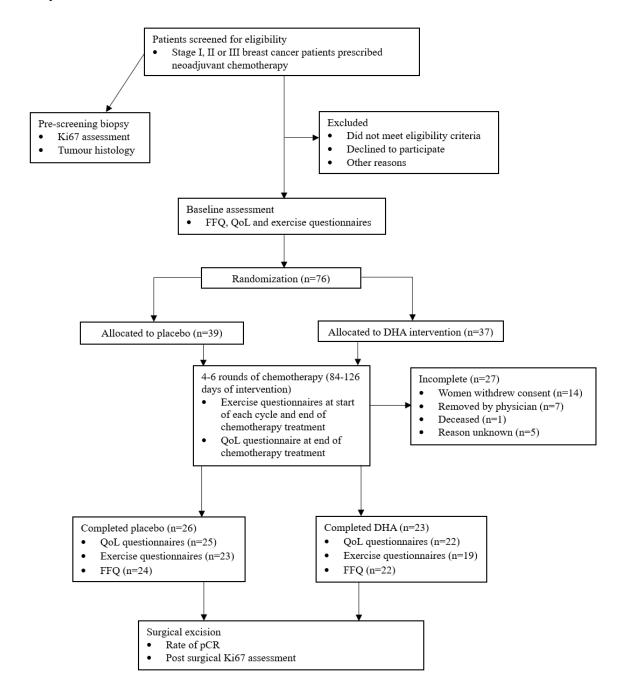


Figure 1. Flowchart of the DHA WIN RCT. The figure was adapted from Newell *et al.* (2019). Abbreviations: Docosahexaenoic acid (DHA), Docosahexaenoic acid for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN), randomized controlled trial (RCT), food frequency questionnaire (FFQ), quality of life (QoL), pathological complete response (pCR).

In addition to the primary outcome of the Ki67 index, several secondary outcomes were measured, including the rate of pCR, baseline dietary intake, QoL and exercise levels (Figure 2) [19]. Classification of pCR was completed after surgical resection as part of the standard-of-care assessment [19]. Resected breast tissue and all sampled axillary nodes were assessed for absence of invasive cancer by Hematoxylin and Eosin evaluation. The C-DHQ-II was completed by participants at baseline. QoL questionnaires were completed at baseline and at the end of chemotherapy treatment. Exercise questionnaires were completed at the start of each 3-week cycle, and the end of cycle 6. Participants were given paper copies of the questionnaires to complete during clinic visits.

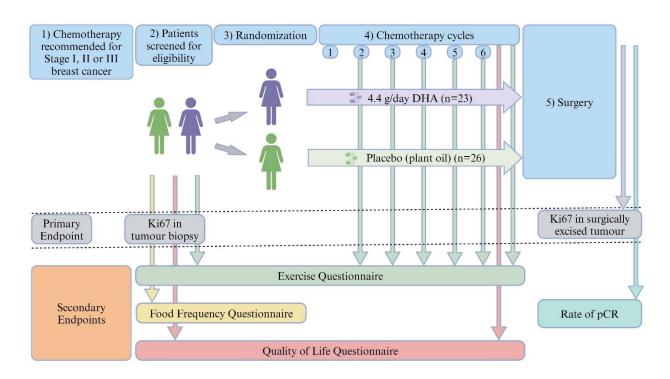


Figure 2. Flowchart of DHA WIN trial design with the primary endpoint and outcomes relevant to the thesis research. The figure was adapted from Newell *et al.* (2019) and created using BioRender.com. Abbreviations: Docosahexaenoic acid (DHA), pathological complete response (pCR).

3.1.2 Ethical Approval, Inclusion Criteria and Recruitment

The DHA WIN RCT received full approval from the Health Research Ethics Board of Alberta – Cancer Committee (Protocol #: HREBA.CC-18-0381) [19]. The study is registered at ClinicalTrials.gov (NCT03831178). The study took place at the Cross Cancer Institute (CCI) in Edmonton, Alberta with central laboratory and clinical analyses being completed at the University of Alberta. Participants were recruited by oncologists and clinical trial nurses at the CCI and screened for eligibility. Eligible patients that were interested in participating received a detailed explanation of the study and written informed consent was obtained prior to their involvement in the study. The target sample size of 26 participants was determined based on the primary objective. All data for the trial is managed through the REDCap trial database.

Inclusion criteria for participants included stage I, II or III invasive breast cancer and prescription of neoadjuvant chemotherapy [19]. Participants needed an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, the ability to take oral medications, adequate tissue specimen for diagnosis and analysis, and normal haematology and biochemistry assessments. Patients were excluded if they received chemotherapy prior to surgery, were currently consuming or had consumed in the previous two months n-3, fish oil or other supplements or foods containing DHA (>200 mg/day) for more than one day per week, or had continued intake of supplements containing vitamin C, vitamin E or β-carotene that was greater than the DRIs or other antioxidant supplements. Individuals that were allergic to soy or corn or were hypersensitive to any component of the container were also excluded. Several medical conditions were also cause for exclusion, including symptomatic but untreated cholelithiasis, a history of deep vein thrombosis, active thrombophlebitis, pulmonary embolism, stroke, acute myocardial infarction, congestive cardiac failure, untreated hypertension and known inherited hypercoagulable disorder

and diagnosis of any other malignancy within the past year except for adequately treated basal cell or squamous cell skin cancer. Lastly, a history of a psychiatric disorder that would preclude consent or a partial or complete loss of vision or diplopia from ophthalmic vascular disease was means for exclusion.

3.1.3 Baseline Characteristics

Baseline demographic and clinical characteristics of participants are shown in Table 1.

Table 1. DHA WIN participant demographic and clinical characteristics.

Variables	Total (n = 49)	Placebo (n = 26)	$ \begin{array}{c} \mathbf{DHA} \\ (n = 23) \end{array} $
Age (years) ¹	50.8 (31-73)	51.2 (31-69)	50.4 (32-73)
BMI $[kg/m^2]^2$	28.8 ± 6.7	27.5 ± 6.0	30.3 ± 7.3
Underweight $(<18.5)^3$	1 (2.0%)	1 (3.8%)	0 (0.0%)
Healthy weight $(18.5-25)^3$	13 (26.5%)	8 (30.8%)	5 (21.7%)
Overweight $(25-30)^3$	18 (36.7%)	10 (38.5%)	8 (34.8%)
Obese $(\geq 30)^3$	17 (34.7%)	7 (26.9%)	10 (43.5%)
Ethnicity ³			
Caucasian	31 (63.3%)	17 (65.4%)	14 (60.9%)
Asian	10 (20.4%)	5 (19.2%)	5 (21.7%)
Black	4 (8.2%)	2 (7.7%)	2 (8.9%)
Indigenous	4 (8.2%)	2 (7.7%)	2 (8.9%)
Menopausal status ³			
No	27 (55.1%)	13 (50.0%)	14 (60.9%)
Yes	22 (44.9%)	13 (50.0%)	9 (39.1%)
Age at menarche (years) ²	12.8 ± 1.5	12.7 ± 1.7	12.8 ± 1.3
Missing values	4 (8.2%)	2 (7.7%)	2 (8.7%)
Diabetes ³			
No	47 (95.9%)	26 (100.0%)	21 (91.3%)
Yes	2 (4.1%)	0 (0%)	2 (8.7%)
Ethanol abuse ³			
No	48 (98.0%)	26 (100.0%)	22 (95.7%)
Yes	1 (2.0%)	0 (0%)	1 (4.3%)

Smokers ³			
No	41 (83.7%)	21 (80.8%)	20 (87.0%)
Yes	8 (16.3%)	5 (19.2%)	3 (13.0%)
Histology ^{3,4}			
HER2+	25 (51.0%)	14 (53.8%)	11 (47.8%)
TNBC	12 (24.5%)	5 (19.2%)	7 (30.4%)
Luminal A	10 (20.4%)	6 (23.1%)	4 (17.4%)
Luminal B	2 (4.1%)	1 (3.8%)	1 (4.3%)
Disease Stage ³			
IIA	13 (26.5%)	6 (23.1%)	7 (30.4%)
IIB	9 (18.4%)	3 (11.5%)	6 (26.1%)
IIIA	14 (28.6%)	9 (34.6%)	5 (21.7%)
IIIB	4 (8.2%)	2 (7.7%)	2 (8.7%)
IIIC	1 (2.0%)	0 (0.0%)	1 (4.3%)
Unknown	8 (16.3%)	6 (23.1%)	2 (8.7%)
Tumour Grade ³			
T1	1 (2.0%)	1 (3.8%)	0 (0.0%)
T2	26 (53.1%)	14 (53.8%)	12 (52.2%)
Т3	11 (22.4%)	5 (19.2%)	6 (26.1%)
T4	5 (10.2%)	3 (11.5%)	2 (8.7%)
Unknown	6 (12.2%)	3 (11.5%)	3 (13.0%)
Axillary Node Status ³			
N0	12 (24.5%)	6 (23.1%)	6 (26.1%)
N1	20 (40.8%)	10 (38.5%)	10 (43.5%)
N2	5 (10.2%)	3 (11.5%)	2 (8.7%)
N3	2 (4.1%)	1 (3.9%)	1 (4.4%)
Unknown	10 (20.4%)	6 (23.1%)	4 (17.4%)
$\mathbf{ECOG}^{3,5}$			
Baseline			
0	44 (89.8%)	24 (92.3%)	20 (87.0%)
1	2 (4.1%)	2 (7.7%)	0 (0.0%)
Unknown	3 (6.1%)	0 (0.0%)	3 (13.0%)
End of treatment		, ,	,
0	35 (71.4%)	22 (84.6%)	13 (56.5%)
1	10 (20.4%)	2 (7.7%)	8 (34.8%)
2	2 (4.1%)	1 (3.8%)	1 (4.3%)
Unknown	2 (4.1%)	1 (3.8%)	1 (4.3%)
Total recruited (n)	76	39	37
Overall compliance ²	83.9 ± 20.0	81.3 ± 22.5	86.3 ± 17.7
Missing values ³	13 (26.5%)	9 (34.6%)	4 (17.4%)

Pathological complete response³

No	32 (65.3%)	19 (73.1%)	13 (56.5%)
Yes	17 (34.7%)	7 (26.9%)	10 (43.5%)

¹Mean (range); ²Mean ± SD; ³Count (percentage of total or given treatment group); ⁴HER2+ (ER-, PR-, HER2+), TNBC (ER-, PR-, HER2-), Luminal A (ER+ and/or PR+, HER2-), Luminal B (ER+ and/or PR+, HER2+); ⁵0 = Fully active, able to carry on all pre-disease performance without restriction [97]; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, i.e., light housework, office work; 2 = Ambulatory and capable of all selfcare but unable to carry out any work activities, up and about more than 50% of waking hours. Abbreviations: Body mass index (BMI), human epidermal growth factor receptor 2 (HER2), triple negative breast cancer (TNBC), Eastern Cooperative Oncology Group (ECOG).

3.2 Questionnaires

3.2.1 Quality of Life Questionnaire

Several assessments were included in the QoL questionnaire completed by participants. These included the Functional Assessment of Cancer Therapy (FACT)-General (FACT-G), FACT-Breast (FACT-B), FACT-Taxane, FACT-Endocrine Symptoms (FACT-ES), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale (FACIT-Fatigue), the Perceived Stress Scale (PSS), the Fordyce Emotions Questionnaire, the Center for Epidemiologic Studies-Depression Scale (CES-D) and the State-Trait Anxiety Inventory (STAI). A copy of the QoL questionnaire is included in Appendix 1. As mentioned previously, QoL questionnaires were completed at baseline (prior to the start of chemotherapy), and at the end of chemotherapy treatment (prior to surgery).

3.2.1.1 FACT and FACIT Questionnaires

The FACT and FACIT questionnaires are validated questionnaires that are commonly used to assess HRQoL in cancer patients [98-102]. The FACT-G is comprised of 27 items that measures four domains of HRQoL in patients with cancer, including physical well-being, social well-being, emotional well-being and functional well-being [103]. A number of other subscales, including the

breast cancer subscale (10 questions), taxane subscale (16 questions) and endocrine symptom subscale (19 questions) have been developed to assess QoL in patients with breast cancer and specific symptoms related to taxane and endocrine therapies [104-106]. They are commonly added to the FACT-G questionnaire, and make up the FACT-B, FACT-Taxane and FACT-ES questionnaires, respectively. It is worth noting that each of these questionnaires produce several subscores. For example, each one produces a subscale score for physical well-being, social wellbeing, emotional well-being, and functional well-being and a FACT-G total score which is the sum of the four previous subscales. Additionally, the FACT-B produces a breast cancer (BC) subscale score, a FACT-B total score (which is the sum of the FACT-G and BC subscale scores) and a FACT-B trial outcome index (TOI) (which is the sum of the physical well-being, functional well-being and BC subscales). The FACT-Taxane produces a taxane subscale score, a FACT-taxane total score (which is the sum of the FACT-G and the taxane subscale scores) and a FACT-taxane TOI (that is the sum of the physical well-being, functional well-being and taxane subscales). Lastly, the FACT-ES generates an endocrine symptoms (ES) subscale score and a FACT-ES total score (which is the sum of the FACT-G and ES subscale scores). The FACIT-Fatigue scale consists of 13 items that assess patients' fatigue and its impact on daily function [107].

Each of these questionnaires had a recall period of seven days, and responses were given on a five-point Likert-type scale, ranging from 0 (not at all) to 4 (very much). Scores for each subscale were determined by summing the score for positive items with the reverse coded score of negative items. Higher scores indicate a better QoL.

3.2.1.2 Perceived Stress Scale (PSS)

The PSS is one of the most widely used stress perception assessments worldwide [108]. The PSS-14 consists of seven negative questions (i.e. felt nervous and stressed) and seven positive questions (i.e. felt that you were on top of things) that relate to how often participants have experienced stressful situations in the past month. Similar to the FACT questionnaires, the responses to the PSS questions were given on a five-point Likert-type scale, from 0 (never) to 4 (very often). The scores for positive items were reverse coded and summed with negative item scores. Higher total scores indicate more perceived stress.

3.2.1.3 Fordyce Emotions Questionnaire

The Fordyce Emotions Questionnaire, also known as the happiness measure, is a measure of an individual's emotional well-being [109]. It consists of an 11-point happiness/unhappiness scale and a question asking for the percentage of time spent in "happy", "unhappy" and "neutral" moods. A combination score can be calculated which combines the scale and happy % scores with equal weights. It is obtained using the following equation: Combination score = [scale score x 10 + happy%]/2. The combination score is generally used as the primary criterion for happiness in research [109].

3.2.1.4 Center for Epidemiologic Studies-Depression Scale (CES-D)

A modified version of the CES-D was included in the QoL questionnaire to assess depressive symptoms. It consisted of 10 statements and asked participants how often they experienced specific feelings or behaviours over the past seven days. Each item was rated from 0 (rarely or none of the time) to 3 (most or all of the time). Positively worded items were reverse

coded, and summed with negatively worded items to obtain a final score, with higher scores indicating greater depressive symptomology [110].

3.2.1.5 State-Trait Anxiety Inventory (STAI)

A modified version of the STAI was utilized to assess participants' levels of anxiety [111]. Respondents were asked to rate 10 statements from 1 (not at all) to 4 (very much so). Items that reflect the absence of anxiety were reverse coded and summed with items that indicated higher anxiety. Therefore, higher scores indicate more severe anxiety.

3.2.2 Godin Leisure-Time Exercise Questionnaire

An adapted version of the Godin Leisure-Time Exercise Questionnaire was used to collect information on the frequency and average duration of light, moderate and vigorous aerobic exercise as well as strength/resistance training per week [112, 113]. Participants were asked to only include exercise that was done during free time (i.e. was not housework or occupation) and lasted at least 10 minutes. Brief descriptions of each exercise category and examples were given for each item on the questionnaire. Light intensity aerobic exercise consisted of activities that took minimal effort and did not lead to perspiration (i.e. easy walking, yoga). Moderate intensity aerobic exercises included those that were not exhausting, and led to light perspiration (i.e. fast walking, easy bicycling). Vigorous intensity exercises included those that caused sweating and a rapid heartbeat (i.e. running, vigorous bicycling). Strength/resistance exercise consisted of activities such as weight lifting, resistance bands, sit-ups and push-ups. A copy of the exercise questionnaire is available in Appendix 2.

Average weekly aerobic exercise was determined by adding the average minutes of moderate aerobic exercise to two times the average minutes of vigorous aerobic exercise. Participants were categorized into those that met WHO's aerobic exercise guidelines (\geq 150 minutes/week), and those that did not meet the guidelines (< 150 minutes/week). A separate categorization also separated participants into those that met WHO's resistance training recommendation (\geq 2 times/week), and those that did not (< 2 times/week). As described in Section 3.1.2, exercise questionnaires were completed at 7 timepoints throughout the trial, including at baseline and the end of chemotherapy.

3.2.3 Food Frequency Questionnaire

As previously mentioned, the FFQ employed in the DHA WIN RCT was the C-DHQ II, and was previously described in Section 1.4.3. A copy of the C-DHQ II is included in Appendix 3. Paper copies of the C-DHQ II were completed by participants at baseline, prior to starting chemotherapy [19]. Paper copies were manually inputted into the C-DHQ II website, and data was analyzed using Diet*Calc software [114, 115].

3.3 Statistical Analyses

Descriptive statistics including means and proportions were used to describe continuous and categorical variables, respectively. Baseline dietary intake data was compared between treatment groups using independent t-tests. Depending on the availability of DRIs, the EAR of a nutrient was used to determine the prevalence of inadequacy within the DHA WIN cohort. When an AI was available, it was compared to the average intake of the cohort. Average nutrient intakes were compared to the UL to determine the prevalence of intakes at risk of being excessive. Lastly,

the AMDRs were used to determine the proportion of participants below, within and above these ranges. The proportion of participants in the DHA WIN trial that were below the DRI for a given nutrient was compared to the proportion of the Albertan women not meeting the DRI (based on data obtained from the 2015 CCHS) using chi-squared or Fisher's exact test.

Scoring of the QoL and exercise questionnaires were completed as previously described (Sections 3.2.1 and 3.2.2). Generalized estimating equations (GEE) were used to assess the effects of time and treatment on the average duration of aerobic exercise and average frequency of strength/resistance training. Unadjusted multiple comparisons were used to measure statistical significance compared to baseline levels of exercise. GEE was also used to examine the effects of time and treatment on QoL scores. Lastly, GEE was used to assess the effect of time and exercise classification on QoL scores. GEE was performed with unadjusted models, as well as models adjusted for age, BMI, histology, menopausal status, disease stage and tumour grade. Fisher's exact test was used to assess associations between categorical variables (i.e. meeting WHO's exercise guidelines and treatment group or achieving a pCR). Only participants that completed the trial (i.e. were not withdrawn due to clinical or personal reasons) were included in analyses. Continuous and categorical baseline characteristics of those that completed the trial were compared to those that did not complete the trial using the independent t-test and chi-squared or Fisher's exact test, respectively. Statistical analyses were conducted using SPSS (V27.0, IBM Corporation, Armonk, NY, USA). Statistical significance was defined as a two-sided p-value ≤ 0.05 . Figures were created using BioRender.com or SPSS.

CHAPTER 4: COMPARING EXERCISE LEVELS AND ESTIMATED BASELINE DIETARY INTAKE TO CURRENT GUIDELINES

4.1 Exercise

Participants were categorized into those that met WHO's aerobic exercise recommendation (\geq 150 minutes/week) and those that did not (< 150 minutes/week) (Table 2; Figure 3). At baseline, 23.8% of the DHA group met this recommendation, compared to 44.0% of the placebo group (p = 0.22). At the end of the sixth cycle of chemotherapy, the percentages meeting the recommendation dropped to 21.1% and 30.4%, respectively (p = 0.73). Treatment group was not associated with meeting WHO's aerobic exercise recommendation at any timepoint throughout the trial (Table 2).

Table 2. Categorization of participants based on treatment group and meeting WHO's aerobic exercise recommendation (≥ 150 minutes/week) over time.

	≥ 150 minute aerobic ex		
	Yes	No	p-value
Week 0 $(n = 46)$			
DHA	5 (23.8%)	16 (76.2%)	0.22
Placebo	11 (44.0%)	14 (56.0%)	0.22
Total	16 (34.8%)	30 (65.2%)	
Week 3 $(n = 45)$			
DHA	5 (23.8%)	16 (76.2%)	0.52
Placebo	8 (33.3%)	16 (66.7%)	0.53
Total	13 (28.9%)	32 (71.1%)	
Week 6 $(n = 47)$			
DHA	5 (22.7%)	17 (77.3%)	0.22
Placebo	10 (40.0%)	15 (60.0%)	0.23
Total	15 (31.9%)	32 (68.1%)	
Week 9 $(n = 47)$			
DHA	7 (31.8%)	15 (68.2%)	1.00
Placebo	8 (32.0%)	17 (68.0%)	1.00
Total	15 (31.9%)	32 (68.1%)	
Week 12 $(n = 47)$			
DHA	5 (22.7%)	17 (77.3%)	1.00
Placebo	6 (24.0%)	19 (76.0%)	1.00
Total	11 (23.4%)	36 (76.6%)	

Week 15 $(n = 45)$			
DHA	4 (20.0%)	16 (80.0%)	0.72
Placebo	7 (28.0%)	18 (72.0%)	0.73
Total	11 (24.4%)	34 (75.6%)	
Week 18 $(n = 42)$			
DHA	4 (21.1%)	15 (78.9%)	0.73
Placebo	7 (30.4%)	16 (69.6%)	0.73
Total	11 (26.2%)	31 (73.8%)	

Percentage of the treatment group or total are shown in parentheses. Fisher's exact test was used to test the association between treatment groups and meeting WHO's aerobic exercise recommendation. No statistically significant associations were observed. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: World Health Organization (WHO), docosahexaenoic acid (DHA).

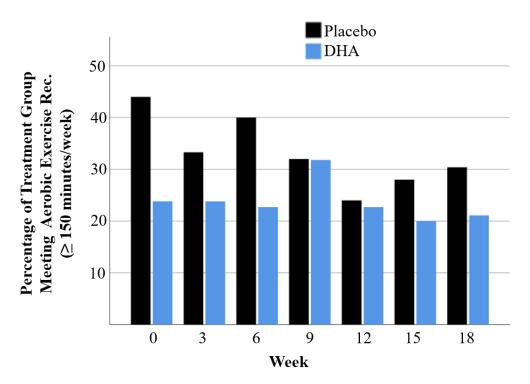


Figure 3. Percentage of the DHA (n = 19) or placebo (n = 23) groups that met WHO's aerobic exercise recommendation (\geq 150 minutes/week) over time. Fisher's exact test was used to test the association between treatment groups and meeting WHO's aerobic exercise recommendation. There were no statistically significant differences between treatment groups at any week. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: World Health Organization (WHO), docosahexaenoic acid (DHA), recommendation (rec).

Similarly, participants were categorized based on meeting WHO's resistance training exercise recommendation (≥ 2 times/week) (Table 3; Figure 4). At baseline, 22.7% of the DHA group met the recommendation, compared to 36.0% of the placebo group (p = 0.36). These dropped to 0% and 34.8% at the end of the sixth cycle of chemotherapy, respectively (p = 0.01). Treatment group was not associated with meeting WHO's resistance training exercise recommendation at any timepoint throughout the trial except at the end of cycle 6 (p = 0.01) (Table 3; Figure 4).

Table 3. Categorization of participants based on treatment group and meeting WHO's resistance training exercise recommendation (≥ 2 times/week) over time.

Yes	Nie		
	No	p-value	
5 (22.7%)	17 (77.3%)	0.36	
9 (36.0%)	16 (64.0%)	0.30	
14 (29.8%)	33 (70.2%)		
4 (19.0%)	17 (81.0%)	1.00	
5 (20.8%)	19 (79.2%)	1.00	
9 (20.0%)	36 (80.0%)		
5 (22.7%)	17 (77.3%)	0.26	
9 (36.0%)	16 (64.0%)	0.36	
14 (29.8%)	33 (70.2%)		
5 (22.7%)	17 (77.3%)	0.52	
8 (32.0%)	17 (68.0%)	0.53	
13 (27.7%)	34 (72.3%)		
3 (13.6%)	19 (86.4%)	0.47	
6 (24.0%)	19 (76.0%)	0.47	
9 (19.1%)	38 (80.9%)		
	9 (36.0%) 14 (29.8%) 4 (19.0%) 5 (20.8%) 9 (20.0%) 5 (22.7%) 9 (36.0%) 14 (29.8%) 5 (22.7%) 8 (32.0%) 13 (27.7%) 3 (13.6%) 6 (24.0%)	9 (36.0%) 16 (64.0%) 14 (29.8%) 33 (70.2%) 4 (19.0%) 17 (81.0%) 5 (20.8%) 19 (79.2%) 9 (20.0%) 36 (80.0%) 5 (22.7%) 17 (77.3%) 9 (36.0%) 16 (64.0%) 14 (29.8%) 33 (70.2%) 5 (22.7%) 17 (77.3%) 8 (32.0%) 17 (68.0%) 13 (27.7%) 34 (72.3%) 3 (13.6%) 19 (86.4%) 6 (24.0%) 19 (76.0%)	

Week 15 $(n = 45)$			
DHA	6 (30.0%)	14 (70.0%)	0.74
Placebo	6 (24.0%)	19 (76.0%)	0.74
Total	12 (26.7%)	33 (73.3%)	
Week 18 $(n = 42)$			
DHA	0 (0.0%)	19 (100.0%)	0.01
Placebo	8 (34.8%)	15 (65.2%)	0.01
Total	8 (19.0%)	34 (81.0%)	

Percentage of the treatment group or total are shown in parentheses. Fisher's exact test was used to test the association between treatment groups and meeting WHO's resistance training exercise recommendation. Bolded p-values indicate a significant difference at p = 0.01. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: World Health Organization (WHO), docosahexaenoic acid (DHA).

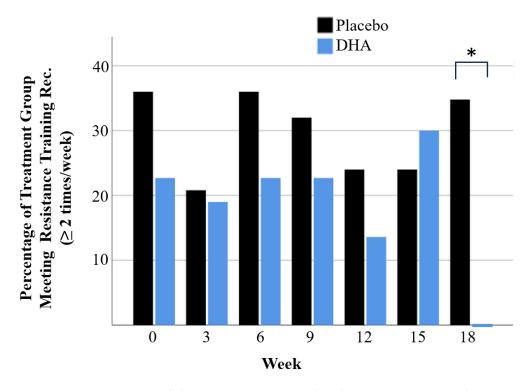


Figure 4. Percentage of the DHA (n = 19) or placebo (n = 23) groups that met WHO's resistance training exercise recommendation (≥ 2 times/week) over time. Fisher's exact test was used to test the association between treatment groups and meeting WHO's resistance training exercise recommendation. *Indicates a statistically significant difference at p = 0.01. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: World Health Organization (WHO), docosahexaenoic acid (DHA), recommendation (rec).

4.2 Dietary Intake

4.2.1 Estimated Baseline Dietary Intake

There were no statistically significant differences between the DHA and placebo groups for estimated baseline daily intake of energy, macronutrients, total monounsaturated fatty acids, total polyunsaturated fatty acids, total saturated fatty acids, cholesterol, sodium, sugar or dietary fiber (Table 4).

Table 4. Estimated baseline daily dietary intake obtained from the C-DHQ II.

	DHA	Placebo	p-value
	(n = 22)	(n = 24)	P , unat
Energy (kcal)	1684 ± 568	1821 ± 1255	0.64
% from carbohydrate	48.7 ± 10.0	48.0 ± 9.5	0.82
% from fat	34.3 ± 6.9	36.4 ± 7.3	0.32
% from protein	17.1 ± 3.6	16.8 ± 3.6	0.79
% from alcohol	2.0 ± 3.1	1.5 ± 2.2	0.57
Carbohydrate (g)	212 ± 109	218 ± 156	0.90
Protein (g)	69.8 ± 21.7	78.2 ± 58.6	0.53
Total fat (g)	62.2 ± 19.5	74.1 ± 54.6	0.34
Total monounsaturated fatty acids (g)	25.1 ± 8.1	29.6 ± 22.1	0.37
Total polyunsaturated fatty acids (g)	10.5 ± 3.4	14.8 ± 14.7	0.19
PUFA 18:2 (Octadecadienoic acid) (g)	8.3 ± 2.9	12.1 ± 12.5	0.17
PUFA 18:3 (Octadecatrienoic acid) (g)	1.8 ± 0.7	2.2 ± 1.8	0.32
Total saturated fatty acids (g)	20.8 ± 8.3	23.1 ± 17.0	0.56
Cholesterol (mg)	233 ± 79	249 ± 156	0.67
Sodium (mg)	2492 ± 934	2880 ± 2237	0.45
Sugar (g)	103 ± 80	93 ± 77	0.65
Dietary fiber (g)	18.3 ± 8.9	22.7 ± 19.4	0.33

Data are presented as mean \pm SD. Independent t-tests were conducted to determine if there was a statistically significant difference in mean daily intake between the DHA and placebo groups. No statistically significant differences were observed between groups. Abbreviations: Canadian-Diet History Questionnaire II (C-DHQ II), docosahexaenoic acid (DHA), polyunsaturated fatty acid (PUFA).

4.2.2 Estimated Daily Dietary Intake Compared to Current Recommendations and the Canadian Community Health Survey

Of the nutrients presented in Table 4, EARs exist for carbohydrates (100 g/day) and protein (0.66 g/kg/day) [116]. Carbohydrate intake below the EAR was reported by 8.7% of the DHA WIN cohort, compared to 3.1% of Albertan women that completed the 2015 CCHS (p = 0.07) [117]. Within the DHA WIN cohort, 23.9% of participants reported a protein intake level below the EAR. This percentage was not compared to the CCHS because the national survey did not report the percentage of participants below the EAR. An AI exists for sodium (1500 mg/day) and dietary fiber (25 g/day for women aged 31-50 and 21 g/day for women aged 51-70). Within the DHA WIN cohort, 82.6% of participants reported sodium intake above the AI, compared to 91.1% of the CCHS women (p = 0.06). It is also worth highlighting that the mean intake of sodium was $2695 \pm$ 1733 mg/day in the DHA WIN cohort (Table 6). Since the average intake exceeds the AI, the prevalence of inadequacy is likely low [87]. The CDRR for sodium is 2300 mg/day, which is the amount of sodium above which intake reduction in an apparently healthy population is expected to reduce the risk of chronic disease development [118]. The percentage of the DHA WIN cohort that reported sodium intake above the CDRR was 45.7%, compared to 40.2% in the CCHS cohort (p = 0.47) [117]. Average reported daily intake was above the AI for dietary fiber for 61.5% of the DHA WIN cohort, but this percentage was not reported on the 2015 CCHS. Average intake of dietary fiber was 20.6 ± 15.3 g/day for the DHA WIN cohort (Table 6), which is less than the AIs provided for this population. Risk of inadequacy increases at some intake level below the AI, but conclusions regarding the prevalence of inadequacy cannot be made without clinical or biochemical assessment [119].

The percentage of participants that reported macronutrient intake below, within or above the AMDRs were determined (Table 5). Carbohydrate intake that exceeded the AMDR was reported among 8.7% of the DHA WIN cohort, compared to < 3% of Albertan women that completed the CCHS (p = 0.008). Similarly, 52.2% of the DHA WIN women reported intake above the AMDR for fat, compared to 32.9% that completed the 2015 CCHS (p = 0.008). A greater percentage of women from the CCHS reported an intake within the AMDR for fat (66.9%) compared to DHA WIN participants (45.7%) (p = 0.003). The two groups did not statistically significantly differ in other AMDR categories (Table 5).

Table 5. Percentages of the DHA WIN or CCHS cohorts that were below, within or above the AMDRs.

	Carbohydrate	Fat	Protein
	$(45-65\% \text{ of energy})^1$	$(20-35\% \text{ of energy})^1$	$(10-35\% \text{ of energy})^1$
% below AMDR			
DHA WIN	32.6%	2.2%	2.2%
CCHS [117]	33.5%	< 3%	< 3%
% within AMDR			
DHA WIN	58.7%	45.7%*	97.8%
CCHS	66.3%	66.9%	99.7%
% above AMDR			
DHA WIN	8.7%*	52.2%*	0.0%
CCHS	< 3%	32.9%	0.0%

¹AMDR for listed macronutrient. Data are presented as the percentage of the given cohort that are within each category. Chi-squared and Fisher's exact test were used to determine if there was a statistically significant difference between the percentage in the DHA WIN cohort (n = 46) compared to the percentage obtained from the CCHS (n = 696) [117]. *Indicates a statistically significant difference between the DHA WIN and CCHS cohorts at p < 0.01. Abbreviations: Acceptable macronutrient distribution range (AMDR), Docosahexaenoic acid for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN), Canadian Community Health Survey (CCHS).

4.2.3 Estimated Daily Dietary Intake Compared to Canadian Community Health Survey

Mean intake of energy and several nutrients were compared between the DHA WIN cohort and Albertan women that completed the 2015 CCHS (Table 6). On average, the estimated daily intake of protein, total fat, monounsaturated fat, sodium and dietary fiber were greater in the DHA WIN cohort compared to the CCHS group (all $p \le 0.05$).

Table 6. Mean estimated daily intake of energy and nutrients in the DHA WIN cohort compared to Albertan women that completed the 2015 CCHS.

	DHA WIN (n = 46)	CCHS (n = 696)	p-value
Energy (kcal/day)	1755 ± 980	1575 ± 923	0.20
% from carbohydrate	48.3 ± 9.7	47.6 ± 13.2	0.71
% from fat	35.4 ± 7.1	33.0 ± 10.6	0.14
% from protein	16.9 ± 3.6	16.7 ± 5.3	0.76
Carbohydrate (g/day)	215 ± 135	188 ± 132	0.18
Protein (g/day)	74.2 ± 44.6	65.0 ± 26.4	0.03
Total fat (g/day)	68.4 ± 41.7	60.0 ± 26.4	0.05
Total monounsaturated fatty acids (g/day)	27.4 ± 16.9	21.9 ± 13.2	0.01
Total polyunsaturated fatty acids (g/day)	12.8 ± 11.0	12.3 ± 7.9	0.71
Total saturated fatty acids (g/day)	22.0 ± 13.5	19.8 ± 13.2	0.27
Cholesterol (mg/day)	241 ± 124	218 ± 185	0.40
Sodium (mg/day)	2695 ± 1733	2206 ± 1398	0.02
Total sugar (g/day)	97.8 ± 77.8	77.0 ± 79.1	0.08
Dietary fiber (g/day)	20.6 ± 15.3	14.9 ± 10.6	< 0.001

Data are presented as mean \pm SD. Independent t-tests were used to assess statistical significance between the DHA and CCHS [117] groups. Bolded p-values indicate statistically significant differences at p \leq 0.05. Abbreviations: Docosahexaenoic acid for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN), Canadian Community Health Survey (CCHS).

CHAPTER 5: RESULTS

Seventy-six participants were recruited to participate in the DHA WIN RCT, of which 49 (65%) completed the trial. Participants that completed the trial (n = 49) were compared with those that did not (n = 27) and there were no statistically significant differences in age, BMI, tumour stage, tumour grade, histology or menopausal status. Adherence to the intervention was 81% for the placebo group and 86% for the DHA group.

5.1 Quality of Life

5.1.1 Comparing Quality of Life Within and Between Treatment Groups

All subscales of the FACT questionnaires significantly decreased from baseline to the end of the sixth cycle of chemotherapy in both the DHA and control groups (p-time \leq 0.03), with the exception of the emotional well-being scores, which significantly increased over time in both groups (p-time = 0.01). The FACIT-Fatigue scale and STAI also decreased over time in both groups (p-time \leq 0.01), while the happiness measure (Fordyce Emotions Combination score) increased (p-time = 0.03). Perceived stress decreased in both groups, while the depression scores increased, but these changes did not reach statistical significance. These changes are shown in Table 7. DHA did not statistically significantly mitigate the change in QoL indicators over time (all p-interactions \geq 0.05).

Table 7. Quality of life scores at baseline (week 0) and end of cycle 6 (week 18) in the DHA and placebo groups.

				Unadjusted				Adjusted		
	Week 0 [mean ± SD]	Week 18 [mean ± SD]	Mean Change (95% CI)	p-int	p- treatment	p-time	p-int	p- treatment	p-time	
FACT-G total									_	
score										
DHA	88.9 ± 14.0	82.2 ± 17.0	-6.7 (-16.0 to 2.7)	0.82	0.44	<0.001	0.65	0.36	<0.001	
Placebo	85.2 ± 14.1	79.4 ± 16.0	-5.9 (-14.9 to 3.1)	0.62	0.44	~0.001	0.03	0.30	~0.001	
Physical WB										
DHA	24.6 ± 4.4	21.8 ± 5.0	-2.8 (-5.6 to 0.0)	0.69	0.79	<0.001	0.85	0.46	<0.001	
Placebo	24.5 ± 4.4	21.1 ± 6.8	-3.4 (-6.7 to 0.1)	0.09	0.79	~0.001	0.83	0.40	~0.001	
Social WB										
DHA	24.8 ± 4.3	23.2 ± 4.8	-1.6 (-4.3 to 1.1)	0.87	0.26	<0.001	0.72	0.14	<0.001	
Placebo	23.3 ± 5.1	21.6 ± 5.4	-1.7 (-4.7 to 1.3)	0.67	0.20	~0.001	0.72	0.14	\0.001	
Emotional WB										
DHA	17.6 ± 4.8	18.8 ± 4.2	+1.2 (-1.5 to 3.9)	0.57	0.83	0.01	0.65	0.87	0.01	
Placebo	17.1 ± 5.1	19.1 ± 3.9	+2.0 (-0.5 to 4.6)	0.57	0.63	0.01	0.03	0.67	0.01	
Functional										
WB										
DHA	21.9 ± 5.9	18.4 ± 5.8	-3.5 (-7.0 to 0.0)	0.33	0.43	< 0.001	0.35	0.52	< 0.001	
Placebo	20.1 ± 5.1	18.0 ± 5.2	-2.1 (-5.0 to 0.8)	0.22	0.15	0,001	0.55	0.02	0.001	
FACT-B total										
score	1106.17	100	100/010							
DHA	118.6 ± 17.0	108.5 ± 21.8	-10.2 (-21.9 to 1.6)	0.86	0.73	< 0.001	0.75	0.64	< 0.001	
Placebo	115.7 ± 18.0	106.9 ± 19.9	-8.8 (-19.8 to 2.2)							
FACT-B TOI										
DHA	76.2 ± 12.5	66.5 ± 15.0	-9.8 (-18.0 to -1.5)	0.91	1.00	< 0.001	0.83	0.95	< 0.001	
Placebo	75.8 ± 11.2	66.3 ± 13.7	-9.5 (-16.6 to -2.3)							

BC subscale									
score									
DHA	29.7 ± 5.9	26.2 ± 6.7	-3.5 (-7.3 to 0.3)	0.88	0.24	<0.001	0.93	0.11	<0.001
Placebo	31.2 ± 4.4	27.8 ± 5.5	-3.3 (-6.1 to -0.5)	0.00	0.24	~0.001	0.93	0.11	~0.001
FACT-Taxane									
total score									
DHA	150.2 ± 18.4	136.9 ± 21.4	-13.3 (-25.3 to -1.3)	0.95	0.72	<0.001	0.84	0.73	< 0.001
Placebo	147.8 ± 15.1	135.1 ± 21.4	-12.7 (-23.6 to -1.8)	0.75	0.72	\0.001	0.04	0.73	\0.001
FACT-Taxane									
TOI									
DHA	107.8 ± 14.8	94.8 ± 14.8	-12.9 (-21.8 to -4.1)	0.75	0.87	<0.001	0.74	0.97	< 0.001
Placebo	105.9 ± 12.2	94.5 ± 17.3	-11.3 (-20.0 to -2.6)	0.75	0.07	\0.001	0.74	0.57	\0.001
Taxane									
subscale score									
DHA	61.3 ± 6.0	54.6 ± 7.1	-6.6 (-10.6 to -2.7)	0.47	0.73	<0.001	0.46	0.12	<0.001
Placebo	60.9 ± 6.5	56.0 ± 9.3	-4.9 (-9.5 to -0.3)	0.47	0.73	<0.001	0.46	0.12	<0.001
FACT-ES total			,						
score									
DHA	154.9 ± 21.5	145.7 ± 22.9	-9.2 (-22.5 to 4.2)	0.62	0.95	<0.001	0.68	0.96	<0.001
Placebo	155.3 ± 17.0	144.6 ± 21.1	-10.7 (-22.0 to 0.6)	0.02	0.93	~0.001	0.08	0.90	~0.001
ES subscale									
score									
DHA	66.0 ± 9.4	63.5 ± 8.1	-2.5 (-7.7 to 2.8)	0.51	0.11	0.01	0.44	0.05	0.03
Placebo	69.6 ± 4.9	65.4 ± 7.7	-4.2 (-7.8 to -0.5)	0.31	0.11	0.01	0.44	0.05	0.03
Fatigue									
subscale score									
DHA	44.3 ± 11.1	38.0 ± 10.7	-6.3 (-12.9 to 0.3)	0.66	0.82	<0.001	0.70	0.66	<0.001
Placebo	43.1 ± 8.2	38.0 ± 10.9	-5.2 (-10.6 to 0.2)	0.00	0.82	~0.001	0.70	0.00	~0.001
PSS score									
DHA	19.7 ± 7.2	18.0 ± 9.2	-1.7 (-6.6 to 3.2)	0.04	0.72	0.22	0.02	0.00	0.20
Placebo	20.2 ± 8.5	19.2 ± 8.7	-1.0 (-5.9 to 3.8)	0.84	0.72	0.22	0.92	0.80	0.29
			(

CES-D score									
DHA	7.0 ± 3.2	7.3 ± 4.0	+0.3 (-1.9 to 2.4)	0.78	0.69	0.38	0.84	0.96	0.37
Placebo	7.3 ± 4.3	7.8 ± 3.9	+0.5 (-1.8 to 2.8)	0.78	0.09	0.36	0.04	0.90	0.57
STAI score									
DHA	20.4 ± 7.0	18.7 ± 6.6	-1.7 (-5.8 to 2.4)	0.89	0.86	0.04	0.79	0.88	0.01
Placebo	20.8 ± 6.1	18.9 ± 6.0	-1.9 (-5.3 to 1.5)	0.89	0.80	0.04	0.79	0.66	0.01
Fordyce Emotions Combination									
score									
DHA	59.4 ± 24.3	63.5 ± 21.8	+4.1 (-10.2 to 18.5)	0.16	0.60	0.01	0.14	0.36	0.03
Placebo	57.6 ± 22.4	68.1 ± 17.4	+10.5 (-1.2 to 22.2)	0.10	0.00	0.01	0.14	0.30	0.03

The sample sizes were 22 for the DHA group and 25 for the placebo group. Generalized estimating equations were used to test statistical significance of differences within and between treatment groups. Statistical significance is indicated by bolded p-values. Adjusted models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: p-interaction (p-int; time*treatment), docosahexaenoic acid (DHA), Functional Assessment of Cancer Therapy-General (FACT-G), well-being (WB), FACT-Breast (FACT-B), Trial Outcome Index (TOI), breast cancer (BC), endocrine symptoms (ES), Perceived Stress Scale (PSS), Center for Epidemiologic Studies-Depression (CES-D), State-Trait Anxiety Inventory (STAI), body mass index (BMI).

5.1.2 Exercise Classification and QoL

Participants were previously categorized based on meeting WHO's aerobic or resistance training exercise recommendation at baseline and after the sixth cycle of chemotherapy (Section 4.1). Consistent with the results reported in Section 5.1.1, all subscales of the FACT questionnaires decreased or remained the same from baseline to end of cycle 6 in all exercise groups (i.e. the groups that met or did not meet the aerobic or resistance training exercise recommendation at baseline or the end of cycle 6) (p-time ≤ 0.06), except emotional well-being, which increased in all groups (p-time ≤ 0.06) (Tables 8-11). Anxiety decreased over time in all groups (p-time ≤ 0.03) while the happiness measure increased over time (p-time ≤ 0.07).

5.1.2.1 Aerobic Exercise Classification at Baseline and QoL

On average, participants that reported ≥ 150 minutes of aerobic exercise per week at baseline experienced a smaller decline in their FACT-G total score (-5.4; 95% CI, -17.1 to 6.4 versus -7.4; 95% CI, -15.6 to 0.7; p-interaction = 0.05) (Figure 5), a greater decrease in their anxiety (-4.7; 95% CI, -9.5 to 0.1 versus -0.2; 95% CI, -3.4 to 3.0; p-interaction = 0.01) (Figure 6), as well as a greater increase in their emotional well-being (+3.3; 95% CI, 0.1 to 6.6 versus +0.9; 95% CI, -1.3 to 3.1; p-interaction = 0.05) (Figure 7) over time. Participants that met the aerobic exercise recommendation at baseline experienced a decrease in their perceived stress (-4.0; 95% CI, -10.4 to 2.3), whereas those that did not meet the exercise recommendation at baseline experienced an increase in stress from baseline to end of treatment (+0.3; 95% CI, -3.8 to 4.4) (p-interaction = 0.01) (Figure 8). Additionally, those that met the recommendation at baseline reported a higher taxane subscale score at baseline (62.5 \pm 3.9 versus 60.1 \pm 7.2) and end of treatment (56.3 \pm 10.7 versus 55.0 \pm 7.2) (p-recommendation < 0.002) and a greater happiness

score at baseline (60.5 ± 21.0 versus 57.2 ± 24.7) and end of treatment (72.4 ± 13.3 versus 60.5 ± 20.9) (p-recommendation = 0.03). These changes are shown in Table 8.

Table 8. Quality of life scores at baseline (week 0) and end of cycle 6 (week 18) in participants that met (≥ 150 minutes/week) or did not meet (< 150 minutes/week) WHO's aerobic exercise recommendation at baseline.

			Unadjusted			Adjusted			
	Week 0 [mean ± SD]	Week 18 [mean ± SD]	Mean Change (95% CI)	p-int	p-rec	p-time	p-int	p-rec	p-time
FACT-G total score									
≥ 150 min/week	85.4 ± 15.6	80.1 ± 15.2	-5.4 (-17.1 to 6.4)	0.12	0.64	<0.001	0.05	0.61	< 0.001
< 150 min/week	87.2 ± 13.5	79.7 ± 16.7	-7.4 (-15.6 to 0.7)	0.12	0.04	~0.001	0.05	0.01	~0.001
Physical WB									
≥ 150 min/week	24.4 ± 5.4	21.2 ± 7.3	-3.2 (-7.9 to 1.6)	0.86	0.96	<0.001	0.78	0.56	< 0.001
< 150 min/week	24.6 ± 3.9	21.3 ± 5.5	-3.3 (-5.8 to -0.9)	0.80	0.90	~0.001	0.78	0.50	~0.001
Social WB									
≥ 150 min/week	24.4 ± 6.0	22.4 ± 6.4	-2.0 (-6.6 to 2.6)	0.76	0.83	<0.001	0.82	0.82	< 0.001
< 150 min/week	23.9 ± 4.2	22.2 ± 4.6	-1.6 (-3.9 to 0.6)	0.70	0.03	~0.001	0.02	0.02	~0.001
Emotional WB									
≥ 150 min/week	14.9 ± 5.5	18.2 ± 3.0	+3.3 (0.1 to 6.6)	0.05	0.07	<0.001	0.05	0.18	< 0.001
< 150 min/week	18.1 ± 4.2	19.0 ± 4.3	+0.9 (-1.3 to 3.1)	0.03	0.07	\0.001	0.03	0.10	~0.001
Functional WB									
≥ 150 min/week	20.1 ± 4.7	18.9 ± 4.9	-1.2 (-4.7 to 2.3)	0.10	0.76	<0.002	0.09	0.82	< 0.001
< 150 min/week	21.0 ± 5.9	17.2 ± 5.3	-3.8 (-6.7 to -0.8)	0.10	0.70	~0.002	0.09	0.62	~0.001
FACT-B total score									
≥ 150 min/week	114.6 ± 21.2	106.2 ± 19.8	-8.4 (-23.8 to 7.0)	0.44	0.70	< 0.001	0.41	0.65	< 0.001
< 150 min/week	117.6 ± 15.5	106.8 ± 20.8	-10.9 (-20.6 to -1.2)	0.44	0.70	\0.001	0.71	0.03	\0.001
FACT-B TOI									
≥ 150 min/week	75.4 ± 13.6	65.8 ± 13.9	-9.5 (-19.8 to 0.7)	0.68	0.99	<0.001	0.68	0.93	< 0.001
< 150 min/week	75.9 ± 11.1	65.5 ± 14.1	-10.3 (-17.0 to -3.7)	0.00	0.55	\0.001	0.00	0.93	~0.001
BC subscale score									
≥ 150 min/week	30.9 ± 6.2	26.8 ± 6.5	-4.1 (-8.8 to 0.6)	0.73	0.88	< 0.001	0.75	0.71	< 0.001
< 150 min/week	30.3 ± 4.9	27.0 ± 5.9	-3.2 (-6.1 to -0.4)	0.73	0.00	~0.001	0.75	0.71	·0.001

FACT-Taxane total									
score									
≥ 150 min/week	148.0 ± 17.5	135.9 ± 24.1	-12.1 (-28.0 to 3.9)	0.59	0.99	<0.001	0.52	0.77	<0.001
< 150 min/week	148.5 ± 16.9	134.7 ± 19.9	-13.8 (-23.5 to -4.0)	0.39	0.99	~0.001	0.32	0.77	~0.001
FACT-Taxane TOI									
≥ 150 min/week	107.8 ± 12.7	95.5 ± 20.2	-12.2 (-25.0 to 0.5)	0.94	0.61	< 0.001	0.95	0.07	<0.001
< 150 min/week	105.6 ± 14.3	93.4 ± 14.0	-12.1 (-19.5 to -4.7)	0.94	0.61	<0.001	0.93	0.07	~0.001
Taxane subscale									
score									
≥ 150 min/week	62.5 ± 3.9	56.3 ± 10.7	-6.2 (-12.2 to -0.2)	0.65	0.32	<0.001	0.73	<0.002	<0.001
< 150 min/week	60.1 ± 7.2	55.0 ± 7.2	-5.2 (-8.9 to -1.4)	0.03	0.32	~0.001	0.73	~0.002	~0.001
FACT-ES total									
score									
\geq 150 min/week	154.6 ± 19.0	143.4 ± 20.8	-11.1 (-26.3 to 4.0)	0.97	0.88	< 0.001	0.98	0.71	< 0.001
< 150 min/week	154.3 ± 19.7	144.5 ± 22.3	-9.9 (-21.0 to 1.3)	0.77	0.00	10.001	0.70	0.71	10.001
ES subscale score									
\geq 150 min/week	69.1 ± 4.9	63.8 ± 8.6	-5.4 (-10.6 to -0.1)	0.26	0.72	0.01	0.31	0.78	0.01
< 150 min/week	67.1 ± 8.7	64.7 ± 7.8	-2.3 (-6.6 to 2.0)	0.20	0.72	0.01	0.51	0.76	0.01
Fatigue subscale									
score									
\geq 150 min/week	44.3 ± 9.6	40.1 ± 13.1	-4.2 (-12.6 to 4.2)	0.30	0.38	< 0.001	0.33	0.09	< 0.001
< 150 min/week	43.0 ± 10.1	36.4 ± 9.5	-6.6 (-11.7 to -1.5)	0.50	0.50	10.001	0.55	0.07	*0.001
PSS score									
\geq 150 min/week	21.6 ± 8.8	17.5 ± 8.4	-4.0 (-10.4 to 2.3)	0.01	0.98	0.02	0.01	0.13	0.02
< 150 min/week	19.4 ± 7.1	19.7 ± 8.7	+0.3 (-3.8 to 4.4)	0.01	0.70	0.02	0.01	0.13	0.02
CES-D score									
≥ 150 min/week	8.1 ± 5.1	7.5 ± 4.2	-0.6 (-4.0 to 2.9)	0.10	0.73	0.66	0.09	0.94	0.64
< 150 min/week	6.9 ± 3.0	7.9 ± 3.7	+1.0 (-0.7 to 2.8)	0.10	0.73	0.00	0.07	0.74	0.04
STAI score									
≥ 150 min/week	22.3 ± 6.9	17.5 ± 6.1	-4.7 (-9.5 to 0.1)	0.01	0.98	< 0.003	0.01	0.46	<0.001
< 150 min/week	20.0 ± 6.3	19.8 ± 6.2	-0.2 (-3.4 to 3.0)	0.01	0.70	\ 0.003	0.01	0.70	*U•UU1

Fordyce Emotions Combination score

≥ 150 min/week	60.5 ± 21.0	72.4 ± 13.3	+12.0 (-1.1 to 25.0)	0.10	0.16	0.01	0.21	0.02	0.01
< 150 min/week	57.2 ± 24.7	60.5 ± 20.9	+3.3 (-9.1 to 15.7)	0.19	0.10	0.01	0.21	0.03	0.01

16 participants reported ≥ 150 minutes/week of aerobic exercise and 30 participants reported < 150 minutes/week. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Statistical significance is indicated by bolded p-values. Adjusted models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), well-being (WB), FACT-Breast (FACT-B), Trial Outcome Index (TOI), breast cancer (BC), endocrine symptoms (ES), Perceived Stress Scale (PSS), Center for Epidemiologic Studies-Depression (CES-D), State-Trait Anxiety Inventory (STAI), body mass index (BMI).

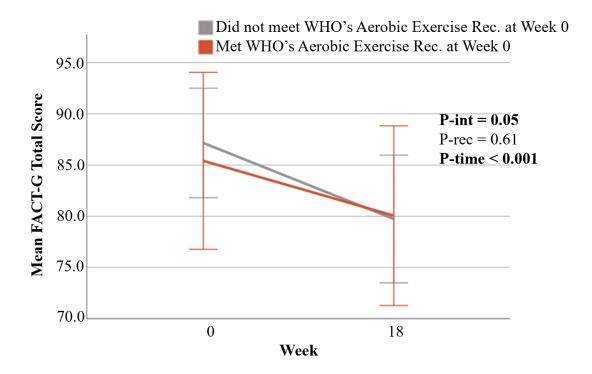


Figure 5. Change in mean FACT-G total scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 16) or did not meet (n = 30) WHO's aerobic exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at p \leq 0.05. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), recommendation (rec), body mass index (BMI).

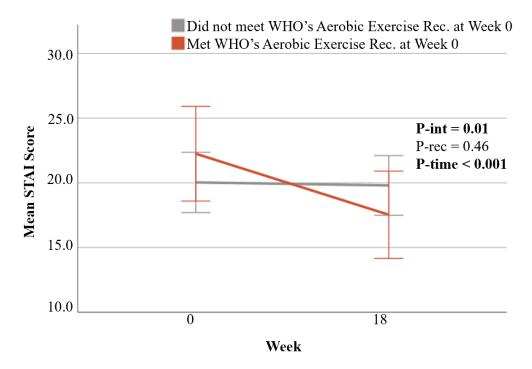


Figure 6. Change in mean STAI scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 16) or did not meet (n = 30) WHO's aerobic exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), State-Trait Anxiety Inventory (STAI), recommendation (rec), body mass index (BMI).

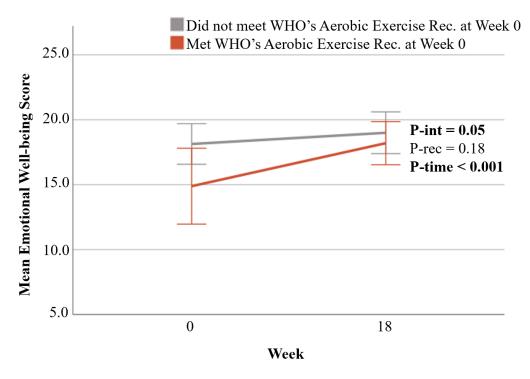


Figure 7. Change in mean emotional well-being scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 16) or did not meet (n = 30) WHO's aerobic exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), recommendation (rec), body mass index (BMI).

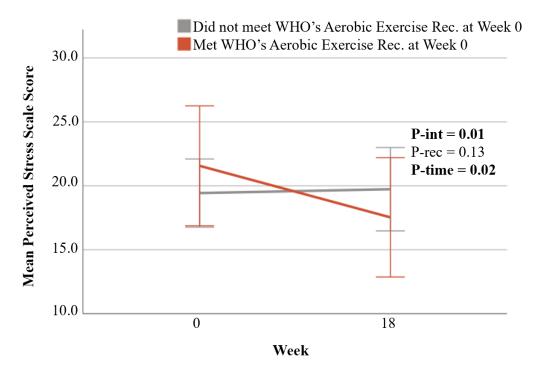


Figure 8. Change in mean perceived stress scale scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 16) or did not meet (n = 30) WHO's aerobic exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), recommendation (rec), body mass index (BMI).

5.1.2.2 Aerobic Exercise Classification at the End of Cycle 6 and QoL

Participants were also categorized based on meeting the aerobic exercise recommendation at the *end* of the sixth cycle of chemotherapy (Table 2). Participants that met the recommendation experienced a smaller decline over time in their FACT-G total score (-2.1; 95% CI, -16.0 to 11.9 versus -8.9; 95% CI, -17.5 to -0.3; p-interaction = 0.01) (Figure 9). They also did not experience a change in their functional well-being over time, whereas the group that did not meet the recommendation experienced a decrease in their functional well-being from baseline to end of

cycle 6 (-4.1; 95% CI, 7.1 to -1.1) (p-interaction = 0.01) (Figure 10). Additionally, those that met the aerobic exercise recommendation after the sixth cycle reported a higher happiness score at baseline (70.0 \pm 15.5 versus 58.0 \pm 25.3) and at end of cycle 6 (78.4 \pm 12.0 versus 61.4 \pm 20.8) compared to those that did not meet the exercise recommendation (p-recommendation < 0.002). These changes are shown in Table 9.

Table 9. Quality of life scores at baseline (week 0) and end of cycle 6 (week 18) in participants that met (≥ 150 minutes/week) or did not meet (< 150 minutes/week) WHO's aerobic exercise recommendation at the end of cycle 6.

			Unadjusted			Adjusted		
Week 0 [mean ± SD]	Week 18 [mean ± SD]	Mean Change (95% CI)	p-int	p-rec	p-time	p-int	p-rec	p-time
87.7 ± 16.7	85.7 ± 13.9	-2.1 (-16.0 to 11.9)	0.01	0.50	<0.001	0.01	0.65	<0.001
88.3 ± 14.6	79.4 ± 18.0	-8.9 (-17.5 to -0.3)	0.01	0.39	<0.001	0.01	0.65	<0.001
25.3 ± 2.5	22.9 ± 5.7	-2.4 (-6.3 to 1.5)	0.46	0.24	<0.001	0.25	0.97	~0 001
24.5 ± 5.1	21.0 ± 6.5	-3.5 (-6.5 to -0.5)		0.34	<0.001	0.33	0.87	<0.001
22.4 ± 6.7	21.6 ± 6.9	-1.1 (-7.2 to 4.9)	0.57	0.26	<0.00 <i>5</i>	0.52	0.11	< 0.005
24.5 ± 4.2	22.9 ± 4.3	-1.6 (-3.8 to 0.6)		0.30	<0.005	0.33	0.11	<0.005
17.9 ± 3.7	19.7 ± 2.5	+1.8 (-1.0 to 4.6)	0.52	0.72	0.01	0.56	0.26	0.01
17.9 ± 5.0	19.0 ± 4.5	+1.1 (-1.3 to 3.6)	0.53	0.73	0.01	0.36	0.30	0.01
21.8 ± 5.3	21.8 ± 2.7	0.0 (-3.8 to 3.8)	0.01	0.05	0.01	0.01	0.00	0.01
21.0 ± 6.1	16.9 ± 5.7	-4.1 (-7.1 to -1.1)	0.01	0.05	0.01	0.01	0.98	0.01
119.7 ± 20.9	112.4 ± 19.9	-7.3 (-25.9 to 11.4)	0.14	0.56	<0.001	0.10	0.76	<0.001
117.8 ± 17.7	106.1 ± 22.3	-11.6 (-22.0 to -1.2)	0.14	0.30	<0.001	0.10	0.76	<0.001
79.2 ± 12.1	71.4 ± 13.1	-7.8 (-19.3 to 3.8)	0.25	0.10	<0.001	0.20	0.01	<0.001
75.8 ± 12.5	64.4 ± 15.2	-11.4 (-18.5 to -4.3)	0.23	0.19	0.19 <0.001		0.81	<0.001
		,						
31.9 ± 5.3	26.7 ± 7.0	-5.2 (-10.9 to 0.5)	0.22	0.70	<0.001	0.10	0.08	<0.001
30.2 ± 5.1	27.0 ± 6.3	-3.2 (-6.1 to -0.3)	0.22	0.70	~0.001	0.19	0.98	<0.001
	[mean \pm SD] 87.7 ± 16.7 88.3 ± 14.6 25.3 ± 2.5 24.5 ± 5.1 22.4 ± 6.7 24.5 ± 4.2 17.9 ± 3.7 17.9 ± 5.0 21.8 ± 5.3 21.0 ± 6.1 119.7 ± 20.9 117.8 ± 17.7 79.2 ± 12.1 75.8 ± 12.5 31.9 ± 5.3	[mean \pm SD] [mean \pm SD] 87.7 ± 16.7 85.7 ± 13.9 88.3 ± 14.6 79.4 ± 18.0 25.3 ± 2.5 22.9 ± 5.7 24.5 ± 5.1 21.0 ± 6.5 22.4 ± 6.7 21.6 ± 6.9 24.5 ± 4.2 22.9 ± 4.3 17.9 ± 3.7 19.7 ± 2.5 19.0 ± 4.5 21.8 ± 5.3 21.8 ± 2.7 16.9 ± 5.7 119.7 ± 20.9 112.4 ± 19.9 117.8 ± 17.7 106.1 ± 22.3 79.2 ± 12.1 71.4 ± 13.1 75.8 ± 12.5 64.4 ± 15.2 31.9 ± 5.3 26.7 ± 7.0	[mean \pm SD] [mean \pm SD] (95% CI) 87.7 \pm 16.7 85.7 \pm 13.9 -2.1 (-16.0 to 11.9) 88.3 \pm 14.6 79.4 \pm 18.0 -8.9 (-17.5 to -0.3) 25.3 \pm 2.5 22.9 \pm 5.7 -2.4 (-6.3 to 1.5) 24.5 \pm 5.1 21.0 \pm 6.5 -3.5 (-6.5 to -0.5) 22.4 \pm 6.7 21.6 \pm 6.9 -1.1 (-7.2 to 4.9) 24.5 \pm 4.2 22.9 \pm 4.3 -1.6 (-3.8 to 0.6) 17.9 \pm 3.7 19.7 \pm 2.5 +1.8 (-1.0 to 4.6) +1.1 (-1.3 to 3.6) 17.9 \pm 5.0 19.0 \pm 4.5 +1.1 (-1.3 to 3.6) 21.8 \pm 5.3 21.8 \pm 2.7 0.0 (-3.8 to 3.8) 21.0 \pm 6.1 16.9 \pm 5.7 -4.1 (-7.1 to -1.1) 119.7 \pm 20.9 112.4 \pm 19.9 -7.3 (-25.9 to 11.4) 117.8 \pm 17.7 106.1 \pm 22.3 -11.6 (-22.0 to -1.2) 79.2 \pm 12.1 71.4 \pm 13.1 -7.8 (-19.3 to 3.8) 75.8 \pm 12.5 64.4 \pm 15.2 -11.4 (-18.5 to -4.3) 31.9 \pm 5.3 26.7 \pm 7.0 -5.2 (-10.9 to 0.5)	Week 0 [mean \pm SD]Week 18 [mean \pm SD]Mean Change (95% CI)p-int 87.7 ± 16.7 88.3 ± 14.6 85.7 ± 13.9 79.4 ± 18.0 $-2.1 (-16.0 \text{ to } 11.9)$ $-8.9 (-17.5 \text{ to } -0.3)$ 0.01 25.3 ± 2.5 24.5 ± 5.1 22.9 ± 5.7 21.0 ± 6.5 $-2.4 (-6.3 \text{ to } 1.5)$ $-3.5 (-6.5 \text{ to } -0.5)$ 0.46 22.4 ± 6.7 24.5 ± 4.2 21.6 ± 6.9 22.9 ± 4.3 $-1.1 (-7.2 \text{ to } 4.9)$ $-1.6 (-3.8 \text{ to } 0.6)$ 0.57 17.9 ± 3.7 17.9 ± 5.0 19.7 ± 2.5 19.0 ± 4.5 $+1.8 (-1.0 \text{ to } 4.6)$ $+1.1 (-1.3 \text{ to } 3.6)$ 0.53 21.8 ± 5.3 21.0 ± 6.1 21.8 ± 2.7 16.9 ± 5.7 $0.0 (-3.8 \text{ to } 3.8)$ $-4.1 (-7.1 \text{ to } -1.1)$ 0.01 119.7 ± 20.9 117.8 ± 17.7 112.4 ± 19.9 106.1 ± 22.3 $-7.3 (-25.9 \text{ to } 11.4)$ $-11.6 (-22.0 \text{ to } -1.2)$ 0.14 79.2 ± 12.1 75.8 ± 12.5 71.4 ± 13.1 64.4 ± 15.2 $-7.8 (-19.3 \text{ to } 3.8)$ $-11.4 (-18.5 \text{ to } -4.3)$ 0.25 31.9 ± 5.3 26.7 ± 7.0 $-5.2 (-10.9 \text{ to } 0.5)$ 0.22	Week 0 [mean \pm SD]Week 18 [mean \pm SD]Mean Change (95% CI)p-intp-rec 87.7 ± 16.7 88.3 ± 14.6 85.7 ± 13.9 79.4 ± 18.0 $-2.1 (-16.0 \text{ to } 11.9)$ $-8.9 (-17.5 \text{ to } -0.3)$ 0.01 0.59 25.3 ± 2.5 24.5 ± 5.1 22.9 ± 5.7 21.0 ± 6.5 $-2.4 (-6.3 \text{ to } 1.5)$ $-3.5 (-6.5 \text{ to } -0.5)$ 0.46 0.34 22.4 ± 6.7 24.5 ± 4.2 21.6 ± 6.9 22.9 ± 4.3 $-1.1 (-7.2 \text{ to } 4.9)$ $-1.6 (-3.8 \text{ to } 0.6)$ 0.57 0.36 17.9 ± 3.7 17.9 ± 5.0 19.7 ± 2.5 19.0 ± 4.5 $+1.8 (-1.0 \text{ to } 4.6)$ $+1.1 (-1.3 \text{ to } 3.6)$ 0.53 0.73 21.8 ± 5.3 21.0 ± 6.1 21.8 ± 2.7 16.9 ± 5.7 $0.0 (-3.8 \text{ to } 3.8)$ $-4.1 (-7.1 \text{ to } -1.1)$ 0.01 0.05 119.7 ± 20.9 117.8 ± 17.7 112.4 ± 19.9 106.1 ± 22.3 $-7.3 (-25.9 \text{ to } 11.4)$ $-11.6 (-22.0 \text{ to } -1.2)$ 0.14 0.56 79.2 ± 12.1 75.8 ± 12.5 71.4 ± 13.1 64.4 ± 15.2 $-7.8 (-19.3 \text{ to } 3.8)$ $-11.4 (-18.5 \text{ to } -4.3)$ 0.25 0.19 31.9 ± 5.3 26.7 ± 7.0 $-5.2 (-10.9 \text{ to } 0.5)$ $-5.2 (-10.9 \text{ to } 0.5)$ 0.22 0.70	Week 0 [mean \pm SD] Week 18 [mean \pm SD] Mean Change (95% CI) p-int p-rec p-time 87.7 ± 16.7 88.3 ± 14.6 85.7 ± 13.9 79.4 ± 18.0 -2.1 (-16.0 to 11.9) -8.9 (-17.5 to -0.3) 0.01 0.59 <0.001 25.3 ± 2.5 22.9 ± 5.7 $24.6 - 6.3$ to 1.5) 24.5 ± 5.1 21.0 ± 6.5 -3.5 (-6.5 to -0.5) 0.46 0.34 <0.001 22.4 ± 6.7 21.6 ± 6.9 $21.6 \pm$	Week 0 [mean \pm SD] Week 18 [mean \pm SD] Mean Change (95% CI) p-int p-rec p-time p-int 87.7 \pm 16.7 \pm 85.7 \pm 13.9 \pm 79.4 \pm 18.0 \pm 8.3 \pm 14.6 \pm 79.4 \pm 18.0 \pm 8.9 (-17.5 to -0.3) 0.01 \pm 0.59 \pm 0.001 \pm 0.01 0.01 25.3 \pm 2.5 \pm 22.9 \pm 5.7 \pm 21.0 \pm 6.5 \pm 21.0 \pm 6.5 \pm 23.5 (-6.5 to -0.5) 0.46 \pm 0.34 \pm 0.001 \pm 0.35 22.4 \pm 6.7 \pm 21.6 \pm 6.9 \pm -1.1 (-7.2 to 4.9) \pm 22.9 \pm 4.3 \pm 1.6 (-3.8 to 0.6) 0.57 \pm 0.36 \pm 0.005 \pm 0.53 17.9 \pm 3.7 \pm 19.7 \pm 2.5 \pm 1.8 (-1.0 to 4.6) \pm 1.1 (-1.3 to 3.6) 0.53 \pm 0.73 \pm 0.01 \pm 0.56 21.8 \pm 5.3 \pm 21.8 \pm 2.7 \pm 0.0 (-3.8 to 3.8) \pm 1.1 (-7.1 to -1.1) 0.01 \pm 0.05 \pm 0.01 \pm 0.01 119.7 \pm 20.9 \pm 112.4 \pm 19.9 \pm 106.1 \pm 22.3 \pm 11.6 (-22.0 to -1.2) 0.14 \pm 0.56 \pm 0.001 \pm 0.10 79.2 \pm 12.1 \pm 71.4 \pm 13.1 \pm 7.8 (-19.3 to 3.8) \pm 11.4 (-18.5 to -4.3) 0.25 \pm 0.19 \pm 0.001 \pm 0.20 31.9 \pm 5.3 \pm 26.7 \pm 7.0 \pm 26.7 \pm 7.0 \pm 27.0 (-10.9 to 0.5) 0.22 \pm 0.70 \pm 0.001 0.19	Week 0 [mean \pm SD] Week 18 [mean \pm SD] Mean Change (95% CI) p-int p-rec p-time p-int <

FACT-Taxane total									
score									
$\geq 150 \text{ min/week}$	151.6 ± 16.7	140.8 ± 16.6	-10.9 (-26.1 to 4.3)	0.34	0.42	< 0.001	0.31	0.51	< 0.001
< 150 min/week	149.5 ± 18.3	134.3 ± 23.9	-15.2 (-26.3 to -4.1)						
FACT-Taxane TOI									
\geq 150 min/week	111.1 ± 7.7	99.8 ± 11.8	-11.3 (-20.5 to -2.1)	0.73	0.08	< 0.001	0.63	0.87	< 0.001
< 150 min/week	105.8 ± 15.7	92.5 ± 17.8	-13.3 (-22.0 to -4.7)	0.75	0.00	10.001	0.05	0.07	10.001
Taxane subscale									
score									
≥ 150 min/week	63.9 ± 0.3	55.1 ± 8.5	-8.8 (-14.6 to -3.1)	0.17	0.26	< 0.001	0.18	0.48	< 0.001
< 150 min/week	59.9 ± 7.3	55.1 ± 8.8	-4.8 (-8.9 to -0.7)	0.17	0.20	~0.001	0.18	0.48	~0.001
FACT-ES total									
score									
≥ 150 min/week	157.1 ± 17.9	149.8 ± 22.0	-7.3 (-25.8 to 11.1)	0.30	0.62	<0.001	0.20	0.40	<0.001
< 150 min/week	156.2 ± 21.3	144.2 ± 23.1	-12.1 (-23.7 to -0.4)	0.30	0.62	<0.001	0.28	0.48	<0.001
ES subscale score			,						
$\geq 150 \text{ min/week}$	70.0 ± 3.6	64.1 ± 10.1	-5.9 (-12.6 to 0.9)	0.22	0.67	.0.000	0.21	0.46	0.01
< 150 min/week	67.5 ± 9.1	64.9 ± 7.4	-2.6 (-6.9 to 1.6)	0.33	0.67	<0.009	0.31	0.46	0.01
Fatigue subscale									
score									
≥ 150 min/week	45.6 ± 7.4	40.9 ± 12.1	-4.8 (-13.7 to 4.2)	0.46	0.20	.0.001	0.20	0.77	.0.004
< 150 min/week	43.2 ± 10.9	36.6 ± 10.9	-6.5 (-12.1 to -1.0)	0.46	0.30	<0.001	0.39	0.77	< 0.001
PSS score			,						
≥ 150 min/week	20.5 ± 8.3	17.9 ± 8.8	-2.6 (-10.3 to 5.0)			0.44		0.6	0.4.6
< 150 min/week	19.3 ± 8.3	18.7 ± 9.6	-0.5 (-5.1 to 4.0)	0.30	0.93	0.12	0.25	0.65	0.16
CES-D score	13.6 0.6	1017 510	0.0 (0.1 00)						
$\geq 150 \text{ min/week}$	7.2 ± 5.3	6.8 ± 4.7	-0.4 (-4.8 to 4.0)						
< 150 min/week	6.7 ± 3.3	7.8 ± 3.9	+1.0 (-0.8 to 2.9)	0.17	0.85	0.54	0.15	0.84	0.49
STAI score	0.7 ± 3.3	7.0 ± 3.7	11.0 (0.0 to 2.7)						
≥ 150 min/week	19.5 ± 5.8	16.6 ± 6.0	-2.9 (-8.1 to 2.3)						
≥ 150 min/week < 150 min/week	19.3 ± 3.8 20.2 ± 6.9	19.2 ± 6.4	-2.9 (-8.1 to 2.3) -1.0 (-4.4 to 2.4)	0.23	0.39	0.01	0.24	0.47	0.01
< 130 IIIII/ WEEK	$\angle 0.2 \pm 0.9$	19.2 ± 0.4	-1.0 (-4.4 10 2.4)						

Fordyce Emotions Combination score

\geq 150 min/week	70.0 ± 15.5	78.4 ± 12.0	+8.4 (-4.4 to 21.2)	0.14 <0.002	<0.002	0.01	0.11	<0.002	Λ Λ1
< 150 min/week	58.0 ± 25.3	61.4 ± 20.8	+3.4 (-8.8 to 15.6)	0.14	<0.003	0.01	0.11	<0.002	0.01

11 participants reported ≥ 150 minutes/week of aerobic exercise and 31 participants reported < 150 minutes/week. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Statistical significance is indicated by bolded p-values. Adjusted models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), well-being (WB), FACT-Breast (FACT-B), Trial Outcome Index (TOI), breast cancer (BC), endocrine symptoms (ES), Perceived Stress Scale (PSS), Center for Epidemiologic Studies-Depression (CES-D), State-Trait Anxiety Inventory (STAI), body mass index (BMI).

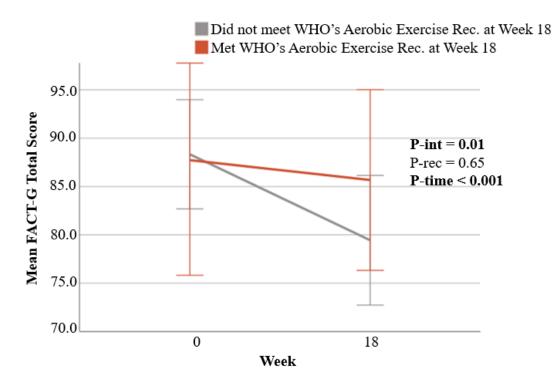


Figure 9. Change in mean FACT-G total scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 11) or did not meet (n = 31)WHO's aerobic exercise recommendation at the end of cycle 6. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded pvalues at 0.05. Abbreviations: p-interaction (p-int; p time*recommendation), p-recommendation (p-rec), Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), recommendation (rec), body mass index (BMI).

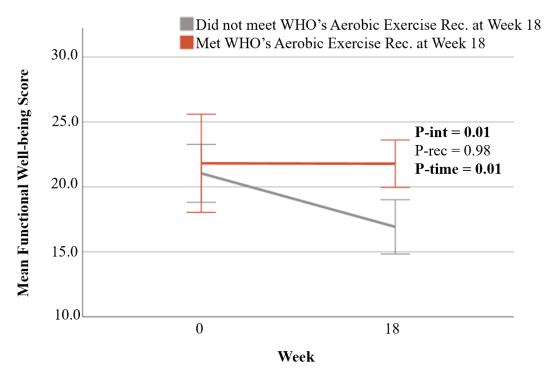


Figure 10. Change in mean functional well-being scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 11) or did not meet (n = 31) WHO's aerobic exercise recommendation at the end of cycle 6. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), recommendation (rec), body mass index (BMI).

5.1.2.3 Resistance Training Exercise Classification at Baseline and QoL

Compared to those that reported < 2 times/week of resistance training exercise at baseline, participants that reported \geq 2 times/week experienced a smaller decline in their FACT-G total score (-2.8; 95% CI, -11.3 to 5.7 versus -8.1; 95% CI, -16.8 to 0.7; p-interaction = 0.04) (Figure 11) and FACT-B total score (-5.8; 95% CI, -18.2 to 6.7 versus -11.3; 95% CI, -21.7 to -0.9; p-interaction = 0.06) (Figure 12) from baseline to the end of cycle 6. Additionally, those that met the resistance training recommendation at baseline reported a lower anxiety score at baseline (19.8 \pm 7.0 versus

 20.9 ± 6.5) and at the end of chemotherapy (17.9 ± 6.6 versus 19.3 ± 6.1) (p-recommendation = 0.02) and a greater happiness score at baseline (68.5 ± 17.3 versus 55.0 ± 24.4) and at the end of chemotherapy (73.1 ± 13.8 versus 61.6 ± 20.8) (p-recommendation = 0.01). These changes are shown in Table 10.

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Table 10. Quality of life scores at baseline (week 0) and end of cycle 6 (week 18) in participants that met (≥ 2 times/week) or did not meet (< 2 times/week) WHO's resistance training exercise recommendation at baseline.

				Unadjusted			Adjusted		
	Week 0 [mean ± SD]	Week 18 [mean ± SD]	Mean Change (95% CI)	p-int	p-rec	p-time	p-int	p-rec	p-time
FACT-G total score									
\geq 2 times/week	88.8 ± 11.6	85.9 ± 10.2	-2.8 (-11.3 to 5.7)	0.06	0.17	<0.001	0.04	0.44	< 0.001
< 2 times/week	86.1 ± 15.4	78.0 ± 18.2	-8.1 (-16.8 to 0.7)	0.00	0.17	~0.001	0.04	0.44	~0.001
Physical WB									
\geq 2 times/week	25.9 ± 2.4	23.6 ± 4.6	-2.2 (-5.1 to 0.7)	0.39	0.02	<0.001	0.24	0.67	<0.001
< 2 times/week	23.9 ± 4.9	20.4 ± 6.4	-3.5 (-6.4 to -0.7)		0.03	<0.001	0.24	0.67	<0.001
Social WB									
\geq 2 times/week	24.6 ± 3.3	23.8 ± 4.2	-0.8 (-3.7 to 2.2)	0.20	0.20	0.01	0.17	0.22	0.01
< 2 times/week	23.9 ± 5.3	21.8 ± 5.5	-2.2 (-4.9 to 0.5)		0.30	0.01	0.17	0.23	0.01
Emotional WB									
$\geq 2 \text{ times/week}$	16.3 ± 6.0	19.0 ± 3.4	+2.7 (-1.1 to 6.5)	0.21	0.73	<0.002	0.20	0.70	<0.003
< 2 times/week	17.5 ± 4.4	18.8 ± 4.2	+1.3 (-0.9 to 3.4)	0.21	0.73	<0.002	0.28	0.79	<0.002
Functional WB									
\geq 2 times/week	22.0 ± 3.4	19.5 ± 4.0	-2.5 (-5.5 to 0.4)	0.79	0.11	<0.001	0.70	0.42	<0.001
< 2 times/week	20.3 ± 6.2	17.4 ± 5.7	-3.0 (-5.9 to 0.0)	0.78	0.11	<0.001	0.70	0.42	<0.001
FACT-B total score			, ,						
\geq 2 times/week	119.9 ± 16.9	114.1 ± 15.2	-5.8 (-18.2 to 6.7)	0.10	0.20	<0.001	0.06	0.67	<0.001
< 2 times/week	115.7 ± 18.1	104.4 ± 22.4	-11.3 (-21.7 to -0.9)	0.10	0.20	<0.001	0.06	0.67	<0.001
FACT-B TOI									
\geq 2 times/week	79.0 ± 10.7	71.3 ± 10.2	-7.7 (-15.9 to 0.4)	0.34	0.00	<0.001	0.20	0.07	رم مرم 1 مرم
< 2 times/week	74.5 ± 12.2	63.9 ± 15.4	-10.6 (-17.6 to -3.6)		0.08	<0.001	0.20	0.87	<0.001
BC subscale score			, ,						
$\geq 2 \text{ times/week}$	31.1 ± 6.1	28.1 ± 6.1	-3.0 (-7.7 to 1.8)	0.74	0.51 -0.001	<0.001	0.64	0.49	<0.001
< 2 times/week	30.3 ± 5.0	26.7 ± 6.2	-3.6 (-6.4 to -0.8)	0.74	0.51	<0.001	0.64	0.48	<0.001
			*						

FACT-Taxane total									
score	1541 + 0.0	1410 + 122	10.2 (21.0 4- 2.5)						
$\geq 2 \text{ times/week}$	154.1 ± 8.0	141.9 ± 13.2	-12.3 (-21.0 to -3.5)	0.55	0.07	< 0.001	0.37	0.58	< 0.001
< 2 times/week FACT-Taxane TOI	146.4 ± 19.2	133.0 ± 23.8	-13.4 (-24.4 to -2.5)						
	110.1 + 4.0	00.1 + 0.7	12.0 (10.0 + - 7.0)						
$\geq 2 \text{ times/week}$	112.1 ± 4.2	99.1 ± 9.7	-13.0 (-19.0 to -7.0)	0.68	0.02	< 0.001	0.97	0.55	< 0.001
< 2 times/week	104.2 ± 15.4	92.5 ± 18.1	-11.7 (-20.2 to -3.3)						
Taxane subscale									
score	(2.1 . 1.0	550 · 54	5 1 (11 5 : 0 0)						
$\geq 2 \text{ times/week}$	63.1 ± 1.8	55.9 ± 7.4	-7.1 (-11.5 to -2.8)	0.32	0.21	< 0.001	0.32	0.78	< 0.001
< 2 times/week	60.1 ± 7.2	55.3 ± 8.8	-4.9 (-8.9 to -0.9)						
FACT-ES total									
score									
$\geq 2 \text{ times/week}$	161.1 ± 10.1	151.1 ± 17.6	-10.0 (-21.5 to 1.5)	0.72	0.09	< 0.001	0.56	0.76	< 0.001
< 2 times/week	152.3 ± 21.7	142.1 ± 23.3	-10.3 (-21.7 to 1.2)	0.72	0.05	0.001	0.00	0.70	0,001
ES subscale score									
\geq 2 times/week	70.1 ± 3.5	65.2 ± 8.8	-4.9 (-10.3 to 0.5)	0.41	0.24	0.01	0.47	0.64	0.01
< 2 times/week	67.0 ± 8.6	64.2 ± 7.6	-2.8 (-6.8 to 1.3)	0.71	0.24	0.01	U. T /	0.04	0.01
Fatigue subscale									
score									
\geq 2 times/week	46.5 ± 7.1	42.9 ± 9.9	-3.6 (-10.3 to 3.0)	0.29	0.03	< 0.001	0.28	0.64	<0.001
< 2 times/week	42.3 ± 10.5	35.7 ± 10.7	-6.5 (-11.8 to -1.3)	0.29	0.03	~0.001	0.28	0.04	\0.001
PSS score									
\geq 2 times/week	20.7 ± 7.6	18.1 ± 7.4	-2.6 (-8.5 to 3.2)	0.20	0.02	0.06	0.25	0.72	0.00
< 2 times/week	19.6 ± 8.0	18.8 ± 9.6	-0.8 (-5.2 to 3.6)	0.30	0.93	0.06	0.25	0.73	0.09
CES-D score									
≥ 2 times/week	6.5 ± 3.5	7.1 ± 3.7	+0.6 (-2.2 to 3.4)	0.06	0.22	0.40	0.01	0.50	0.27
< 2 times/week	7.6 ± 4.0	8.0 ± 4.0	+0.4 (-1.6 to 2.4)	0.86	0.33	0.40	0.91	0.59	0.37
STAI score	,		,,, (= <u>=.</u>)						
≥ 2 times/week	19.8 ± 7.0	17.9 ± 6.6	-1.9 (-7.2 to 3.4)						
< 2 times/week	20.9 ± 6.5	19.3 ± 6.1	-1.7 (-4.8 to 1.5)	0.84	0.47	0.05	0.96	0.02	0.03
2 111100/ 11001	20.7 ± 0.5	17.5 - 0.1	1.7 (1.0 to 1.5)						

Fordyce Emotions Combination score

\geq 2 times/week	68.5 ± 17.3	73.1 ± 13.8	+4.7 (-7.7 to 17.0)	0.80	0.01	0.04	0.90	0.01	0.04
< 2 times/week		61.6 ± 20.8	+6.6 (-5.1 to 18.3)		0.01	0.04	0.90	0.01	0.04

14 participants reported resistance training exercise ≥ 2 times/week and 33 participants reported < 2 times/week at baseline. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Statistical significance is indicated by bolded p-values. Adjusted models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), well-being (WB), FACT-Breast (FACT-B), Trial Outcome Index (TOI), breast cancer (BC), endocrine symptoms (ES), Perceived Stress Scale (PSS), Center for Epidemiologic Studies-Depression (CES-D), State-Trait Anxiety Inventory (STAI), body mass index (BMI).

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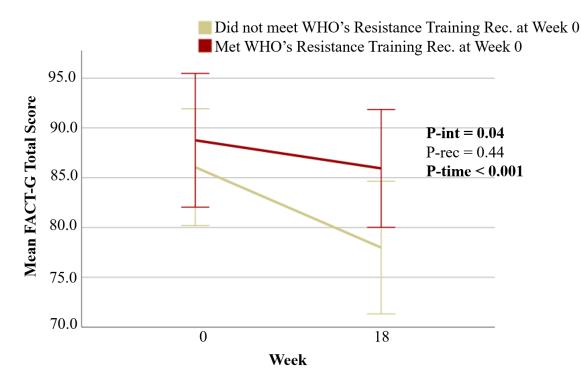


Figure 11. Change in mean FACT-G total scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 14) or did not meet (n = 33) WHO's resistance training exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), recommendation (rec), body mass index (BMI).

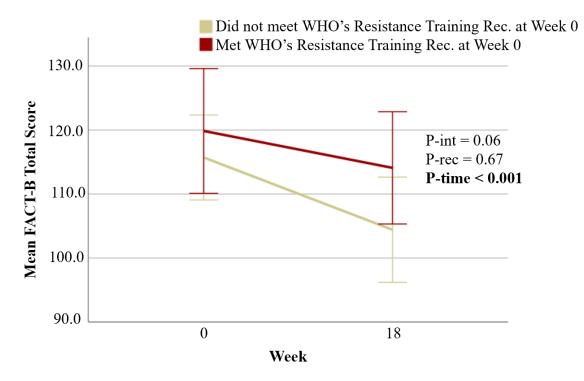


Figure 12. Change in mean FACT-B total scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 14) or did not meet (n = 33) WHO's resistance training exercise recommendation at baseline. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-Breast (FACT-B), recommendation (rec), body mass index (BMI).

5.1.2.4 Resistance Training Exercise Classification at the End of Cycle 6 and QoL

Compared to those that reported < 2 times/week of resistance training exercise after the sixth cycle of chemotherapy, participants that reported \geq 2 times/week experienced a smaller decline in their functional well-being (-0.5; 95% CI, -5.3 to 4.3 versus -3.6; 95% CI, -6.5 to -0.7; p-interaction = 0.07) (Figure 13) and FACT-B TOI (-6.2; 95% CI, -18.8 to 6.5 versus -11.3; 95% CI, -18.3 to -4.4; p-interaction = 0.06) (Figure 14). These changes are shown in Table 11.

Table 11. Quality of life scores at baseline (week 0) and end of cycle 6 (week 18) in participants that met (≥ 2 times/week) or did not meet (< 2 times/week) WHO's resistance training exercise recommendation at the end of cycle 6.

			_	U	nadjust	ed		Adjuste	d
	Week 0 [mean ± SD]	Week 18 [mean ± SD]	Mean Change (95% CI)	p-int	p-rec	p-time	p-int	p-rec	p-time
FACT-G total score									
\geq 2 times/week	88.0 ± 16.1	84.6 ± 12.7	-3.4 (-19.5 to 12.7)	0.44	0.58	<0.003	0.44	0.93	<0.002
< 2 times/week	88.2 ± 14.9	80.3 ± 18.0	-8.0 (-16.2 to 0.3)	0.44	0.38	~0.003	0.44	0.93	~0.002
Physical WB									
\geq 2 times/week	25.5 ± 3.0	22.5 ± 5.6	-3.0 (-7.8 to 1.8)	0.01	0.43	<0.003	0.81	0.61	<0.002
< 2 times/week	24.5 ± 4.8	21.2 ± 6.5	-3.2 (-6.1 to -0.4)	0.91	0.43	<0.003	0.81	0.61	<0.002
Social WB									
\geq 2 times/week	24.3 ± 3.3	22.1 ± 5.1	-2.2 (-6.8 to 2.4)	0.41	0.97	<0.001	0.44	0.41	<0.001
< 2 times/week	23.8 ± 5.3	22.5 ± 5.2	-1.3 (-3.9 to 1.3)		0.97	~0.001	0.44	0.41	~0.001
Emotional WB									
\geq 2 times/week	17.6 ± 6.8	19.5 ± 4.0	+1.9 (-4.1 to 7.9)	0.67	0.98	0.06	0.69	0.70	0.06
< 2 times/week	17.9 ± 4.1	19.1 ± 4.1	+1.2 (-0.8 to 3.2)	0.07	0.98	0.00	0.09	0.70	0.00
Functional WB									
\geq 2 times/week	21.0 ± 4.8	20.5 ± 4.1	-0.5 (-5.3 to 4.3)	0.08	0.41	0.02	0.07	0.68	0.02
< 2 times/week	21.3 ± 6.1	17.7 ± 5.7	-3.6 (-6.5 to -0.7)	0.08	0.41	0.02	0.07	0.08	0.02
FACT-B total score									
\geq 2 times/week	117.5 ± 20.6	112.4 ± 18.9	-5.1 (-27.1 to 16.9)	0.30	0.63	< 0.001	0.25	0.60	<0.001
< 2 times/week	118.4 ± 18.1	106.8 ± 22.4	-11.6 (-21.7 to -1.6)	0.30	0.03	~0.001	0.23	0.00	~0.001
FACT-B TOI									
\geq 2 times/week	76.9 ± 11.5	70.8 ± 12.0	-6.2 (-18.8 to 6.5)	0.11	0.49	< 0.001	0.06	0.51	<0.001
< 2 times/week	76.5 ± 12.7	65.2 ± 15.5	-11.3 (-18.3 to -4.4)	0.11	0.49	~U.UU1	0.00	0.31	~0.001
BC subscale score									
\geq 2 times/week	30.4 ± 5.5	27.8 ± 7.4	-2.7 (-9.7 to 4.4)	0.39	0.88 <0.001	<0.001	0.27	0.08	<0.001
< 2 times/week	30.7 ± 5.1	26.8 ± 6.2	-3.9 (-6.7 to -1.2)	0.59	0.00	~0.001	0.27	0.00	~0.001

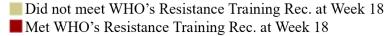
FACT-Taxane total score									
≥ 2 times/week	155.9 ± 10.5	139.0 ± 15.7	-16.9 (-33.1 to -0.6)						
< 2 times/week	149.0 ± 18.7	135.3 ± 23.6	-13.7 (-24.1 to -3.2)	0.61	0.34	< 0.001	0.79	0.78	< 0.001
FACT-Taxane TOI	119.0 = 10.7	155.5 = 25.0	13.7 (21.1 to 3.2)						
$\geq 2 \text{ times/week}$	107.3 ± 14.5	97.4 ± 11.1	-9.9 (-24.2 to 4.3)						
< 2 times/week	107.1 ± 14.4	93.7 ± 17.7	-13.4 (-21.3 to -5.4)	0.54	0.66	< 0.001	0.39	0.40	< 0.001
Taxane subscale	107.11 — 11.1	75.7 – 17.7	13.1 (21.5 to 5.1)						
score									
≥ 2 times/week	59.0 ± 10.8	54.4 ± 8.2	-4.6 (-15.2 to 6.0)	0.70	0.62	-0.004	0.75	0.06	-0.003
< 2 times/week	61.4 ± 5.3	55.3 ± 8.8	-6.1 (-9.6 to -2.6)	0.78	0.62	<0.004	0.75	0.06	< 0.003
FACT-ES total			,						
score									
$\geq 2 \text{ times/week}$	164.7 ± 11.5	150.5 ± 22.9	-14.2 (-36.5 to 8.2)	0.48	0.18	<0.001	0.58	0.76	<0.001
< 2 times/week	155.0 ± 21.3	144.5 ± 22.9	-10.4 (-21.3 to 0.4)	0.46	0.10	~0.001	0.38	0.70	~0.001
ES subscale score									
\geq 2 times/week	71.1 ± 2.3	65.9 ± 11.7	-5.2 (-15.0 to 4.5)	0.59	0.25	0.04	0.72	0.84	0.06
< 2 times/week	67.5 ± 8.7	64.4 ± 7.2	-3.1 (-7.0 to 0.7)	0.39	0.23	0.04	0.72	0.64	0.00
Fatigue subscale									
score									
\geq 2 times/week	43.1 ± 9.8	39.4 ± 11.9	-3.8 (-15.4 to 7.9)	0.30	0.88	< 0.001	0.26	0.22	< 0.001
< 2 times/week	44.0 ± 10.3	37.4 ± 11.2	-6.6 (-11.8 to -1.4)	0.50	0.00	10.001	0.20	0.22	10.001
PSS score									
\geq 2 times/week	20.3 ± 9.3	18.3 ± 8.2	-2.0 (-11.4 to 7.4)	0.61	0.94	0.20	0.54	0.56	0.24
< 2 times/week	19.4 ± 8.1	18.6 ± 9.6	-0.8 (-5.1 to 3.5)	0.01	0.71	0.20	0.51	0.50	0.21
CES-D score									
\geq 2 times/week	6.6 ± 3.2	7.5 ± 4.8	+0.9 (-3.5 to 5.3)	0.85	0.91	0.32	0.88	0.76	0.30
< 2 times/week	6.9 ± 4.0	7.5 ± 4.0	+0.6 (-1.4 to 2.6)	0.02	0.71	0.52	0.00	0.70	0.50
STAI score									
\geq 2 times/week	20.8 ± 6.0	19.0 ± 8.1	-1.8 (-9.5 to 5.8)	0.80	0.75	0.03	0.81	0.62	0.03
< 2 times/week	19.9 ± 6.8	18.4 ± 6.0	-1.4 (-4.5 to 1.7)	0.00	0.75	0.00	0.01	0.02	0.00

Fordyce Emotions Combination score

\geq 2 times/week	64.7 ± 20.1	74.3 ± 15.8	+9.6 (-9.8 to 28.9) +3.1 (-8.4 to 14.6)	0.20	0.20	0.07	0.20	0.40	0.07
< 2 times/week	60.4 ± 24.5	63.5 ± 20.9	+3.1 (-8.4 to 14.6)	0.39	0.20	0.07	0.39	0.49	0.07

8 participants reported resistance training exercise ≥ 2 times/week and 34 participants reported < 2 times/week at the end of cycle 6. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Statistical significance is indicated by bolded p-values. Adjusted models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), well-being (WB), FACT-Breast (FACT-B), Trial Outcome Index (TOI), breast cancer (BC), endocrine symptoms (ES), Perceived Stress Scale (PSS), Center for Epidemiologic Studies-Depression (CES-D), State-Trait Anxiety Inventory (STAI), body mass index (BMI).

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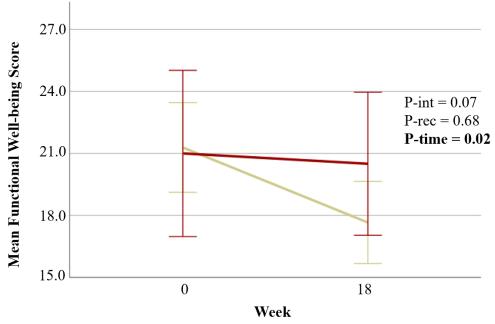
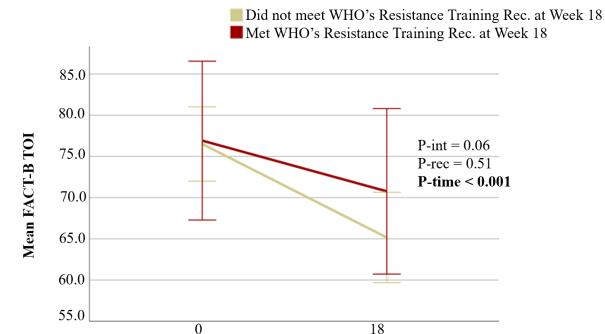


Figure 13. Change in mean functional well-being scores from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 8) or did not meet (n = 34) WHO's resistance training exercise recommendation at the end of cycle 6. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), World Health Organization (WHO), recommendation (rec), body mass index (BMI).



Week

Figure 14. Change in mean FACT-B TOIs from baseline (week 0) to end of cycle 6 (week 18) in participants that met (n = 8) or did not meet (n = 34) WHO's resistance training exercise recommendation at the end of cycle 6. Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between exercise categories. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Statistical significance is indicated by bolded p-values at $p \le 0.05$. Abbreviations: p-interaction (p-int; time*recommendation), p-recommendation (p-rec), trial outcome index (TOI), World Health Organization (WHO), recommendation (rec), body mass index (BMI).

5.2 Exercise

5.2.1 Comparing Exercise Behaviour Within and Between Treatment Groups

A change over time was observed for mean weekly aerobic exercise (p-time < 0.001) and resistance training frequency (p-time = 0.01). However, treatment group did not significantly affect the change in mean weekly aerobic exercise (p-interaction = 0.56) or resistance training frequency (p-interaction = 0.28) over time. Therefore, groups were combined to assess changes over time.

Overall, mean aerobic exercise was statistically significantly lower at week 12 (-53.5 minutes/week; 95% CI, -100.5 to -6.3; p = 0.03) and week 18 (-70.8; 95% CI, -123.0 to -18.6; p = 0.008) compared to baseline (Figure 15). Similarly, mean resistance training frequency was lower at week 12 (-0.57 times/week; 95% CI, -1.0 to -0.13; p = 0.01) compared to baseline in the whole sample (Figure 16).

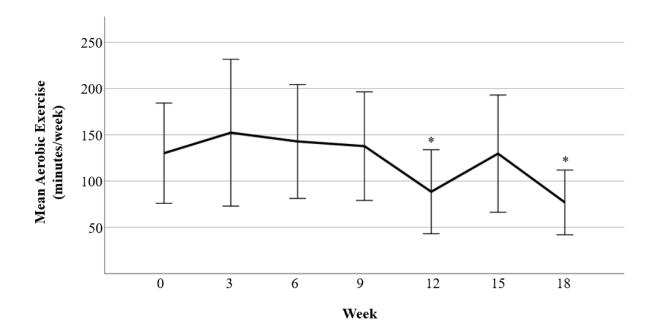


Figure 15. Daily aerobic exercise over time in the DHA and placebo groups combined (n = 42). Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between treatment groups. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Each week was compared to baseline using unadjusted multiple comparisons. *Indicates statistically significantly different from baseline at $p \le 0.03$. Not all statistically significant differences are shown on the graph. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: Docosahexaenoic acid (DHA), body mass index (BMI).

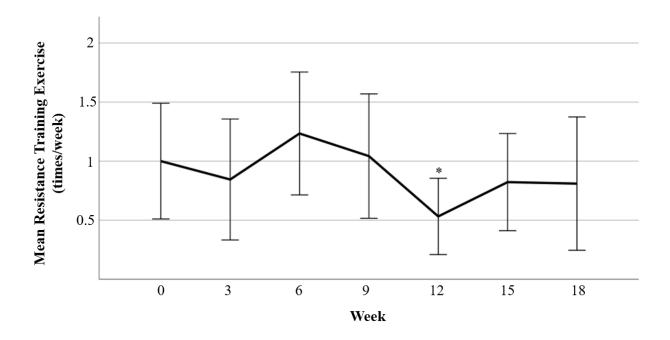


Figure 16. Daily resistance training exercise frequency over time in the DHA and placebo groups combined (n = 42). Error bars represent 95% confidence intervals. Generalized estimating equations were used to test statistical significance of differences within and between treatment groups. Models were adjusted for age, BMI, histology, menopausal status, tumour stage and grade. Each week was compared to baseline using unadjusted multiple comparisons. *Indicates statistically significantly different from baseline at p = 0.01. Not all statistically significant differences are shown on the graph. Week 0 indicates baseline. Week 18 indicates the end of cycle 6. Abbreviations: Docosahexaenoic acid (DHA), body mass index (BMI).

5.2.2 Associations Between Exercise Levels and pCR

Meeting WHO's aerobic exercise recommendation at any timepoint throughout the trial was not associated with achieving a pCR (Table 12). Similarly, meeting WHO's recommendation for resistance training at any timepoint was not associated with pCR (Table 13).

Table 12. Categorization of participants based on meeting WHO's aerobic exercise recommendation (≥ 150 minutes/week) and achieving a pathological complete response.

	Achieved a pCR				
	Yes	No	p-value		
≥ 150 min/week					
Week 0 (n = 46)					
Yes	7 (43.8%)	9 (56.3%)	0.52		
No	9 (30.0%)	21 (70.0%)	0.52		
Total	16 (34.8%)	30 (65.2%)			
Week 3 $(n = 45)$					
Yes	5 (38.5%)	8 (61.5%)	1.00		
No	11 (34.4%)	21 (65.6%)	1.00		
Total	16 (35.6%)	29 (64.4%)			
Week 6 $(n = 47)$					
Yes	6 (40.0%)	9 (60.0%)	0.75		
No	11 (34.4%)	21 (65.6%)	0.73		
Total	17 (36.2%)	30 (63.9%)			
Week 9 $(n = 47)$					
Yes	4 (26.7%)	11 (73.3%)	0.52		
No	13 (40.6%)	19 (59.4%)	0.32		
Total	17 (36.2%)	30 (63.8%)			
Week 12 $(n = 47)$					
Yes	4 (36.4%)	7 (63.6%)	1.00		
No	13 (36.1%)	23 (63.9%)	1.00		
Total	17 (36.2%)	30 (63.8%)			
Week 15 $(n = 45)$					
Yes	2 (18.2%)	9 (81.8%)	0.17		
No	15 (44.1%)	19 (55.9%)	0.17		
Total	17 (37.8%)	28 (62.2%)			
Week 18 $(n = 42)$					
Yes	3 (27.3%)	8 (72.7%)	0.48		
No	14 (45.2%)	17 (54.8%)	0.40		
Total	17 (40.5%)	25 (59.5%)			

Percentage of given exercise category or the total are shown in parentheses. Fisher's exact test was used to test the association between meeting WHO's aerobic exercise recommendation and achieving a pCR. No statistically significant associations were observed. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: World Health Organization (WHO), pathological complete response (pCR).

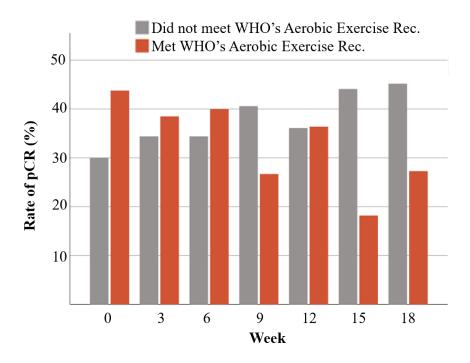


Figure 17. Rate of pCR in each aerobic exercise category over time. Fisher's exact test was used to test the association between meeting (n = 11) or not meeting (n = 30) WHO's aerobic exercise recommendation and achieving a pCR. No statistically significant differences between aerobic exercise categories were observed. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: World Health Organization (WHO), pathological complete response (pCR), recommendation (rec).

Table 13. Categorization of participants based on meeting WHO's resistance training exercise recommendation (≥ 2 times/week) and achieving a pathological complete response.

	Achieved a pCR				
	Yes	No	p-value		
≥ 2 times/week					
Week 0 (n = 46)					
Yes	4 (28.6%)	10 (71.4%)	0.53		
No	13 (39.4%)	20 (60.6%)	0.55		
Total	17 (36.2%)	30 (63.8%)			
Week 3 $(n = 45)$					
Yes	2 (22.2%)	7 (77.8%)	0.46		
No	14 (38.9%)	22 (61.1%)	0.46		
Total	16 (35.6%)	29 (64.4%)			
Week 6 $(n = 47)$					
Yes	4 (28.6%)	10 (71.4%)	0.52		
No	13 (39.4%)	20 (60.6%)	0.53		
Total	17 (36.2%)	30 (63.8%)			
Week 9 $(n = 47)$					
Yes	4 (30.8%)	9 (69.2%)	0.74		
No	13 (38.2%)	21 (61.8%)	0.74		
Total	17 (36.2%)	30 (63.8%)			
Week 12 $(n = 47)$, ,	,			
Yes	4 (44.4%)	5 (55.6%)	0.70		
No	13 (34.2%)	25 (65.8%)	0.70		
Total	17 (36.2%)	30 (63.8%)			
Week 15 $(n = 45)$					
Yes	3 (25.0%)	9 (75.0%)	0.22		
No	14 (42.4%)	19 (57.6%)	0.33		
Total	17 (37.8%)	28 (62.2%)			
Week 18 $(n = 42)$	` '	` '			
Yes	2 (25.0%)	6 (75.0%)	0.44		
No	15 (44.1%)	19 (55.9%)	0.44		
Total	17 (40.5%)	25 (59.5%)			

Percentage of given exercise category or the total are shown in parentheses. Fisher's exact test was used to test the association between meeting WHO's aerobic exercise recommendation and achieving a pCR. No statistically significant associations were observed. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: World Health Organization (WHO), pathological complete response (pCR).

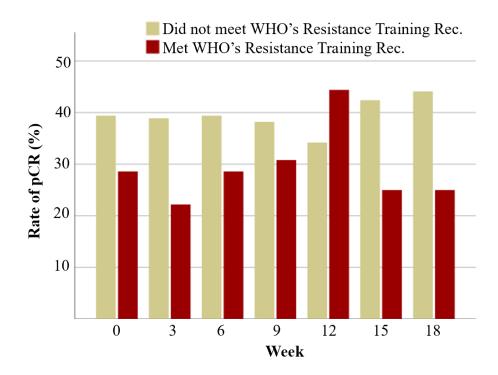


Figure 18. Rate of pCR in each resistance training exercise category over time. Fisher's exact test was used to test the association between meeting (n = 8) or not meeting (n = 33) WHO's resistance training exercise recommendation and achieving a pCR. No statistically significant differences between resistance training exercise categories were observed. Week 0 indicates baseline. Week 18 indicates end of cycle 6. Abbreviations: World Health Organization (WHO), pathological complete response (pCR), recommendation (rec).

CHAPTER 6: CONCLUSIONS, LIMITATIONS AND FUTURE DIRECTIONS

6.1 Summary of Results by Thesis Objective

Objective 1: Determine how QoL changed from baseline to the end of neoadjuvant chemotherapy among breast cancer patients in the DHA WIN cohort and determine the role of DHA and exercise in mitigating potential changes.

It was hypothesized that perceived QoL would decrease from baseline to the end of chemotherapy and that this decrease would be less severe in the DHA group. All subscales of the FACT questionnaires (except emotional well-being) and the FACIT-Fatigue scale decreased from baseline to the end of cycle 6. However, emotional well-being, anxiety and happiness measures all improved over time. DHA did not statistically significantly mitigate the change over time in any QoL indicator.

It was also hypothesized that participants that met WHO's aerobic or resistance training exercise recommendation at baseline or the end of cycle 6 would experience a less severe decrease in QoL over time. Meeting WHO's aerobic exercise recommendation at baseline was associated with several maintained QoL indicators over time, including participants' FACT-G total scores, stress, anxiety and emotional well-being. Meeting this recommendation at the end of cycle 6 was also associated with maintained QoL indicators over time, including participants' FACT-G total scores and functional well-being.

Meeting WHO's resistance training recommendation at baseline was associated with maintained FACT-G and FACT-B total scores over time. Meeting

this recommendation at the end of cycle 6 was associated with maintained functional well-being and FACT-B trial outcome indices over time.

Objective 2: Describe participants' aerobic and resistance training exercise levels throughout the trial and compare them between treatment groups, and determine whether meeting exercise recommendations predicted achieving a pCR.

Most women did not meet WHO's aerobic or resistance training exercise guidelines in either treatment group. Less than 35% of total participants met the aerobic exercise recommendation and less than 30% of total participants met the resistance training recommendation at any given timepoint throughout the trial.

The DHA treatment did not significantly affect the change in mean weekly aerobic exercise or resistance training frequency over time. Overall, mean aerobic exercise was statistically significantly lower at week 12 and week 18 compared to baseline. Similarly, mean resistance training frequency was lower at week 12 compared to baseline in the whole sample.

There were no statistically significant differences in the percentage of the DHA or placebo groups that met either the aerobic or resistance training exercise recommendation at baseline. It was hypothesized that a greater percentage of the DHA group would meet WHO's aerobic and resistance training guidelines compared to the placebo group at the end of chemotherapy. Contrary to this hypothesis, a greater percentage of the placebo group met WHO's resistance training guideline at the end of cycle 6, compared to the DHA group. The

percentages of the DHA and placebo groups that met WHO's aerobic exercise recommendation at the end of cycle 6 were not significantly different.

It was hypothesized that meeting WHO's aerobic or resistance training exercise recommendations at baseline or the end of cycle 6 would increase the likelihood of achieving a pCR. However, meeting either recommendation at any timepoint was not associated with achieving a pCR.

Objective 3: Describe the estimated daily dietary intake of DHA WIN participants at study entry with the CCHS and Canadian DRIs and compare daily intake between the DHA and placebo groups.

Estimated average daily dietary intake of macronutrients, cholesterol, sodium, sugar and dietary fiber were not statistically significantly different between the DHA and placebo groups at baseline. Compared to Albertan women that completed the 2015 CCHS, the estimated daily intake of the DHA WIN cohort was greater for protein, total fat, total monounsaturated fatty acids, sodium and dietary fiber. Compared to the CCHS cohort, a greater percentage of the DHA WIN cohort was above the AMDR for fat and carbohydrate.

6.2 Discussion of the Major Findings

This study examined several secondary outcomes from the DHA WIN clinical trial, which was designed to assess the effect of DHA supplementation (4.4 g/day) on treatment efficacy in women with breast cancer undergoing neoadjuvant chemotherapy. The outcomes analyzed in this thesis research included estimated daily dietary intake at study entry, exercise levels at baseline,

the start of cycles 2 to 6 and the end of cycle 6, QoL at baseline and the end of chemotherapy, and pCR after surgery.

Compared to Albertan women that completed the 2015 CCHS, estimated mean dietary intake of total protein, fat, monounsaturated fat, sodium and dietary fiber were higher in the DHA WIN cohort. Consistent with these findings, Tapan *et al.* (2020) found that estimated daily intake of total fat and monounsaturated fat was significantly greater in breast cancer patients compared to a group of apparently healthy controls [120]. However, the authors did not find significant differences between the groups for estimated daily intake of total protein, sodium or dietary fiber. These inconsistent findings, as well as ASCO's conclusion that there is insufficient evidence to recommend specific dietary interventions during cancer treatment [68] highlights the need for further investigation regarding nutrient intake and breast cancer risk as well as optimal dietary intake during chemotherapy.

A greater percentage of the DHA WIN cohort had diets that were above the AMDRs for carbohydrate and fat compared to the CCHS cohort. This finding is important to highlight because intake within the AMDRs have been associated with reduced risk of chronic disease [85, 121]. In addition, the World Cancer Research Fund International has developed recommendations for cancer prevention, including eating at least 30 g of fiber and 400 g of fruit and vegetables per day [122], while limiting intake of 'fast foods' and other processed foods high in fat, starches or sugars [123]. On average, the estimated daily intake of the DHA WIN cohort was 20.6 g/day of dietary fiber, about 10 g/day below the recommended intake for cancer prevention. However, the World Cancer Research Fund International and American Institute for Cancer Research have also concluded that there is limited evidence on the associations between *breast cancer* risk and various nutrients, including fat, carbohydrates, protein, dietary fiber, cholesterol and sugar [124]. This

further emphasizes the importance of future studies investigating the relationship between dietary intake and risk of breast cancer.

All subscales of the FACT questionnaires (except emotional well-being) as well as the FACIT-Fatigue scale decreased from baseline to the end of cycle 6 in both the DHA and placebo groups, indicating a poorer perceived QoL and greater level of perceived fatigue at the end of chemotherapy. These findings are consistent with previous studies that have reported a reduction in QoL and increased fatigue among breast cancer patients receiving neoadjuvant chemotherapy [47-49]. Anxiety decreased, while emotional well-being and happiness measures improved from baseline to the end of cycle 6. These are in line with findings from Lee *et al.* (2022), who found that anxiety in breast cancer patients was highest prior to beginning neoadjuvant chemotherapy, which gradually improved during treatment [51]. Lee *et al.* (2022) also found that depression was higher during neoadjuvant chemotherapy, compared to before and after treatment, highlighting the possibility that certain QoL indicators decreased during treatment in the present study, but rebounded at the end of chemotherapy.

There have been mixed findings regarding the effects of DHA on QoL among breast cancer patients [7, 54]. In the current study, DHA did not appear to mitigate changes in QoL. This is consistent with the previous study done by de la Rosa Oliva *et al.* (2019), who found that supplementation of EPA and DHA during six months of chemotherapy did not result in significant differences in fatigue, nausea, drowsiness, appetite and dyspnea [54].

It is important to consider clinical significance when interpreting the results of the current study. The minimal clinically important difference (MCID) is defined as "the smallest change that is important to patients" [125, 126] and is important when considering clinical relevance [126]. One can consider whether changes over time within a given group are clinically relevant.

Furthermore, one can assess whether the difference between groups' mean changes (i.e. the mean difference) is clinically significant. MCIDs have previously been determined for several of the QoL subscales that were included in this study, including the FACT-G (4-7 points), physical well-being (2-3 points), social well-being (0.7-2 points), emotional well-being (1-2 points), functional well-being (2-3 points), fatigue subscale (3-4), FACT-B (7-8 points), BC subscale (2-3 points) and the FACT-B TOI (5-6 points) [127-131]. The changes in these subscales over time were clinically significant in both the DHA and placebo groups (Table 7), and mean differences between groups were not clinically relevant for any of the aforementioned subscales. This supports the finding that DHA did not mitigate changes in these QoL indicators.

Meeting WHO's aerobic exercise recommendation at baseline appeared to have statistically significant positive effects on participants' FACT-G total scores, taxane subscale scores, anxiety, emotional well-being, stress and happiness. Mean differences between groups were considered clinically relevant for emotional well-being and functional well-being, and favoured the group that met the recommendation at baseline. Similarly, meeting WHO's aerobic exercise recommendation at the end of cycle 6 appeared to have a statistically significant positive effect on participants' FACT-G total scores, functional well-being and happiness. Clinically meaningful mean differences were observed for the FACT-G subscale and functional well-being, which favoured the group that met the recommendation at the end of cycle 6. The positive effects of aerobic exercise observed in the current study are consistent with previous studies that have demonstrated the ability of physical activity to alleviate fatigue and improve HRQoL in patients with cancer [3, 4]. In contrast, the BC subscale decreased more in the group that met the recommendation, and the mean difference between groups for this subscale was clinically meaningful, but did not reach statistical significance.

Similar to aerobic exercise, resistance training exercise appeared to positively affect several QoL indicators. With regards to statistical significance, meeting WHO's resistance training recommendation at baseline appeared to have a positive effect on participants' FACT-G total scores, FACT-B total scores, anxiety and happiness. Mean differences between groups were clinically relevant for the FACT-G subscale, social well-being, emotional well-being and FACT-B total scores, which all favoured the group that met the recommendation. Meeting WHO's resistance training recommendation at the end of cycle 6 appeared to have positive effects on participants' functional well-being and FACT-B TOIs. In addition to these statistically significant effects, there were clinically meaningful differences between groups for the FACT-G subscale, functional well-being, FACT-B subscale, FACT-B TOI and social well-being. Outcomes for all of these subscales favoured the group that met the recommendation, except the social well-being subscale, which decreased less among those that did not meet the recommendation at the end of cycle 6, but this group effect was not statistically significant. Together, these findings suggest that aerobic and resistance training exercise before and during treatment may mitigate the negative effect of neoadjuvant chemotherapy on various QoL indicators in patients with breast cancer which offers further support for the recommendations provided by WHO, ASCO and ACSM for cancer survivors [66, 67, 132].

On average, aerobic exercise and resistance training frequency declined over time in the DHA WIN cohort. Mean aerobic exercise was significantly lower at week 12 and 18 compared to baseline, while mean resistance training frequency was significantly lower at week 12 compared to baseline. This was expected as side effects of chemotherapy have been shown to impede physical activity in breast cancer patients [133]. It is important to note that recall or response bias

inherent to self-report methods for physical activity may have contributed to the fluctuation in exercise levels over time [134].

Meeting WHO's exercise recommendations was not associated with achieving a pCR. This is consistent with Baker *et al.* (2022) who found no relationship between pre-treatment levels of physical activity and pCR [73]. In contrast, Sanft *et al.* (2023) found that breast cancer patients randomized to a home-based exercise and nutrition intervention were more likely to achieve a pCR than the control group [74]. The intervention in the study by Sanft *et al.* (2023) consisted of exercise and nutrition counselling that promoted adherence to physical activity guidelines (i.e. ≥ 150 minutes/week of aerobic exercise and twice-weekly resistance training) and a predominantly plant-based diet, but did not specifically consider DHA intake. These mixed findings highlight the need for additional RCTs investigating the association between exercise and pCR in breast cancer patients.

6.3 Strengths and Limitations of the Thesis Research

The DHA WIN clinical trial was the first phase II RCT designed to assess the effects of DHA supplementation concomitant with neoadjuvant chemotherapy on patients with non-metastatic breast cancer [19]. The DHA intervention was minimally invasive, and self-administered dietary, exercise and QoL questionnaires were cost-effective and resulted in a small respondent burden [93]. QoL questionnaires combined measures for several indicators, which provided a comprehensive assessment of patients' QoL.

The thesis research was also subject to several limitations that are important to consider. First, the DHA WIN RCT was powered to assess changes in the Ki67 index, which was the primary outcome of the trial. Lack of statistical significance observed for QoL and exercise outcomes may

be due, in part, to lack of statistical power to examine these secondary outcomes. The quality and quantity of dietary intake has been shown to change in women with breast cancer undergoing chemotherapy [135]. However, since FFQs were only completed at study entry, estimated baseline dietary intake could not be compared to intake during or after treatment. Limitations inherent to FFQs are also important to consider. For example, recall of food intake over the past year may be imprecise, and actual intake may influence reporting of past intake [93]. In addition, a diagnosis of breast cancer may contribute to bias of dietary history collected after diagnosis [136]. It is also possible that the pre-specified food list did not accurately reflect items and portions that the individual typically consumed [87]. Similarly, recall and response bias must be considered for the exercise questionnaires [134].

6.4 Future Directions and Recommendations

In addition to supportive care benefits, exercise has the potential to be utilized as a cancer treatment [96]. However, exercise must demonstrate benefit in a specific clinical setting (i.e. specific cancer type and treatment protocol) before it can be integrated into clinical practice guidelines as a cancer treatment [96]. Therefore, it is important to conduct RCTs that examine the effects of different types and doses of exercise on long-term and patient-reported outcomes in this population.

Further, meeting the Physical Activity Guidelines for Americans both before and after treatment has been associated with reduced recurrence and mortality in patients with breast cancer [137]. This highlights the importance of assessing relapse-free survival and overall survival in future studies to better understand the long-term implications of physical activity in patients with breast cancer.

Previous studies have demonstrated that dietary interventions, such as nutritional counselling and dietary supplementation (i.e. with EPA and/or DHA) during treatment may reduce drug-induced side effects [10]. However, ASCO has concluded that there is insufficient evidence to develop recommendations for dietary interventions to improve outcomes related to QoL or treatment toxicity [68]. This highlights the need for large clinical trials to help establish definitive dietary recommendations [10].

6.5 Final Conclusions

In conclusion, most QoL indicators declined from baseline to the end of chemotherapy in both the DHA and placebo groups. However, emotional well-being, anxiety and happiness all improved over time. DHA did not significantly mitigate the change in any QoL indicators. Meeting WHO's guidelines for aerobic or resistance training exercise at baseline or the end of cycle 6 was associated with several maintained QoL indicators, including stress, anxiety, emotional well-being, functional well-being, FACT-G total scores, FACT-B total scores and FACT-B TOIs. These findings suggest that aerobic and resistance training exercise before and during treatment may mitigate the negative effect of neoadjuvant chemotherapy on various QoL indicators in patients with breast cancer. Meeting WHO's aerobic or resistance training exercise recommendation at baseline or at the end of cycle 6 was not associated with achieving a pCR, but future research investigating this potential relationship is warranted.

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APPENDIX 1

Identi	fication #_	 _
Date:		 _

Docosahexaenoic acid (<u>DHA</u>) for <u>Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN)</u>

Post-intervention Questionnaire

Investigators: C. Field, RD, PhD, J. Mackey, MD, S. Basi, MD, X. Zhu, MD, A. Joy, MD, K. King, MD, J. Price-Hiller, MD, J. Meza-Junco, MD, S. Ghosh, PhD

Funded by the Canadian Institutes of Health Research and Cross Cancer Institute Investigator Initiated Trials

Instructions

Thank you for your continued participation in this study. At this post-intervention assessment, we are going to ask you many of the same questions as in the previous questionnaires. However, it is important to answer these questions based on what you are thinking and feeling right now, and not on how you answered the questions the last time. This will give us important information about how your thoughts and feelings have changed. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for each. Also, if at all possible, it is important to answer all questions. However, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete. If you have any questions about completing the questionnaire, please contact Marnie Newell (PhD Candidate for DHA WIN) at 492-4240 or marnie.newell@ualberta.ca.

Below is a list of statements that other people with cancer have said are important to their quality of life. Please indicate the extent to which you have experienced each of the statements <u>during the past 7 days</u> by circling the appropriate number using the following scale.

During the PAST WEEK:

	not at all	a little bit	some- what	quite a bit	very much
1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. I feel close to my friends	0	1	2	3	4
9. I get emotional support from my family	0	1	2	3	4
10. I get support from my friends	0	1	2	3	4
11. My family has accepted my illness	0	1	2	3	4
12. I am satisfied with family communication about my illness	0	1	2	3	4
13. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
14. I am satisfied with my sex life	0	1	2	3	4
15. I feel sad	0	1	2	3	4
16. I am satisfied with how I am coping with my illness	0	1	2	3	4

During the **PAST WEEK**:

Daing div <u>11101 WDDR</u> .	not at all	a little bit	some- what	quite a bit	very much
17. I am losing hope in the fight against my illness	0	1	2	3	4
18. I feel nervous	0	1	2	3	4
19. I worry about dying	0	1	2	3	4
20. I worry that my condition will get worse	0	1	2	3	4
21. I am able to work (include work at home)	0	1	2	3	4
22. My work (include work at home) is fulfilling	0	1	2	3	4
23. I am able to enjoy life	0	1	2	3	4
24. I have accepted my illness	0	1	2	3	4
25. I am sleeping well	0	1	2	3	4
26. I am enjoying the things I usually do for fun	0	1	2	3	4
27. I am content with the quality of my life right now	0	1	2	3	4
28. I have been short of breath	0	1	2	3	4
29. I am self-conscious about the way I dress	0	1	2	3	4
30. My arms are swollen or tender	0	1	2	3	4
31. I feel sexually attractive	0	1	2	3	4
32. I have been bothered by hair loss	0	1	2	3	4
33. I worry about the risk of cancer in my family	0	1	2	3	4
34. I worry about the effect of stress on my illness	0	1	2	3	4
35. I am bothered by a change in weight	0	1	2	3	4
36. I am able to feel like a woman	0	1	2	3	4
37. I have certain parts of my body where I experience significant pain.	0	1	2	3	4

During the <u>PAST WEEK</u>:

FATIGUE SYMPTOMS

	not at all	a little bit	some- what	quite a bit	very much
1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ("washed out")	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble <u>finishing</u> things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I am able to do my usual activities	0	1	2	3	4
9. I need to sleep during the day	0	1	2	3	4
10. I am too tired to eat	0	1	2	3	4
11. I need help doing my usual activities	0	1	2	3	4
12. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
13. I have to limit my social activity because I am tired	0	1	2	3	4

During the <u>PAST WEEK</u>:

TAXANE SYMPTOMS

	not at all	a little bit	some- what	quite a bit	very much
1. I have numbness or tingling in my hands	0	1	2	3	4
2. I have numbness or tingling in my feet	0	1	2	3	4
3. I feel discomfort in my hands	0	1	2	3	4
4. I feel discomfort in my feet	0	1	2	3	4
5. I have joint pain or muscle cramps	0	1	2	3	4
6. I feel weak all over	0	1	2	3	4
7. I have trouble hearing	0	1	2	3	4
8. I get a ringing or buzzing in my ears	0	1	2	3	4
9. I have trouble buttoning buttons	0	1	2	3	4
10. I have trouble feeling the shape of small objects when they are in my hand	0	1	2	3	4
11. I have trouble walking	0	1	2	3	4
12. I feel bloated	0	1	2	3	4
13. My hands are swollen	0	1	2	3	4
14. My legs or feet are swollen	0	1	2	3	4
15. I have pain in my fingertips	0	1	2	3	4
16. I am bothered by the way my hands or nails look	0	1	2	3	4

During the <u>PAST WEEK</u>:

ENDOCRINE SYMPTOMS

	not at all	a little bit	some- what	quite a bit	very much
1. I have hot flashes	0	1	2	3	4
2. I have cold sweats	0	1	2	3	4
3. I have night sweats	0	1	2	3	4
4. I have vaginal discharge	0	1	2	3	4
5. I have vaginal itching/irritation	0	1	2	3	4
6. I have vaginal bleeding or spotting		0	1 4	2	3
7. I have vaginal dryness	0	1	2	3	4
8. I have pain or discomfort with intercourse	0	1	2	3	4
9. I have lost interest in sex	0	1	2	3	4
10. I have gained weight	0	1	2	3	4
11. I feel lightheaded (dizzy)	0	1	2	3	4
12. I have been vomiting	0	1	2	3	4
13. I have diarrhea	0	1	2	3	4
14. I get headaches	0	1	2	3	4
15. I feel bloated	0	1	2	3	4
16. I have breast sensitivity/tenderness	0	1	2	3	4
17. I have mood swings	0	1	2	3	4
18. I am irritable	0	1	2	3	4
19. I have pain in my joints	0	1	2	3	4

The questions in this scale ask you about your feelings and thoughts during the last month. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

	0 never		2 some- times	3 fairly often	4 very often
In the last month, how often have you					
been upset because of something that happened unexpectedly	0	1	2	3	4
2. felt that you were unable to control the important things in your life	0	1	2	3	4
3. felt nervous and stressed	0	1	2	3	4
4. dealt successfully with irritating life hassles	0	1	2	3	4
5. felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
felt confident about your ability to handle your personal problems	0	1	2	3	4
7. felt that things were going your way	0	1	2	3	4
8. found that you could not cope with all the things	4	0	1	2	3
that you had to do	W *				
9. been able to control irritations in your life	0	1	2	3	4
10. felt that you were on top of things	0	1	2	3	4
11. been angered because of things that happened that were outside of your control	0	1	2	3	4
12. found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. been able to control the way you spend your time	0	1	2	3	4
14. felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

The following question asks you to rate, on average, how <u>happy or unhappy</u> you felt <u>over the past week</u>. Please read all the statements first and then check the one statement (between 0 and 10) that best describes your average level of happiness over the past week. Check only <u>ONE</u> item.

On average, over the PAST WEEK I have felt:
10. Extremely happy (feeling ecstatic, joyous, fantastic!).
9. Very happy (feeling really good, elated!).
8. Pretty happy (spirits high, feeling good).
7. Mildly happy (feeling fairly good, somewhat cheerful).
6. Slightly happy (just a bit above neutral).
5. Neutral (not particularly happy or unhappy).
4. Slightly unhappy (just a bit below neutral).
3. Mildly unhappy (just a little low).
2. Pretty unhappy (somewhat "blue," spirits down).
1. Very unhappy (depressed, spirits very low).
0. Extremely unhappy (utterly depressed, completely down).
This next question asks you to estimate the <u>percentage of time</u> , on average, that you felt happy unhappy, and neutral (neither happy nor unhappy) <u>over the past week</u> . Write down your best estimates in the spaces below. Make sure the three figures add up to 100 percent.
Over the <u>PAST WEEK</u> :
The percentage of time I felt <u>happy</u> was:%
The percentage of time I felt unhappy was:%
The percentage of time I felt neutral was:%
Total: 100 %

Below is a list of statements concerning how you might have felt or behaved in the <u>past week</u>. Please use the following scale to indicate <u>how often</u> you felt or behaved in these ways in the past week.

Rarely or noneof the	time Some of the time	ne	Much of th	e time	Most or all of the
time (< 1 day)	(1-2 days)		(3-4 d	ays)	(5-7 days)
During the PAST WE	EEK:				
1. I felt depressed.		0	1	2	3
2. I felt that everythin	g I did was an effort.	0	1	2	3
3. My sleep was restle	ess.	0	1	2	3
4. I was happy.		0	1	2	3
5. I felt lonely.		0	1	2	3
6.People were unfrier	ndly.	0	1	2	3
7. I enjoyed life.		0	1	2	3
8. I felt sad.		0	1	2	3
9. I felt that people di	sliked me.	0	1	2	3
10. I could not get "ge	oing".	0	1	2	3

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number that best indicates how you have felt during the <u>past week</u>. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer that best describes how you felt.

During the PAST WEEK:

	not at all	somewhat	moderately so	very much so
1. I felt calm	1	2	3	4
2. I was tense	1	2	3	4
3. I felt at ease	1	2	3	4
4. I worried over possible misfortunes	1	2	3	4
5. I felt frightened	1	2	3	4
6. I felt self-confident	1	2	3	4
7. I was jittery	1	2	3	4
8. I was relaxed	1	2	3	4
9. I was worried	1	2	3	4
10. I felt steady	1	2	3	4

APPENDIX 2

Docosahexaenoic acid (DHA) for Women with Breast Cancer in the Neoadjuvant Setting (DHA WIN) Exercise Questionnaire

For this question, we would like you to recall your average weekly exercise <u>during the past 3</u> <u>weeks</u>. We will ask you separate questions about <u>aerobic or endurance exercise</u> (i.e., exercise that improves the heart and lungs such as walking or swimming) and <u>strength or resistance</u> <u>exercise</u> (i.e., exercise that improves muscular strength such as weight lifting).

When answering these questions please remember:

- > only count exercise sessions that lasted 10 minutes or longer in duration.
- > only count exercise that was done during free time (i.e., not occupation or housework).
- > note that the main difference between the categories 'a,' 'b', and 'c' is the intensity of the aerobic (endurance) exercise and category 'd' is for strength (resistance) exercise.
- > please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) over the <u>PAST 3 WEEKS</u> how many days on average did you do the following kinds of aerobic and strength exercise and what was the average duration each time?

	Average Frequency (days per week)	Average Duration (minutes per session)
a. VIGOROUS INTENSITY AEROBIC EXERCISE (HEART BEATS RAPIDLY, SWEATING) (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).		
b. MODERATE INTENSITY AEROBIC EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) (e.g., fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).		
c. LIGHT INTENSITY AEROBIC EXERCISE (MINIMAL EFFORT, NO PERSPIRATION) (e.g., easy walking, yoga, bowling, lawn bowling, shuffleboard).	***************************************	
d. STRENGTH/RESISTANCE EXERCISE (MODERATE TO INTENSE EFFORT) (e.g., weight lifting, resistance bands, sit-ups, push-ups)		

APPENDIX 3

Diet History Questionnaire II

Adapted for Canada from the National Institutes of Health **Diet History Questionnaire II**



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GENERAL INSTRUCTION	

- Use only a black ball-point pen. Do not use a pencil or felt-tip pen. Do not fold, staple, or tear the pages.
- Shade the box next to your answer, like this:
- If you make any changes, cross out the incorrect answer and shade in the box next to the correct answer. Also draw a circle around the correct answer.
- If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.
- Questions on portion size use measures like cups, ounces, teaspoons and tablespoons. Metric conversions are provided below.

<u>Volume</u> 1 cup = 8 ounces = 250ml 1 ounce = 30g

Weight

1 fluid ounce = 30ml 1 teaspoon = 5ml

1 tablespoon = 15ml

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:	in what you bor	montn were n?	In what year were you born?	Are you male or female?
	Jan	Jul	1 9	Male
	Feb	Aug		Female
month day year	Mar	Sep		
	Apr	Oct	BAR CODE I	ABEL OR SUBJECT ID
	May	Nov	BAR CODE L	HERE
	Jun	Dec		

DHQ II PastYear

		ı					
1.	Over the <u>past 12 months</u> , how often did you drink tomato juice ?		3b.	How often was the orar you drank calcium-for	nge juice or grapefruit juic tified?		
	 NEVER (GO TO QUESTION 2) ☐ 1 time per month or less ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 3-4 times per week ☐ 6 or more times per day ☐ 5-6 times per week 	4.	. Ove	☐ Almost never or never ☐ About 1/2 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or alway			
	1a. Each time you drank tomato juice , how much did you usually drink?		mix	er 100% fruit juice or 10 tures (such as apple, gra ers)?			
	☐ Less than ½ cup (4 ounces) ☐ ½ to 1¼ cups (4 to 10 ounces) ☐ More than 1¼ cups (10 ounces)		1	EVER (GO TO QUESTION time per month or less	☐ 1 time per day		
2.	Over the <u>past 12 months</u> , how often did you drink other vegetable juice? (Please do not include tomato juice.)		□ 1- □ 3-	3 times per month 2 times per week 4 times per week 6 times per week	☐ 2-3 times per day ☐ 4-5 times per day ☐ 6 or more times per day		
	 NEVER (GO TO QUESTION 3) ☐ 1 time per month or less ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 3-4 times per week ☐ 6 or more times per day ☐ 5-6 times per week 	4a	4a. Each time you drank other 100% fruit or 100% fruit juice mixtures, how must you usually drink? ☐ Less than ¾ cup (6 ounces) ☐ ¾ to 1½ cups (6 to 12 ounces) ☐ More than 1½ cups (12 ounces)				
	how much did you usually drink? Less than ¾ cup (6 ounces) ¾ to 1¼ cups (6 to 10 ounces) More than 1¼ cups (10 ounces)	Fr		v often did you drink othe té, Fruitopia, Five Alive, or regular)?	Sunny D, or Kool-Aid,		
3.	drink 100% orange juice or grapefruit juice? NEVER (GO TO QUESTION 4) 1 time per month or less 2-3 times per month 1-2 times per week 3-4 times per week 5-6 times per week day		□ 1 □ 2- □ 1- □ 3-	EVER (GO TO QUESTION time per month or less 3 times per month 2 times per week 4 times per week 6 times per week	☐ 1 time per day ☐ 2-3 times per day ☐ 4-5 times per day ☐ 6 or more times per day		
	 3a. Each time you drank 100% orange juice or grapefruit juice, how much did you usually drink? ☐ Less than ¾ cup (6 ounces) ☐ ¾ to 1¼ cups (6 to 10 ounces) ☐ More than 1¼ cups (10 ounces) 						
▼ Oı	uestion 4 appears in the next column	0	uestion 6	appears on the next page	1465		

			1			
Over the	past 12 months		7	a.	Each time you drank c chocolate , how much	
5a.	Each time you drank of much did you usually of much did you usually of □ Less than 1 cup (8 our □ 1 to 2 cups (8 to 16 our □ More than 2 cups (16 or □ More than 2 cups (16 o	nces) nces)			Less than 1 cup (8 our 1 to 2 cups (8 to 16 ou More than 2 cups (16 o	nces) nces) punces)
5b.	How often were your of low calorie? Almost never or never hout 1/4 of the time About 1/2 of the time About 3/4 of the time Almost always or always			b. 	How often was the chochocolate you drank reconstruction and reconstruc	educed-fat or fat-free?
as a (Ple cho repl N 1 2 1 3 5 6a 6b 7 Hov cho	as a beverage, how modrink? Less than 1 cup (8 out 1 to 1½ cups (8 to 12 out 1 to 1½ cups (11 to 12 out 1)) What kind of milk or moderate you usually drink? Whole milk 2% fat milk 1% fat milk Skim, nonfat, or 0.5% Soy milk Rice milk Almond milk Other often did you drink choolecolate? EVER (GO TO QUESTION	ee, NOT in cereal)? colate milk, hot hakes or meal N 7) 1 time per day 2-3 times per day 4-5 times per day 6 or more times per day nilk or milk substitutes nuch did you usually nces) counces) counces) hilk substitutes did fat milk colate milk or hot	9.	11:12-13-15-14:15-15-15-15-15-15-15-15-15-15-15-15-15-1	did you usually drink? Less than 1 cup (8 our 1 to 2 cups (8 to 16 ou More than 2 cups (16 our often did you drink me	1 time per day 2-3 times per day 4-5 times per day 6 or more times per day nilkshakes, how much nces) nces) nuces) al replacement or such as Boost, Breakfast or others)? N 10) 1 time per day 2-3 times per day 4-5 times per day 6 or more times per day 7 day 8 ear replacement or 9 es, how much did you nces) nces)
2- 1- 3-	time per month or less 3 times per month 2 times per week 4 times per week 6 times per week	☐ 1 time per day ☐ 2-3 times per day ☐ 4-5 times per day ☐ 6 or more times per day				
Question 8	appears in the next column		Questi	on 10	appears on the next page	1465

Over the <u>past 12 months</u>	11b. How often did you drink sports drinks DURING THE REST OF THE YEAR?
10. How often did you drink soft drinks or pop?	□ NEVER
☐ NEVER (GO TO QUESTION 11)	_
☐ 1 time per month or less ☐ 1 time per day ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 4-5 times per day ☐ 3-4 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ per day	☐ 1 time per month or less ☐ 1 time per day ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 4-5 times per day ☐ 3-4 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times
10a. Each time you drank soft drinks or pop , how much did you usually drink? ☐ Less than 12 ounces or less than 1 regular size can or bottle (355 ml)	11c. Each time you drank sports drinks , how much did you usually drink? ☐ Less than 1½ cups (12 ounces) ☐ 1½ to 3 cups (12 to 24 ounces) ☐ More than 3 cups (24 ounces)
☐ 12 to 16 ounces or 1 regular size can or bottle (355 ml) ☐ More than 16 ounces or more than 1 regular size can or bottle (355 ml)	12. How often did you drink energy drinks (such as Red Bull, Rock Star, Full Throttle, or Monster)?
10b. How often were your soft drinks or pop diet or calorie-free ?	□ NEVER (GO TO QUESTION 13) □ 1 time per month or less □ 1 time per day
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 2-3 times per month ☐ 1-2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 5-6 times per week ☐ 2-3 times per day ☐ 4-5 times per day ☐ 6 or more times ☐ per day
10c. How often were your soft drinks or pop	12a. Each time you drank energy drinks , how much did you usually drink?
☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time	☐ Less than 1 cup (8 ounces) ☐ 1 to 2 cups (8 to 16 ounces) ☐ More than 2 cups (16 ounces) 13. How often did you driply boar?
☐ Almost always or always	13. How often did you drink beer ? NEVER (GO TO QUESTION 14)
11. Over the past 12 months, did you drink sports drinks (such as PowerAde or Gatorade)? □ NO (GO TO QUESTION 12) □ YES	☐ 1 time per month or less ☐ 1 time per day ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 4-5 times per day ☐ 3-4 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ per day
11a. How often did you drink sports drinks IN THE SUMMER?	13a. Each time you drank beer , how much did you usually drink?
□ NEVER	☐ Less than 1 regular size can or bottle (341 ml) ☐ 1 to 3 regular size cans or bottles ☐ More than 3 regular size cans or bottles
☐ 1 time per month or less ☐ 2-3 times per month ☐ 1-2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2-3 times per day ☐ 4-5 times per day ☐ 6 or more times ☐ per day	

Question 12 appears in the next column

Question 14 appears on the next page

Over th	e past	12 n	nonths
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over the past 12 months	15. How often did you drink wine ?				
4. How often did you drink water (including tap, bottled, carbonated, flavoured, or vitamin added water)?	NEVER (GO TO QUESTION 16)				
□ NEVER (GO TO QUESTION 15) □ 1 time per month or less □ 1 time per day □ 2-3 times per day	☐ 1 time per month or less ☐ 1 time per day ☐ 2-3 times per month ☐ 2-3 times per day ☐ 1-2 times per week ☐ 4-5 times per day ☐ 6 or more times ☐ 5-6 times per week ☐ per day ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 5-6 times per week ☐ 6 or more times ☐ 5-6 times per week ☐ 5-6				
☐ 1-2 times per week ☐ 4-5 times per day ☐ 6 or more times ☐ 5-6 times per week ☐ per day	15a. Each time you drank wine , how much did you usually drink?				
14a. Each time you drank water, how much did you usually drink?☐ Less than 1 cup (8 ounces)	☐ Less than 1 glass (5 ounces) ☐ 1 to 2 glasses (5 to 12 ounces) ☐ More than 2 glasses (12 ounces)				
☐ 1 to 4 cups (8 to 32 ounces) ☐ More than 4 cups (32 ounces)	15b. How often was the wine you drank red wine ?				
14b. How often was the water you drank tap water ? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always 16. How often did you drink liquor or mixed drinks?				
14c. How often was the water you drank bottled , sweetened water (with low or no-calorie sweetener, including carbonated water)? ☐ Almost never or never ☐ About ¼ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always	□ NEVER (GO TO QUESTION 17) □ 1 time per month or less □ 1 time per day □ 2-3 times per month □ 2-3 times per day □ 1-2 times per week □ 4-5 times per day □ 3-4 times per week □ 6 or more times □ 5-6 times per week per day 16a. Each time you drank liquor or mixed drinks, how much did you usually drink?				
14d. How often was the bottled sweetened water you drank with added vitamins or minerals (such as Aquafina Plus, Vitaminwater, or others)? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	Less than 1 shot of liquor 1 to 3 shots of liquor More than 3 shots of liquor				

Question 15 appears in the next column

Question 17 appears on the next page



Over the past 12 months...

Over the past 12 months			17e. Was milk added to yo		
17. Did you eat oatmeal, Cream of Wheat, Red River,			Wheat, Red River, or ☐ NO (GO TO QUESTI		
or o	other cooked cereal?			•	ON 16)
\Box	IO (GO TO QUESTION 18)			↓ □YES	
<u>-</u> \				17f. What kind of milk was	s usually added?
17a.	7a. How often did you eat oatme Wheat, Red River, or other THE WINTER?			☐ Whole milk☐ 2% fat milk☐ 1% fat milk☐ Skim, nonfat, or 0.5%	fat milk
	□ NEVED			☐ Soy milk ☐ Rice milk	
	□ NEVER			☐ Almond milk	
	☐ 1-6 times per winter☐ 7-11 times per winter	☐ 2 times per week☐ 3-4 times per week		☐ Other	
	1 time per month 2-3 times per month 1 time per week	5-6 times per week 1 time per day 2 or more times per day		cereal, how much was	River, or other cooked
17b.	How often did you eat oat Wheat, Red River, or oth DURING THE REST OF T	er cooked cereal		☐ Less than ½ cup☐ ½ to 1 cup☐ More than 1 cup☐	
	☐ NEVER		18.	. How often did you eat co l	d cereal?
	☐ 1-6 times per year	☐ 2 times per week	$ $ \vdash	— □ NEVER (GO TO QUEST)	TON 19)
	☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 3-4 times per week☐ 5-6 times per week☐ 1 time per day☐ 2 or more times☐ per day☐ 3-4 times☐ 3-4		☐ 1-6 times per year☐ 7-11 times per year☐ 1 time per month☐ 2-3 times per month☐ 1 time per week☐	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day
17c.		h time you ate oatmeal, Cream of Wheat, I River, or other cooked cereal, how much you usually eat?		18a. Each time you ate col you usually eat?	, ,
	☐ Less than ¾ cup ☐ ¾ to 1¼ cups ☐ More than 1¼ cups			☐ Less than 1 cup☐ 1 to 2½ cups☐ More than 2½ cups	
17d.	d. How often was butter or margarine added to your oatmeal, Cream of Wheat, Red River, or other cooked cereal? Almost never or never About ½ of the time About ½ of the time About ¾ of the time Almost always or always			18b. How often was the co	d cereal you ate Vector or
			☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or alw		
				18c. How often was the co Bran, Fibre 1, Fibre 1 All-Bran Buds?	
				☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or alw	
\			\		
Question 2	18 appears in the next column		Que	estion 19 appears on the next page	1465

Over the past 12 months	19a. Each time you ate applesauce , how much did you usually eat?				
18d. How often was the cold cereal you ate some other bran or fibre cereal (such as Cheerios (regular), Shredded Wheat, Raisin Bran, Bran Flakes, Mini-Wheats, Shreddies, Honey	Less than ¼ cup ¼ to ¾ cup More than ¾ cup				
Bunches of Oats, Oatmeal Crisp or others)?	20. How often did you eat apples ?				
☐ Almost never or never	☐ NEVER (GO TO QUESTION 21)				
☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always 18e. How often was the cold cereal you ate any other type of cold cereal (such as Corn Flakes, Rice	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day				
Krispies, Frosted Flakes, Special K, Froot Loops, Cap'n Crunch, Honey Nut Cheerios, Honeycomb, or others)?	20a. Each time you ate apples , how many did you usually eat?				
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time	☐ Less than 1 apple ☐ 1 apple ☐ More than 1 apple ▼				
☐ About ¾ of the time ☐ Almost always or always	21. How often did you eat pears (fresh, canned, or frozen)?				
18f. Was milk added to your cold cereal?	☐ NEVER (GO TO QUESTION 22)				
□ NO (GO TO QUESTION 19) □ YES 18g. What kind of milk was usually added?	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day				
□ Whole milk □ 2% fat milk □ 1% fat milk □ Skim, nonfat, or 0.5% fat milk □ Soy milk □ Rice milk □ Almond milk □ Other	21a. Each time you ate pears , how many did you usually eat? Less than 1 pear 1 pear More than 1 pear 22. How often did you eat bananas ?				
18h. Each time milk was added to your cold cereal, how much was usually added?	NEVER (GO TO QUESTION 23)				
☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup	☐ 1-6 times per year ☐ 2 times per week☐ 7-11 times per year☐ 3-4 times per week☐ 1 time per month☐ 5-6 times per week☐ 2-3 times per month☐ 1 time per day☐ 1 time per week☐ 2 or more times☐ 2 or more times☐ 2 times per week☐ 3-4 times per week☐ 3-4 times per week☐ 5-6 times per week☐ 2 times per week☐ 3-4 times per week☐ 3-4 times per week☐ 2 times per week☐ 3-4 times per week☐ 3-6				
19. How often did you eat applesauce?	per day				
NEVER (GO TO QUESTION 20)					
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day					
Question 20 appears in the next column	Question 23 appears on the next page 1465				

Over the <u>past 12 months</u>			24c. Each time you ate peaches , nectarines , or plums , how much did you usually eat?			
22a. Each time you ate bananas , how many did you usually eat?			Less than 1 fruit or less than ½ cup 1 to 2 fruits or ½ to ¾ cup More than 2 fruits or more than ¾ cup			
☐ Less than 1 banana ☐ 1 banana				More than 2 huits of the	ore t	пап 74 сир
☐ More than 1 banana		2	.5. Ho	w often did you eat gra p	oes?	?
23. How often did you eat dried	I fruit (such as prunes		\Box	NEVER (GO TO QUESTIC)N 2	6)
or raisins)? (Please do not include dried apricots.) ☐ □ NEVER (GO TO QUESTION 24)			□ 7	1-6 times per year7-11 times per year1 time per month		☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week
☐ 1-6 times per year☐ 7-11 times per year☐ 1 time per month☐	☐ 2 times per week☐ 3-4 times per week☐ 5-6 times per week			2-3 times per month 1 time per week		☐ 1 time per day ☐ 2 or more times per day
☐ 2-3 times per month☐ 1 time per week	☐ 1 time per day ☐ 2 or more times per day		25a. Each time you ate grapes , how much did you usually eat?			
23a. Each time you ate driec you usually eat?	d fruit, how much did			☐ ½ to 1 cup or 10 to 30 graphs.	½ cup or less than 10 grapes o or 10 to 30 grapes of 1 cup or more than 30 grapes	
☐ Less than 2 tablespoons☐ 2 to 5 tablespoons☐ More than 5 tablespoon		2		er the <u>past 12 months,</u> ontaloupe?	did y	/ou eat
◆ 24. Over the past 12 months, d nectarines, or plums?	id you eat peaches ,		— <u> </u>	NO (GO TO QUESTION 2 'ES	7)	
NO (GO TO QUESTION 25)			26a. How often did you eat fresh cantaloupe WHEN IN SEASON?			
	resh neaches nectarines			☐ NEVER		
or plums WHEN IN SE.				☐ 1-6 times per season☐ 7-11 times per season☐ 1 time per month☐ 2-3 times per month		☐ 2 times per week☐ 3-4 times per week☐ 5-6 times per week☐ 1 time per day
☐ 1-6 times per season☐ 7-11 times per season☐ 1 time per month	☐ 2 times per week☐ 3-4 times per week☐ 5-6 times per week			☐ 1 time per week		2 or more times per day
☐ 2-3 times per month☐ 1 time per week	☐ 1 time per day ☐ 2 or more times per day			How often did you eat of frozen) DURING THE I		
24b. How often did you eat p	eaches. nectarines. or			☐ NEVER		
	or frozen) DURING THE			☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month		☐ 2 times per week☐ 3-4 times per week☐ 5-6 times per week☐
□ NEVER				2-3 times per month 1 time per week		☐ 1 time per day ☐ 2 or more times
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day			□ i tille bei week		per day
•			,			
Question 25 appears in the next column		Q	uestion 2	27 appears on the next page		1465

Over the <u>past 12 months</u>		2	28. Over the past 12 months, did you eat strawberries ?					
26c. Each time you ate cantaloupe , how much did you usually eat? ☐ Less than ¼ melon or less than ½ cup ☐ ¼ melon or ½ to 1 cup ☐ More than ¼ melon or more than 1 cup			NO (GO TO QUESTION 29) YES 28a. How often did you eat fresh strawberries					
_			WHEN IN SEASON?					
2	7. Over the <u>past 12 months</u> , did you eat melon , other than cantaloupe (such as watermelon or honeydew)?		☐ NEVER ☐ 1-6 times per season ☐ 2 times per week					
	 NO (GO TO QUESTION 28) YES ↓ 27a. How often did you eat fresh melon, other than 		☐ 7-11 times per season ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 or more times ☐ 2 or more times ☐ 2 or more times					
	cantaloupe, WHEN IN SEASON?		28b. How often did you eat strawberries (fresh or					
	□ NEVER		frozen) DURING THE REST OF THE YEAR?					
	☐ 1-6 times per season ☐ 7-11 times per season ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		□ NEVER □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times					
	27b. How often did you eat melon other than cantaloupe (fresh or frozen) DURING THE REST OF THE YEAR?		per day 28c. Each time you ate strawberries , how much did you usually eat?					
	□ NEVER □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week		Less than ¼ cup or less than 4 berries ¼ to ¾ cup or 4 to 10 berries More than ¾ cup or more than 10 berries					
	☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day	2	29. Over the <u>past 12 months</u> , did you eat blueberries , raspberries, saskatoon berries or blackberries?					
	27c. Each time you ate melon other than cantaloupe , how much did you usually eat?		NO (GO TO QUESTION 30)					
	☐ Less than 1 cup or 2 small wedges☐ 1 to 3 cups or 2 medium wedges☐ More than 3 cups or 2 large wedges		▼ 29a. How often did you eat fresh blueberries, raspberries, saskatoon berries or blackberries WHEN IN SEASON?					
			□ NEVER					
			☐ 1-6 times per season ☐ 7-11 times per season ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 or more times per day ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day					

Question 28 appears in the next column

Question 30 appears on the next page



Over the past 12 months 29b. How often did you eat blueberries, raspberries, saskatoon berries or blackberries (fresh or frozen) DURING THE REST OF THE YEAR?		30c. Each time you ate oranges , tangelos , mandarins , or clementines , how many did you usually eat? ☐ Less than 1 fruit ☐ 1 fruit ☐ More than 1 fruit
☐ NEVER ☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	2 times per week 3-4 times per week 5-6 times per week 1 time per day 2 or more times per day	31. Over the past 12 months, did you eat grapefruit? NO (GO TO QUESTION 32) YES 31a. How often did you eat fresh grapefruit WHEN
29c. Each time you ate blueber saskatoon berries or black did you usually eat? Less than ¼ cup 1¼ to ¾ cup More than ¾ cup 30. Over the past 12 months, did y tangelos, mandarins, or clery	ekberries, how much	IN SEASON? NEVER 1-6 times per season 7-11 times per season 1 time per month 2-3 times per month 1 time per week 1 time per week 2-3 times per month 1 time per day
NO (GO TO QUESTION 31) ☐ YES ↓ 30a. How often did you eat fresl mandarins, or clementine SEASON? ☐ NEVER	n oranges, tangelos,	31b. How often did you eat grapefruit (fresh or canned) DURING THE REST OF THE YEAR? NEVER 1-6 times per year 7-11 times per year 1 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 2 or more times
☐ 1-6 times per season☐ 7-11 times per season☐ 1 time per month☐ 2-3 times per month☐ 1 time per week☐ 1 time 1 time per week☐ 1 time 1	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day	per day 31c. Each time you ate grapefruit , how much did you usually eat? Less than ½ grapefruit ½ to 1 grapefruit More than 1 grapefruit
30b. How often did you eat oran mandarins, or clementine DURING THE REST OF TI	s (fresh or canned)	32. How often did you eat pineapple ? NEVER (GO TO QUESTION 33) 1-6 times per year 2 times per week
☐ 1-6 times per year☐ 7-11 times per year☐ 1 time per month☐ 2-3 times per month☐ 1 time per week☐ 1 time p	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day	□ 7-11 times per year □ 1 time per month □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day 32a. Each time you ate pineapple , how much did you usually eat? □ Less than ¼ cup or less than 1 medium slice □ ¼ to ¾ cup or 1 to 2 medium slices
Question 31 appears in the next column		More than 3/4 cup or more than 2 medium slices Ouestion 33 appears on the next page 1465

Over the <u>past 12 months</u>	36. How often did you eat coleslaw ?
33. How often did you eat other kinds of fruit?	NEVER (GO TO QUESTION 37)
□ NEVER (GO TO QUESTION 34) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day 33a. Each time you ate other kinds of fruit , how much did you usually eat?	☐ 1-6 times per year ☐ 2 times per week☐ 7-11 times per year ☐ 3-4 times per week☐ 1 time per month☐ 5-6 times per week☐ 2-3 times per month☐ 1 time per day☐ 1 time per week☐ 2 or more times per day☐ 36a. Each time you ate coleslaw , how much did you usually eat?☐ Less than ¼ cup☐ ½ to ¾ cup☐ 1½ to ¼
Less than ½ cup ⅓ to ¾ cup ⅓ times per week ⅓ to 1 time per day ⅓ to 1 cup ⅓ to 3 cups ⅓ More than 3 cups	¼ to ¾ cup

Question 36 appears in the next column

Question 39 appears on the next page

		1		
Over the past 12 months		4	11b. How often did you eat of frozen) DURING THE	
39. How often did you eat strin beans (fresh, canned, or fro			□ NEVER	KEST OF THE TEAK!
□ NEVER (GO TO QUESTION □ 1-6 times per year □ 7-11 times per year □ 1 time per month □ 2-3 times per month □ 1 time per week 39a. Each time you ate string	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day	4	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week 11c. Each time you ate corrusually eat? ☐ Less than 1 ear or less	
beans, how much did you Less than ½ cup ½ to 1 cup More than 1 cup ▼	ou usually eat?		☐ 1 ear or ½ to 1 cup ☐ More than 1 ear or mo	
40. How often did you eat peas frozen)?				F. F.
■ NEVER (GO TO QUESTION	l 41)	42.	How often did you eat broo	ccoli (fresh or frozen)?
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day		■ NEVER (GO TO QUESTI ■ 1-6 times per year ■ 7-11 times per year ■ 1 time per month ■ 2-3 times per month	ON 43) 2 times per week 3-4 times per week 5-6 times per week 1 time per day
40a. Each time you ate peas usually eat?	, now much did you		☐ 1 time per week	☐ 2 or more times per day
Less than ¼ cup ¼ to ½ cup More than ½ cup		4	2a. Each time you ate bro ousually eat?	ccoli, how much did you
41. Over the past 12 months, d	-		☐ Less than ¼ cup☐ ¼ to 1 cup☐ More than 1 cup	
↓		43.	How often did you eat caul	liflower (fresh or frozen)?
41a. How often did you eat fr SEASON ?	esh corn WHEN IN		- ☐ NEVER (GO TO QUESTI	ON 44)
☐ NEVER ☐ 1-6 times per season ☐ 7-11 times per season ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day
	poi day		you usually eat? Less than ¼ cup ¼ to 1 cup More than 1 cup	imower, now much ald

Question 42 appears in the next column

Question 44 appears on the next page

Over the p	oast 12	mont	<u>hs</u>
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Over the <u>past 12 months</u>	47. How often did you eat mixed vege vegetable stir fry, frozen or canne	
44. How often did you eat Brussels sprouts (fresh or frozen)?	vegetables)?	
☐ NEVER (GO TO QUESTION 45)	NEVER (GO TO QUESTION 48)	
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day	☐ 7-11 times per year ☐ 3-4 ☐ 1 time per month ☐ 5-6 ☐ 2-3 times per month ☐ 1 time per week ☐ 2 o	mes per week times per week times per week me per day r more times
44a. Each time you ate Brussels sprouts , how	47a. Each time you ate mixed vege much did you usually eat?	etables, how
much did you usually eat? Less than 4 Brussels sprouts or less than ½ cup Brussels sprouts or ½ to 1 cup	☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup	
☐ More than 7 Brussels sprouts or more than 1 cup	48. How often did you eat onions ?	
45. How often did you eat asparagus (fresh or	☐ NEVER (GO TO QUESTION 49)	
frozen)? NEVER (GO TO QUESTION 46) 1-6 times per year 7-11 times per year 1 times per week 1 times per month 5-6 times per week	☐ 7-11 times per year ☐ 3-4 ☐ 1 time per month ☐ 5-6 ☐ 2-3 times per month ☐ 1 time per week ☐ 2 o	mes per week times per week times per week me per day r more times
☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day ☐ 2 or more times per day	48a. Each time you ate onions , how usually eat?	•
45a. Each time you ate asparagus , how much did you usually eat?	Less than 1 slice or less than 1 1 to 5 slices or 1 to 4 tablespoo More than 5 slices or more than	ons
☐ Less than 5 spears or less than ½ cup ☐ 5 to 9 spears or ½ to ¾ cup ☐ More than 9 spears or more than ¾ cup	49. Now think about all the cooked ve ate in the <u>past 12 months</u> and how prepared. How often were your ve	v they were egetables
46. How often did you eat winter squash (such as pumpkin, butternut, or acorn)?	COOKED WITH some sort of fat, spray? (Please do not include pot	
☐ NEVER (GO TO QUESTION 47)	☐ NEVER (GO TO QUESTION 50)	
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day	☐ 7-11 times per year ☐ 3-4 ☐ 1 time per month ☐ 5-6 ☐ 2-3 times per month ☐ 1 time ☐ 1 time per week ☐ 2 o	mes per week times per week times per week me per day r more times
46a. Each time you ate winter squash , how much did you usually eat? ☐ Less than 1/₃ cup ☐ 1/₃ to 1 cup ☐ More than 1 cup		- Tables
♥ Ouestion 47 annears in the next column	Ouestion 50 annears on the next page	1/65

Over the past 12 months	51. How often did you eat sweet peppers (green, red, or yellow)?
49a. Which fats were usually added to your vegetables DURING COOKING? (Please do not include potatoes. Mark all that apply.) Margarine	□ NEVER (GO TO QUESTION 52) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day 51a. Each time you ate sweet peppers , how much did you usually eat? □ Less than 1/8 pepper □ 1/8 to 1/2 pepper □ More than 1/2 pepper □ More than 1/2 pepper ▼ 52. Over the <u>past 12 months</u> , did you eat fresh tomatoes (including those in salads)? □ NO (GO TO QUESTION 53) □ YES ↓ 52a. How often did you eat fresh tomatoes (including those in salads) WHEN IN SEASON ?
50a. Which fats, sauces, or dressings were usually added AFTER COOKING OR AT THE TABLE? (Please do not include potatoes. Mark all that apply.) Margarine	□ NEVER □ 1-6 times per season □ 2 times per week □ 7-11 times per season □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day 52b. How often did you eat fresh tomatoes (including those in salads) DURING THE REST OF THE YEAR? □ NEVER
50b. If margarine, butter, vegetable oil, lard, fatback, or bacon fat was added to your cooked vegetables AFTER COOKING OR AT THE TABLE, how much did you usually add? Did not usually add these Less than 1 teaspoon 1 to 3 teaspoons More than 3 teaspoons 50c. If salad dressing, cheese sauce, or white sauce was added to your cooked vegetables AFTER COOKING OR AT THE TABLE, how much did you usually add? Did not usually add these Less than 1 tablespoon 1 to 3 tablespoons More than 3 tablespoons	□ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 2 or more times per day 52c. Each time you ate fresh tomatoes , how much did you usually eat? □ Less than ¼ tomato □ ¼ to 1 tomato □ More than 1 tomato
Question 51 appears in the next column	Question 53 appears on the next page 1465

Over the <u>past 12 months</u>			55a. Each time you ate swe how much did you usua	
53. How often did you eat lettue without other vegetables)?	ce salads (with or		☐ 1 small potato or less th☐ 1 medium potato or ½ t	nan ½ cup o 1 cup
☐ NEVER (GO TO QUESTION	l 54)		☐ 1 large potato or more t	than 1 cup
☐ 1-6 times per year☐ 7-11 times per year	☐ 2 times per week ☐ 3-4 times per week	56	 How often did you eat Fren hash browned potatoes, 	
☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		 NEVER (GO TO QUESTION □ 1-6 times per year □ 7-11 times per year □ 1 time per month 	N 57) 2 times per week 3-4 times per week 5-6 times per week
53a. Each time you ate lettud you usually eat?	ce salads, how much did		2-3 times per month 1 time per week	1 time per day 2 or more times per day
☐ Less than ¼ cup ☐ ¼ to 1½ cups ☐ More than 1½ cups			56a. Each time you ate Fren hash browned potato much did you usually ea	ch fries, home fries, es, or tater tots how
53b. How often did the lettuce dark green lettuce?	e salads you ate include		☐ Less than 10 fries or les☐ 10 to 25 fries or ½ to 1☐ More than 25 fries or m	cup
☐ Almost never or never ☐ About ¹¼ of the time ☐ About ¹½ of the time ☐ About ³¼ of the time ☐ Almost always or always	S		56b. How often did the Fren	ch fries, home fries, hash ater tots you ate include
↓ How often did you eat salact low-fat) on salads?	I dressing (including		☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time	
■ NEVER (GO TO QUESTION	I 55)	↓	☐ Almost always or alway	s
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day	57	 How often did you eat pota NEVER (GO TO QUESTION □ 1-6 times per year □ 7-11 times per year □ 1 time per month □ 2 3 times per month 	N 58) 2 times per week 3-4 times per week 5-6 times per week
54a. Each time you ate salad how much did you usual			☐ 2-3 times per month☐ 1 time per week	☐ 1 time per day ☐ 2 or more times per day
☐ Less than 2 tablespoons☐ 2 to 4 tablespoons☐ More than 4 tablespoons			57a. Each time you ate pota you usually eat?	to salad, how much did
♦ 55. How often did you eat swee	et potatoes or yams?		☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup	
■ NEVER (GO TO QUESTION	I 56)	58		ed, boiled, or mashed
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		potatoes? NEVER (GO TO QUESTION 1-6 times per year 7-11 times per year 1 time per month 2-3 times per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times
Question 56 appears in the next column		▼ Que	estion 59 appears on the next page	per day 1465

Over the <u>past 12 months</u>	58h. Each time cheese or cheese sauce was added to your potatoes, how much was usually added?
58a. Each time you ate baked , boiled , or mashed potatoes , how much did you usually eat? ☐ 1 small potato or less than ½ cup ☐ 1 medium potato or ½ to 1 cup ☐ 1 large potato or more than 1 cup	Less than 1 tablespoon 1 to 3 tablespoons More than 3 tablespoons
EQUITION Office was a surround (including law fat)	59. How often did you eat salsa?
58b. How often was sour cream (including low-fat) added to your potatoes, EITHER IN COOKING OR AT THE TABLE? Almost never or never (GO TO QUESTION 58d) About 1/4 of the time About 1/2 of the time	☐ NEVER (GO TO QUESTION 60) ☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day
□ Almost always or always 58c. Each time sour cream was added to your potatoes, how much was usually added? □ Less than 1 tablespoon □ 1 to 4 tablespoons □ More than 4 tablespoons	59a. Each time you ate salsa , how much did you usually eat? ☐ Less than 2 tablespoons ☐ 2 tablespoons to ½ cup ☐ More than ½ cup
58d. How often was margarine (including light) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?	60. How often did you eat ketchup ? NEVER (GO TO QUESTION 61)
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day
58e. How often was butter (including light) added to your potatoes, EITHER IN COOKING OR AT THE TABLE? ☐ Almost never or never ☐ About 1/2 of the time ☐ About 3/2 of the time ☐ About 3/4 of the time	60a. Each time you ate ketchup , how much did you usually eat? Less than 2 teaspoons 2 to 6 teaspoons More than 6 teaspoons
☐ Almost always or always	61. How often did you eat stuffing, dressing, or dumplings?
58f. Each time margarine or butter was added to your potatoes, how much was usually added?	☐ NEVER (GO TO QUESTION 62)
Never addedLess than 1 teaspoon1 to 3 teaspoonsMore than 3 teaspoons	☐ 1-6 times per year ☐ 2 times per week ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times
58g. How often was cheese or cheese sauce added to your potatoes, EITHER IN COOKING OR AT THE TABLE ?	per day 61a. Each time you ate stuffing , dressing , or
Almost never or never (GO TO QUESTION 59) About ¼ of the time About ½ of the time About ¾ of the time Almost always or always	dumplings, how much did you usually eat? ☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup
Question 59 appears in the next column	Question 62 appears on the next page 1465
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				-
Over the past 12 months			v often did you eat othe r ch as pintos, kidney, blad	
62. How often did you eat chili ?		lenti	lls, soybeans, or refried	beans)? (Please do not
☐ NEVER (GO TO QUESTION 63)			<i>ude bean, pea or lentil s</i> EVER (GO TO QUESTION	
☐ 7-11 times per year ☐ 3 ☐ 1 time per month ☐ 5 ☐ 2-3 times per month ☐ 1 ☐ 1 time per week ☐ 2	2 times per week 3-4 times per week 5-6 times per week time per day 2 or more times per day		6 times per year 11 times per year time per month 3 times per month time per week	2 times per week 3-4 times per week 5-6 times per week 1 time per day 2 or more times per day
62a. Each time you ate chili , how usually eat?	much did you	65a.	Each time you ate oth you usually eat?	er beans, how much did
☐ Less than 1 cup ☐ 1 to 1¾ cups ☐ More than 1¾ cups			☐ Less than ¼ cup☐ ¼ to ¾ cup☐ More than ¾ cup	
63. How often did you eat Mexican tacos, tostados, burritos, tamale enchiladas, quesadillas, or chim ■ □ NEVER (GO TO QUESTION 64)	s, fajitas,	65b.		her beans you ate refried ed with any type of fat,
☐ 1-6 times per year ☐ 2 ☐ 7-11 times per year ☐ 3 ☐ 1 time per month ☐ 5 ☐ 2-3 times per month ☐ 1 ☐ 1 time per week ☐ 2	2 times per week 3-4 times per week 5-6 times per week 1 time per day 2 or more times per day	↓ 66. How	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or alway ✓ often did you eat other	ıys
63a. Each time you ate Mexican find did you usually eat? Less than 1 taco, burrito, etc.		□ 1- □ 7- □ 1	EVER (GO TO QUESTION 6 times per year 11 times per year time per month 3 times per month	☐ 2 times per week☐ 3-4 times per week☐ 5-6 times per week☐ 1 time per day
☐ More than 2 tacos, burritos, e			time per week	2 or more times per day
 How often did you eat baked be include canned, ready-made, or 		66a.	Each time you ate oth how much did you usu	er kinds of vegetables,
☐ 7-11 times per year ☐ 3 ☐ 1 time per month ☐ 5 ☐ 2-3 times per month ☐ 1 ☐ 1 time per week ☐ 2	2 times per week 3-4 times per week 5-6 times per week time per day 2 or more times per day	(suc	Less than ¼ cup ¼ to ½ cup More than ½ cup	or other cooked grains neat, or millet)?
64a. Each time you ate baked be did you usually eat? Less than ½ cup ½ to 1 cup More than 1 cup	eans, how much	□ 7- □ 1 □ 2-	6 times per year 11 times per year time per month 3 times per month time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day
Question 65 appears in the next column		Question 68	3 appears on the next page	1465

Over the past 12 months 67a. Each time you ate rice or other cooked grains, how much did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups	68d. Each time margarine or butter was added to your pancakes, waffles, or French toast, how much was usually added? Never added Less than 1 teaspoon 1 to 3 teaspoons More than 3 teaspoons
67b. How often was butter, margarine, or oil added to your rice or other cooked grains IN COOKING OR AT THE TABLE? Almost never or never About ¼ of the time About ½ of the time About ¾ of the time About ¾ of the time About ¾ of the time About 34 of the time Almost always or always 68. How often did you eat pancakes, waffles, or French toast?	68e. How often was syrup added to your pancakes, waffles, or French toast? Almost never or never (GO TO QUESTION 69) About ½ of the time About ½ of the time About ¾ of the time Almost always or always 68f. Each time syrup was added to your pancakes, waffles, or French toast, how much was usually added?
□ NEVER (GO TO QUESTION 69) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times □ 2 per day	□ Less than 1 tablespoon □ 1 to 3 tablespoons □ More than 3 tablespoons 69. How often did you eat lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini? (Please do not include spaghetti or other pasta.) □ NEVER (GO TO QUESTION 70)
68a. Each time you ate pancakes, waffles, or French toast, how much did you usually eat? ☐ Less than 1 medium piece ☐ 1 to 3 medium pieces ☐ More than 3 medium pieces	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day
68b. How often was margarine (including light) added to your pancakes, waffles, or French toast AFTER COOKING OR AT THE TABLE? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	69a. Each time you ate lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini, how much did you usually eat? Less than 1 cup 1 to 2 cups More than 2 cups 70. How often did you eat macaroni and cheese?
68c. How often was butter (including light) added to your pancakes, waffles, or French toast AFTER COOKING OR AT THE TABLE? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 2 times per week☐ 7-11 times per year☐ 3-4 times per week☐ 1 time per month☐ 5-6 times per week☐ 2-3 times per month☐ 1 time per day☐ 1 time per week☐ 2 or more times per day☐ 70a. Each time you ate macaroni and cheese, how much did you usually eat?☐ Less than 1 cup☐ 1 to 1½ cups☐ 1 to 1 t
♥ Question 69 appears in the next column	☐ More than 1½ cups V Question 71 appears on the next page 1465

О	Over the past 12 months		72d. How often did you eat your pasta, spaghetti, or other noodles with margarine, butter, oil, or		
71. How often did you eat pasta salad or macaroni salad?		cream sauce?			
1	☐ NEVER (GO TO QUESTION 72)		☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time		
	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times	7	☐ About ¾ of the time ☐ Almost always or always 73. How often did you eat bagels or English muffins ? ☐ NEVER (GO TO INTRODUCTION TO QUESTION 74)		
	per day 71a. Each time you ate pasta salad or macaroni salad , how much did you usually eat? Less than ½ cup ½ to 1 cup More than 1 cup		☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 1 time per day ☐ 2 or more times ☐ 2 per day		
7	 Other than the pastas listed in Questions 69, 70, and 71, how often did you eat pasta, spaghetti, or other noodles? 		73a. How often were the bagels or English muffins you ate whole wheat ? ☐ Almost never or never ☐ About ¼ of the time		
	☐ NEVER (GO TO QUESTION 73)		☐ About ½ of the time ☐ About ¾ of the time		
	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day		☐ Almost always or always 73b. Each time you ate bagels or English muffins , how many did you usually eat? ☐ Less than 1 bagel or English muffin		
	72a. Each time you ate pasta, spaghetti, or other noodles, how much did you usually eat?		☐ 1 bagel or English muffin ☐ More than 1 bagel or English muffin		
	Less than 1 cup 1 to 3 cups More than 3 cups 72b. How often did you eat your pasta, spaghetti, or		73c. How often was margarine (including light) added to your bagels or English muffins? ☐ Almost never or never ☐ About ¹⁄₂ of the time ☐ About ³⁄₂ of the time ☐ About ³⁄₂ of the time		
	other noodles with tomato sauce or spaghetti sauce made WITH meat? ☐ Almost never or never		☐ Almost always or always 73d. How often was butter (including light) added to		
	☐ About ¼ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always		your bagels or English muffins? ☐ Almost never or never ☐ About ½ of the time ☐ About ½ of the time ☐ About ¾ of the time		
	72c. How often did you eat your pasta, spaghetti, or other noodles with tomato sauce or spaghetti sauce made WITHOUT meat? ☐ Almost never or never ☐ About 1/4 of the time		☐ Almost always or always 73e. Each time margarine or butter was added to your bagels or English muffins, how much was usually added? ☐ Never added		
	☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always		Less than 1 teaspoon 1 to 2 teaspoons More than 2 teaspoons		

Question 73 appears in the next column

Introduction to Question 74 appears on the next page



Over the past 12 months	74c. How often was mayonnaise or mayonnaise-
73f. How often was cream cheese (including low-fat) spread on your bagels or English muffins?	type dressing (including low-fat) added to the breads, rolls or flatbreads used for your sandwiches or wraps?
☐ Almost never or never (GO TO INTRODUCTION TO QUESTION 74) ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ Almost never or never (GO TO QUESTION 74e) ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always
73g. Each time cream cheese was added to your bagels or English muffins, how much was usually added?	74d. Each time mayonnaise or mayonnaise-type dressing was added to the breads, rolls or flatbreads used for your sandwiches or wraps, how much was usually added?
☐ Less than 1 tablespoon ☐ 1 to 2 tablespoons ☐ More than 2 tablespoons	Less than 1 teaspoon 1 to 3 teaspoons More than 3 teaspoons
The next questions ask about your intake of breads other than bagels or English muffins. First, we will	74e. How often was margarine (including light) added to the breads, rolls or flatbreads used for your sandwiches or wraps?
ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate. 74. How often did you eat breads, rolls or flatbreads (such as pita, roti and tortillas) AS PART OF SANDWICHES (including burger and hot dog rolls)?	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
☐ NEVER (GO TO QUESTION 75)	74f. How often was butter (including low-fat) added to the breads, rolls or flatbreads used for your
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day	sandwiches or wraps? Almost never or never About ¼ of the time About ¾ of the time About ¾ of the time Almost always or always
74a. Each time you ate breads , rolls or flatbreads AS PART OF SANDWICHES , how many did you usually eat?	74g. Each time margarine or butter was added to the breads, rolls or flatbreads used for your sandwiches or wraps, how much was usually added?
☐ 1 slice or ½ roll or flatbread ☐ 2 slices or 1 roll or flatbread ☐ More than 2 slices or more than 1 roll or flatbread	☐ Never added ☐ Less than 1 teaspoon ☐ 1 to 2 teaspoons
74b. How often were the breads, rolls or flatbreads that you used for your sandwiches white (including burger and hot dog rolls)?	☐ More than 2 teaspoons 75. How often did you eat breads, dinner rolls or flatbreads, NOT AS PART OF SANDWICHES?
☐ Almost never or never ☐ About ¼ of the time	☐ NEVER (GO TO QUESTION 76)
☐ About ½ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day
▼ Question 75 appears in the next column	Question 76 appears on the next page 1465

Over the past 12 months	75g. Each time cream cheese was added to your breads, rolls or flatbreads, how much was
75a. Each time you ate breads , dinner rolls or flatbreads , NOT AS PART OF SANDWICHES , how much did you usually eat?	usually added? Less than 1 tablespoon 1 to 2 tablespoons
☐ 1 slice or 1 dinner roll or ½ flatbread ☐ 2 slices or 2 dinner rolls or 1 flatbread ☐ More than 2 slices or dinner rolls or more than 1 flatbread	 More than 2 tablespoons 76. How often did you eat jam, jelly, or honey on bagels, muffins, bread, rolls, or crackers?
75b. How often were the breads, rolls or flatbreads you ate white ?	□ NEVER (GO TO QUESTION 77) □ 1-6 times per year □ 2 times per week
☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always	☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 or more times ☐ 2 or more times ☐ 2 or more times ☐ 1 time per day ☐ 2 or more times ☐ 2 or more times
75c. How often was margarine (including light) added to your breads, rolls or flatbreads?	76a. Each time you ate jam , jelly , or honey , how much did you usually eat?
☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always	☐ Less than 2 teaspoons ☐ 2 to 4 teaspoons ☐ More than 4 teaspoons ▼
☐ Almost always or always 75d. How often was butter (including light) added to your breads, rolls or flatbreads?	77. How often did you eat peanut butter or other nut butter? NEVER (GO TO QUESTION 78)
☐ Almost never or never ☐ About 1⁄2 of the time ☐ About 1⁄2 of the time ☐ About 3⁄4 of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day
75e. Each time margarine or butter was added to your breads, rolls or flatbreads, how much was usually added?	77a. Each time you ate peanut butter or other nut butter , how much did you usually eat?
☐ Never added ☐ Less than 1 teaspoon ☐ 1 to 2 teaspoons	☐ Less than 1 tablespoon ☐ 1 to 2 tablespoons ☐ More than 2 tablespoons ▼
☐ More than 2 teaspoons	78. How often did you eat roast beef or steak IN SANDWICHES ?
75f. How often was cream cheese (including low-fat) added to your breads, rolls or flatbreads?	NEVER (GO TO QUESTION 79)
☐ Almost never or never (GO TO QUESTION 76) ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day
Question 76 appears in the next column	Question 79 appears on the next page 1465

Over the <u>past 12 months</u>	81. How often did you eat other cold cuts or luncheon
78a. Each time you ate roast beef or steak IN SANDWICHES , how much did you usually eat?	meats (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? (Please do not include ham, turkey, or chicken cold cuts.)
☐ Less than 1 slice or less than 2 ounces☐ 1 to 2 slices or 2 to 4 ounces☐ More than 2 slices or more than 4 ounces	□ NEVER (GO TO QUESTION 82) □ 1-6 times per year □ 2 times per week
79. How often did you eat turkey or chicken COLD CUTS (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? (We will ask about other turkey or chicken later.)	☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 or more times
NEVER (GO TO QUESTION 80) 1-6 times per year	81a. Each time you ate other cold cuts or luncheon meats, how much did you usually eat? Less than 1 slice 1 to 3 slices More than 3 slices 81b. How often were the other cold cuts or luncheon meats you ate light, low-fat, or fat-free? (Please do not include ham, turkey, or chicken cold cuts.) Almost never or never About ¼ of the time About ¾ of the time About ¾ of the time Almost always or always 82. How often did you eat canned tuna (including in salads, sandwiches, or casseroles)? NEVER (GO TO QUESTION 83) 1-6 times per year 7-11 times per year 1 time per month 5-6 times per week 1 time per month 1 time per day
80a. Each time you ate luncheon or deli-style ham , how much did you usually eat?	☐ 1 time per week ☐ 2 or more times per day
□ Less than 1 slice □ 1 to 3 slices □ More than 3 slices 80b. How often was the luncheon or deli-style ham you ate light, low-fat, or fat-free? □ Almost never or never □ About 1/4 of the time □ About 1/2 of the time □ About 3/4 of the time □ Almost always or always	82a. Each time you ate canned tuna, how much did you usually eat? Less than ¼ cup or less than 2 ounces ⅓ to ½ cup or 2 to 3 ounces More than ½ cup or more than 3 ounces 82b. How often was the canned tuna you ate water-packed? Almost never or never About ¼ of the time About ¾ of the time About ¾ of the time About ¾ of the time Almost always or always
↓	' ↓

Question 81 appears in the next column

Question 83 appears on the next page

Over the past 12 months 82c. How often was the canned tuna you ate prepared with mayonnaise or other dressing (including low-fat)? Almost never or never About ¼ of the time About ½ of the time About ¾ of the time Almost always or always		84b. Each time you ate beef hamburgers or cheeseburgers from a FAST FOOD or OTHER	
		RESTAURANT, how much did you usually eat? ☐ Less than 1 burger ☐ 1 burger	
		☐ More than 1 burger	
		84c. How often did you have cheeseburgers rather than hamburgers from a FAST FOOD or OTHER RESTAURANT?	
 83. How often did you eat GROUND chicken turkey? (We will ask about other chicker turkey later.) □ NEVER (GO TO QUESTION 84) 		☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	
☐ 1-6 times per year ☐ 2 times per ☐ 7-11 times per year ☐ 3-4 times per ☐ 1 time per month ☐ 5-6 times per ☐ 2-3 times per month ☐ 1 time per o	er week er week day	85. How often did you eat beef hamburgers or cheeseburgers that were NOT from a FAST FOOD or OTHER RESTAURANT?	
□ 1 time per week □ 2 or more tiper day 83a. Each time you ate GROUND chicken how much did you usually eat? □ Less than 2 ounces or less than ½ cup□ 2 to 4 ounces or ½ to 1 cup□ More than 4 ounces or more than 1 cup	or turkey ,	□ NEVER (GO TO QUESTION 86) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day	
84. How often did you eat beef hamburgers cheeseburgers from a FAST FOOD or C RESTAURANT?	or	85a. Each time you ate beef hamburgers or cheeseburgers that were NOT from a FAST FOOD or OTHER RESTAURANT , how much did you usually eat?	
☐ NEVER (GO TO QUESTION 85)		Less than 1 patty or less than 2 ounces 1 patty or 2 to 4 ounces	
☐ 1-6 times per year ☐ 2 times per ☐ 7-11 times per year ☐ 3-4 times per ☐ 1 time per month ☐ 5-6 times per ☐ 1 time per week ☐ 2 or more time per day ☐ 1 time per day ☐ 2 times per ☐ 2 times per ☐ 1 time per day ☐ 2 times per ☐ 2 times per ☐ 2 times per ☐ 2 times per ☐ 3-4 times per ☐ 5-6 times per ☐ 2 times per ☐ 5-6 times per ☐ 1 time per ſ ☐ 2 times per ☐ 5-6 times per ☐ 1 time per ſ ☐ 2 times per ☐ 1 time per ſ ☐ 1 time per ſ ☐ 1 time per ſ ☐ 2 times per ☐ 1 time per ſ ☐ 1 time per ſ ☐ 1 time per ſ ☐ 2 times per ☐ 1 time per ſ ☐ 1 time per ſ ☐ 1 time per ſ ☐ 2 times per ☐ 2 times per ☐ 1 time per ſ ☐ 1 time per ſ ☐ 2 times per ☐ 2 times ☐ 2 time	er week er week day		
84a. Each time you ate beef hamburgers cheeseburgers from a FAST FOOD RESTAURANT, what size did you usu	or OTHER ually eat?	☐ About ¹¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always	
 ☐ Small hamburger (such as a regular Burger King or McDonald's Hamburger) ☐ Medium (such as McDonald's or Burger King Double Burger or Cheeseburger) ☐ Large (such as Burger King Whopper or 		86. How often did you eat ground beef in mixtures (such as meatballs, casseroles, chili, or meatloaf)?	
Double Whopper or a McDonald's Double Quarter Pounder)	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day		
▼		▼	

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Question 85 appears in the next column

	1
Over the past 12 months 86a. Each time you ate ground beef in mixtures, how much did you usually eat?	89. How often did you eat roast beef or pot roast ? (Please do not include roast beef or pot roast in sandwiches.)
□ Less than 3 ounces or less than ½ cup □ 3 to 8 ounces or ½ to 1 cup □ More than 8 ounces or more than 1 cup 87. How often did you eat hot dogs, wieners or frankfurters? (Please do not include sausages or	☐ NEVER (GO TO QUESTION 90) ☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times ☐ per day
NEVER (GO TO QUESTION 88)	89a. Each time you ate roast beef or pot roast, how much did you usually eat? Less than 2 ounces 2 to 6 ounces More than 6 ounces
88a. Each time you ate beef mixtures , how much did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 times per week ☐ 5-6 times per day
Question 89 appears in the next column	Question 92 appears on the next page 1465

91a. Each time you ate pork or beef spareribs, how much did you usually eat? Less than 4 ribs A to 12 ribs A to 14 times per week A times per week A times per week A times per week A times per week A times per week A times per week A times per week A times per week A times per week A times per week A times per week	Over the past 12 months	94. How often did you eat baked, broiled, roasted,			
Less than 4 ribs 4 to 12 ribs 2 times per week 3.4 times per week 3.4 times per week 3.4 times per week 5.6 times per		, ,			
1-6 times per year 2 times per week 1-1 times per year 3 times per week 1-1 times per year 2 times per week 1-1 times per year 3 times per week 1-1 times per year 1-1 times per week 1-1 time per day 1-1 times per year 2 times per week 1-1 time per month 1 time per day 1-1 times per week 1-1 time per month 1 time per day 1-1 times per week 1-1 time per week 1	·	☐ NEVER (GO TO QUESTION 95)			
cutilets, or turkey nuggets (including in sandwiches)? Never (Go To QUESTION 93)	4 to 12 ribs	☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day			
stewed, or fried chicken (including nuggets), how much did you usually eat? 1-6 times per year	cutlets, or turkey nuggets (including in	per day			
Till times per year 3-4 times per week 1 time per month 5-6 times per week 2-3 times per month 1 time per day 2 or more times per day 92a. Each time you ate chicken mixtures, stews, or turkey nuggets, how much did you usually eat? 2 for more times per day 93a. Each time per week 2 times per week 3-4 times per week 3-8		stewed, or fried chicken (including nuggets),			
1 time per week	☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week				
92a. Each time you ate roast turkey, turkey cutlets, or turkey nuggets, how much did you usually eat? (<i>Please note: 4 to 8 turkey nuggets = 3 ounces.</i> .) Less than 2 ounces 2 to 5 ounces About ½ of the time Abou	☐ 1 time per week ☐ 2 or more times	8 nuggets			
Class than 2 ounces Class than 3 ounces Class than 4 ounces Class than 5 ounces Class than 5 ounces Class than 5 ounces Class than 6 ounces Class than 7 ounces Class than 6 ounces					
2 to 5 ounces	,				
salads, sandwiches, casseroles, chicken curries, stews, or other mixtures)? NEVER (GO TO QUESTION 94)	☐ 2 to 5 ounces ☐ More than 5 ounces	☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time			
About ½ of the time About ½ of the time About ¾ of the time	salads, sandwiches, casseroles, chicken curries,				
□ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 1 time per day □ 2 or more times per day □ 1 time per day □ 2 or more times per day □ 1 time per day □ 2 or more times per day □ 4. How often did you eat chicken WITH skin? □ About ½ of the time □ About ¾ of the time □ About	☐ NEVER (GO TO QUESTION 94)				
□ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 1 time per month □ 1 time per day □ 1 time per week □ 2 or more times per day □ 3 a. Each time you ate chicken mixtures , how much did you usually eat? □ Less than ½ cup □ ½ to 1½ cups □ More than 1½ cups □ More than 1½ cups □ NEVER (GO TO QUESTION 96) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per day □ 1 time per day □ 1 time per week □ 2-3 times per month □ 1 time per day □ 1 time per day □ 1 time per week □ 2 or more times per day □ 2 times per week □ 2 or more times per day □ 2 times per week □ 2 or more times	☐ 1-6 times per vear ☐ 2 times per week				
2-3 times per month 1 time per day 2 or more times per day 93a. Each time you ate chicken mixtures , how much did you usually eat? Almost never or never About ½ of the time About ½ of the time About ½ of the time Almost always or always More than 1½ cups Never (GO TO QUESTION 96) 1-6 times per year 2 times per week 1 time per month 1 time per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day 1 time per week 2 or more times per day	☐ 7-11 times per year ☐ 3-4 times per week				
93a. Each time you ate chicken mixtures , how much did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups NEVER (GO TO QUESTION 96) 1-6 times per year 3-4 times per week 7-11 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 2 or more times per day		☐ Almost always or always			
93a. Each time you ate chicken mixtures , how much did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups More than 1½ cups Less than ½ cups Was to 1½ cups Less than ½ cups	☐ 1 time per week ☐ 2 or more times	94d. How often did you eat chicken WITH skin?			
did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups 95. How often did you eat baked ham or ham steak? NEVER (GO TO QUESTION 96) 1-6 times per year 7-11 times per year 1 time per month 5-6 times per week 1 time per month 1 time per day 1 time per week 2 or more times per day	020 Footh time you ato chicken mixtures how much				
□ Less than ½ cup □ ½ to 1½ cups □ More than 1½ cups □ Second 1½ to 1½ cups □ More than 1½ cups □ NEVER (GO TO QUESTION 96) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day □ 1 time per week □ 2 or more times per day					
More than 1½ cups 95. How often did you eat baked ham or ham steak? NEVER (GO TO QUESTION 96) 1-6 times per year 2 times per week 7-11 times per year 3-4 times per week 1 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 2 or more times per day					
95. How often did you eat baked ham or ham steak ? NEVER (GO TO QUESTION 96) 1-6 times per year		☐ Almost always or always			
☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day	☐ More than 1½ cups	95. How often did you eat baked ham or ham steak ?			
☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day		☐ NEVER (GO TO QUESTION 96)			
Question 94 appears in the next column Ouestion 96 appears on the next page 1465		☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times			
	▼ Ouestion 94 appears in the next column	♦ Ouestion 96 appears on the next page 1465			

Over the past 12 months	98a. Each time you ate liver or liverwurst , how much did you usually eat?
95a. Each time you ate baked ham or ham steak , how much did you usually eat?	Less than ½ ounce ½ to 3 ounces More than 3 ounces
☐ Less than 1 ounce ☐ 1 to 3 ounces ☐ More than 3 ounces	99. How often did you eat bacon (including low-fat)?
96. How often did you eat pork (including chops, roasts, and in mixed dishes)? (Please do not include ham, ham steak, or sausage.) NEVER (GO TO QUESTION 97) 1-6 times per year	□ NEVER (GO TO QUESTION 100) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times per day 99a. Each time you ate bacon , how much did you usually eat?
96a. Each time you ate pork , how much did you usually eat?	☐ Fewer than 2 slices ☐ 2 to 4 slices ☐ More than 4 slices
☐ Less than 2 ounces or less than 1 chop ☐ 2 to 5 ounces or 1 chop ☐ More than 5 ounces or more than 1 chop	99b. How often was the bacon you ate light , low-fat , or lean ?
 ♦ 97. How often did you eat gravy on meat, chicken, potatoes (NOT including poutine), rice, etc.? ☐ NEVER (GO TO QUESTION 98) 	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day	100. How often did you eat sausage (including low-fat)? □ NEVER (GO TO QUESTION 101)
97a. Each time you ate gravy on meat, chicken, potatoes, rice, etc., how much did you usually eat? Less than 1/8 cup 1/8 to ½ cup More than ½ cup	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day 100a. Each time you ate sausage, how much did you
*	usually eat?
98. How often did you eat liver (all kinds) or liverwurst? ☐ □ NEVER (GO TO QUESTION 99)	☐ Less than 2 small links or less than 1 large link☐ 2 to 5 small links or 1 to 2 large links☐ More than 5 small links or more than 2 large links
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day	100b. How often was the sausage you ate light, low-fat, or lean? ☐ Almost never or never ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always

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Question 99 appears in the next column

Over the past 12 months	104. How often did you eat ready-to-eat battered fish or fish sticks , including in fast food sandwiches		
101. How often did you eat fried shellfish (such as crab lobster, scallops, or shrimp)?	(not including shellfish)?		
☐ NEVER (GO TO QUESTION 102)	NEVER (GO TO QUESTION 105)		
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per month ☐ 1 time per day ☐ 2 or more times per day ☐ 2 or more times per day		
101a. Each time you ate fried shellfish , how much did you usually eat?	104a. Each time you ate ready-to-eat battered fish or fish sticks , how much did you usually eat? ☐ Less than 2 ounces or less than 1 fillet		
Less than 1 ounce 1 to 3 ounces More than 3 ounces	☐ 2 to 6 ounces or 1 fillet☐ More than 6 ounces or more than 1 fillet☐		
 Involve than 3 outlies How often did you eat shellfish (such as crab, lobster, scallops, or shrimp) that was NOT FRIED? 	105. How often did you eat white or lean fish like cod, sole, perch, or pike (do not include ready-to-eat battered fish or fish sticks)?		
☐ NEVER (GO TO QUESTION 103)	NEVER (GO TO INTRODUCTION TO QUESTION 106)		
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day		
102a. Each time you ate shellfish that was NOT FRIED , how much did you usually eat?	105a. Each time you ate white or lean fish , how much did you usually eat?		
☐ Less than 1 ounce☐ 1 to 4 ounces☐ More than 4 ounces☐	Less than 2 ounces or less than 1 fillet 2 to 5 ounces or 1 fillet More than 5 ounces or more than 1 fillet		
103. How often did you eat dark or oily fish like salmon, fresh tuna, trout, or mackerel?	Now think about all the meat, poultry, and fish you ate in the past 12 months and how they were prepared.		
☐ NEVER (GO TO QUESTION 104)	in the past 12 months and now they were prepared.		
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per week ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ per day	106. How often was oil, butter, margarine, or other fat used to FRY, SAUTE, BASTE, OR MARINATE any meat, poultry, or fish you ate? (Please do not include deep frying.) NEVER (GO TO QUESTION 107)		
103a. Each time you ate dark or oily fish , how much did you usually eat? ☐ Less than 2 ounces ☐ 2 to 6 ounces ☐ More than 6 ounces	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times ☐ 2 per day		
	Ouestion 107 annears on the next hage 1465		
Ouestion 104 annears in the next column	Ouestion 107 annears on the next nage 1465		

Over the past 12 months		10	99. How often did you eat soy b meat-substitutes?	urgers or soy
to prepare your me	ving fats were regularly used eat, poultry, or fish?		■ NEVER (GO TO QUESTION	110)
(Mark all that app ☐ Margarine (including light) ☐ Butter (including light) ☐ Lard, fatback, or bacon fat ☐ Olive oil	ly.) ☐ Corn oil ☐ Canola or rapeseed oil ☐ Oil spray, such as Pam or others ☐ Other kinds of oils ☐ None of the above		☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week 109a. Each time you ate soy b	_
107. Thinking about the ME was it cooked by broili	AT you ate, how often ng, grilling, barbecuing, t include poultry or fish).		meat-substitutes, how ☐ Less than ¼ cup or less ☐ ¼ to 1 cup or 2 to 8 ound ☐ More than 1 cup or more	ces
☐ NEVER (GO TO QUES	TION 108)	11	10. Over the past 12 months, dic	you eat soups ?
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		→ NO (GO TO QUESTION 111 □ YES ↓ 110a. How often did you eat so	
broiling, grilling, ba	meat that was cooked by arbecuing, or pan-frying, what ppearance of the meat?		☐ NEVER ☐ 1-6 times per winter ☐ 7-11 times per winter ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day
broiling, grilling, ba was the inside ap	meat that was cooked by arbecuing, or pan-frying, what pearance of the meat?		110b. How often did you eat so OF THE YEAR? □ NEVER	oup DURING THE REST
☐ Red (rare) ☐ Pink (medium) ☐ Brown (well-done) 108. How often did you eat t			☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times
NEVER (GO TO QUES	TION 109)		- Tunic per week	per day
☐ 1-6 times per year☐ 7-11 times per year☐ 1 time per month☐ 2-3 times per month☐ 1 time per week☐ 1 time p	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		110c. Each time you ate soup usually eat? ☐ Less than 1 cup ☐ 1 to 2 cups ☐ More than 2 cups	how much did you
☐ ¼ to ¾ cup or 2 to	or less than 2 ounces			
↓		' ↓		
Question 109 appears in the next co	lumn	Qu	estion 111 appears on the next page	1465

Over the past 12 months	112. How often did you eat crackers ?
110d. How often were the soups you ate bean , pea ,	☐ NEVER (GO TO QUESTION 113)
or lentil soups? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day
110e. How often were the soups you ate cream soups (including chowders)?	112a. Each time you ate crackers , how many did you usually eat?
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	Fewer than 4 crackers 4 to 8 crackers More than 8 crackers
110f. How often were the soups you ate tomato or	113. How often did you eat corn bread or corn muffins?
vegetable soups (NOT cream soups)?	☐ NEVER (GO TO QUESTION 114)
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day
110g. How often were the soups you ate broth soups (including chicken) with or without noodles or rice?	113a. Each time you ate corn bread or corn muffins , how much did you usually eat?
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	Less than 1 piece or muffin 1 to 2 pieces or muffins More than 2 pieces or muffins
111. How often did you eat pizza ?	114. How often did you eat baking powder biscuits, including scones or tea biscuits?
☐ NEVER (GO TO QUESTION 112)	☐ NEVER (GO TO QUESTION 115)
☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day
111a. Each time you ate pizza , how much did you usually eat? ☐ Less than 1 slice or less than 1 mini pizza	114a. Each time you ate baking powder biscuits including scones or tea biscuits , how many did
☐ 1 to 3 slices or 1 to 2 mini pizzas ☐ More than 3 slices or more than 2 mini pizzas	you usually eat?
111b. How often did you eat pizza with pepperoni , sausage , or other meat ?	☐ 1 to 2 biscuits ☐ More than 2 biscuits
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	
Question 112 appears in the next column	Question 115 appears on the next page 1465

118. How often did you eat pretzels? 118. How often did you eat pretzels 118. How often did you							
low-fat, baked, or low-salt)? NEVER (GO TO QUESTION 116)	Over the past 12 months		11	18. Ho	w often did you eat pretz	els?	
NEVER (GO TO QUESTION 116)						_	week
Fewer than 10 chips or less than 1 cup Gindle of the company o	☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day		□ 7 □ 1 □ 2 □ 1	-11 times per year time per month -3 times per month time per week Each time you ate pretz	☐ 3-4 times po ☐ 5-6 times po ☐ 1 time per c ☐ 2 or more ti per day	er week er week lay mes
More than 25 chips or more than 2 cups	you usually eat? ☐ Fewer than 10 chips or	to chips, how much did			☐ Fewer than 7 average tv☐ 7 to 20 average twists☐ More than 20 average tv	vists	
116. How offen did you eat corn chips or tortilla chips (including low-fat, baked, or low-salt)? 1-6 times per year 3-4 times per week 1-6 times per year 1-6 times per year 1-6 times per week 1-6 times per week 1-6 times per week 1-6 times per year 1-6 times per			11			uts, walnuts,	almonds,
(including low-fat, baked, or low-salt)? 1-6 times per year 3-4 times per week 3-4 times per week 1-6 times per year 3-4 times per week 2-3 times per month 1 time per day 1 time per week 2-3 times per month 1 time per day 1-6 times per year 3-4 times per week 2-3 times per month 1 time per day 1-6 times per year 3-4 times per week 2-3 times per month 1 time per day 1-6 times per year 3-4 times per week 3-4 times per week	★			- □ N	IEVER (GO TO QUESTION	l 120)	
1 time per month	(including low-fat, baked, or NEVER (GO TO QUESTION 1-6 times per year	low-salt)? N 117) □ 2 times per week		□ 7 □ 1 □ 2	-11 times per year time per month -3 times per month	☐ 3-4 times po☐ 5-6 times po☐ 1 time per c☐ 2 or more ti	er week er week lay
Fewer than 10 chips or less than 1 cup 10 to 25 chips or 1 to 2 cups More than 25 chips or more than 2 cups Almost never or never About ½ of the time About ¾ of the	☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week 116a. Each time you ate corn	☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day			or other nuts , how muc ☐ Less than ¼ cup ☐ ¼ to ½ cup		
NEVER (GO TO QUESTION 118) 120. How often did you eat flaxseeds? 120. How often	☐ Fewer than 10 chips or ☐ 10 to 25 chips or 1 to 2	cups			☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time	s you ate pear	nuts?
□ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week □ 2-3 times per month □ 1 time per day □ 2 or more times per day □ 117a. Each time you ate popcorn, how much did you usually eat? □ 1½ cups, popped □ 1½ to 5 cups, popped □ 1 to 2 tablespoons □ More than 2 tablespoons		corn (including				5	
☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day ☐ 1 time per week ☐ 2 or more times per day ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 1 time per month ☐ 1 time per day ☐ 1 time per week ☐ 2 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per week ☐ 1 time per week ☐ 2 or more times per week ☐ 1 time per week ☐ 2 or more times per week ☐ 1 time per week ☐ 2 or more times per week ☐ 1 time per week ☐ 2 or more times per week ☐ 1 time per week ☐ 2 or more times per week ☐ 2 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per week ☐ 2 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per week ☐ 2 times per week ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per week ☐ 2 times per week ☐ 2 times per week ☐ 3 times per week ☐ 2 times per week ☐ 3 times per week ☐ 2 times per week ☐ 3 times per week ☐ 3 times per week ☐ 2 times per week ☐ 3 times per week ☐ 2 times per week </td <td>■ NEVER (GO TO QUESTION</td> <td>N 118)</td> <td>12</td> <td>20. Ho</td> <td>w often did you eat flaxs</td> <td>seeds?</td> <td></td>	■ NEVER (GO TO QUESTION	N 118)	12	20. Ho	w often did you eat flaxs	seeds?	
usually eat? Less than 1½ cups, popped 1½ to 5 cups, popped More than 5 cups, popped 1 to 2 tablespoon More than 2 tablespoons	☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day		□ 1 □ 7 □ 1 □ 2	-6 times per year -11 times per year time per month -3 times per month	☐ 2 times per☐ 3-4 times pe☐ 5-6 times pe☐ 1 time per c☐ 2 or more ti	er week er week lay
☐ 1½ to 5 cups, popped ☐ More than 5 cups, popped ☐ 1 to 2 tablespoons ☐ More than 2 tablespoons	usually eat?	•	1	20a.			ıch did you
♦ Ouestion 118 appears in the next column Ouestion 121 appears on the next page 1465	☐ 1½ to 5 cups, popped				☐ Less than 1 tablespoon☐ 1 to 2 tablespoons	s	
	♥ Question 118 appears in the next column	1	♦	estion 1	21 appears on the next page		1465

Question 121 appears on the next page

Over the past 12 months	123b. How often was the yogurt you ate low-fat or fat-free ?
121. How often did you eat other seeds, like sunflower or pumpkin seeds?	☐ Almost never or never ☐ About ¼ of the time
☐ NEVER (GO TO QUESTION 122)	About ½ of the time About ½ of the time About ¾ of the time
□ 1-6 times per year □ 7-11 times per year □ 1 time per month □ 1 time per week □ 2-3 times per month □ 1 time per day □ 1 time per week □ 2 or more times □ 2 tablespoons □ 2 tablespoons □ 2 tablespoons □ 2 tablespoons to ½ cup □ More than ½ cup □ More than ½ cup □ NEVER (GO TO QUESTION 123) □ 1-6 times per year □ 1 time per week □ 1 time per week □ 2 or more times □ 2 tablespoons □ 2 tablespoons □ 2 tablespoons □ 2 tablespoons to ½ cup □ More than ½ cup □ More than ½ cup □ 1-6 times per year □ 1 times per year □ 1 time per month □ 2-3 times per month □ 1 time per day □ 1 time per day □ 1 time per week □ 2 or more times □ 3-4 times per week □ 3-4 times per week □ 3 -4 times per week □ 4 -4 -4 -4 -4 -4 -4 -4 -4 -4 -4 -4 -4 -	□ Almost always or always 124. How often did you eat cottage cheese (including low-fat)? □ NEVER (GO TO QUESTION 125) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 1 time per day □ 2 or more times per day 124a. Each time you ate cottage cheese, how much did you usually eat? □ Less than ¼ cup □ ¼ to ¾ cup □ ¼ to ¾ cup □ More than ¾ cup ■ More than ¾ cup ■ NEVER (GO TO QUESTION 126) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week □ 7-11 times per year □ 3-4 times per week □ 1 time per month □ 5-6 times per week
☐ Less than 1 bar ☐ 1 bar ☐ More than 1 bar	☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day
123. How often did you eat yogurt (NOT including frozen yogurt)? NEVER (GO TO QUESTION 124) 1-6 times per year	125a. Each time you ate cheese , how much did you usually eat? Less than ½ ounce or less than 1 slice ½ to 2 ounces or 1 to 2 slices More than 2 ounces or more than 2 slices 125b. How often was the cheese you ate low-fat ? Almost never or never About ¼ of the time About ½ of the time About ¾ of the time Almost always or always

Question 124 appears in the next column

Question 126 appears on the next page $\,$

Over the <u>past 12 months</u>	128a. Each time you ate cake , how much did you
126. How often did you eat frozen yogurt , sorbet , or ices (including low-fat or fat-free)? ☐ NEVER (GO TO QUESTION 127)	usually eat? ☐ Less than 1 medium piece ☐ 1 medium piece ☐ More than 1 medium piece
1-6 times per year 2 times per week 7-11 times per year 3-4 times per week 1 time per month 5-6 times per week 1 time per day 1 time per week 2-3 times per month 1 time per day 1 time per week 2 or more times per day 126a. Each time you ate frozen yogurt, sorbet, or ices, how much did you usually eat? Less than ½ cup or less than 1 scoop ½ to 1 cup or 1 to 2 scoops More than 1 cup or more than 2 scoops 127. How often did you eat ice cream or ice cream bars (including low-fat or fat-free)? NEVER (GO TO QUESTION 128) 1-6 times per year 2 times per week 1 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 2 or more times per day 127a. Each time you ate ice cream or ice cream bars, how much did you usually eat? Less than ½ cup or less than 1 scoop ½ to 1 cup or 1 to 2 scoops More than 1 cup or more than 2 scoops More than 1 cup or more than 2 scoops About ½ of the time About ½ of the time About ¾ of the time Almost always or always 128. How often did you eat cake (including low-fat or fat-free)? NEVER (GO TO QUESTION 129) 1-6 times per year 2 times per week 1 time per month 1 time per day 1 time per month 1 time per day 1 time per week 2-3 times per week 2-3 times per week 2 or more times 2 or mor	More than 1 medium piece 129. How often did you eat cookies or brownies (including low-fat or fat-free)? NEVER (GO TO QUESTION 130) 1-6 times per year 2 times per week 7-11 times per year 3-4 times per week 1 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 2 or more times per day 129a. Each time you ate cookies or brownies, how much did you usually eat? Less than 2 cookies or 1 small brownie 2 to 4 cookies or 1 medium brownie More than 4 cookies or 1 large brownie 130. How often did you eat doughnuts, sweet rolls, Danish, or Pop-Tarts? NEVER (GO TO QUESTION 131) 1-6 times per year 2 times per week 1 time per month 5-6 times per week 2-3 times per month 1 time per day 1 time per week 1 time per week 1 time per week 1 time per week 1 time per day 1 time per week 2-3 times per week 2-3 tim
per day ▼	↓

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Question 129 appears in the next column

Over the past 12 months	133c. How often were the pies you ate cream, pudding, custard, or meringue pie?
131a. Each time you ate sweet muffins or dessert breads, how much did you usually eat? ☐ Less than 1 medium piece ☐ 1 medium piece ☐ More than 1 medium piece	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
132. How often did you eat fruit crisp, cobbler, or strudel?	133d. How often were the pies you ate pumpkin or sweet potato pie ?
☐ NEVER (GO TO QUESTION 133) ☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 1 time per day ☐ 1 time per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day 132a. Each time you ate fruit crisp, cobbler , or strudel , how much did you usually eat? ☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup 133. How often did you eat pie ? ☐ NEVER (GO TO QUESTION 134) ☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times per day 133a. Each time you ate pie , how much did you usually eat?	Almost never or never
usually eat? ☐ Less than 1/s of a pie ☐ About 1/s of a pie ☐ More than 1/s of a pie	☐ 1 average bar or 1 to 2 ounces ☐ More than 1 average bar or more than 2 ounces ☐ More than 1 average bar or more than 2 ounces 135. How often did you eat other candy ? ☐ NEVER (GO TO QUESTION 136)
The next four questions ask about the kinds of pie you ate. Please read all four questions before answering. 133b. How often were the pies you ate fruit pie (such as apple, blueberry, others)?	☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 2 or more times per day
☐ Almost never or never ☐ About 1⁄4 of the time ☐ About 1⁄2 of the time ☐ About 3⁄4 of the time ☐ Almost always or always	135a. Each time you ate other candy , how much did you usually eat? ☐ Fewer than 2 pieces ☐ 2 to 6 pieces ☐ More than 6 pieces
Question 134 appears in the next column	Question 136 appears on the next page 1465

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Over the past 12 months...

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00.11	salad?
36. How often did you eat eggs, egg whites, or egg substitutes (NOT counting eggs in baked goods or desserts)? (Please include eggs in salads, quiche, soufflés, and sandwiches.)	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
☐ NEVER (GO TO QUESTION 137)	
☐ 1-6 times per year ☐ 2 times per week ☐ 7-11 times per year ☐ 3-4 times per week ☐ 1 time per month ☐ 5-6 times per week ☐ 2-3 times per month ☐ 1 time per day ☐ 1 time per week ☐ 2 or more times	137. How many cups of coffee , caffeinated or decaffeinated, did you drink? (Please do not include coffee drinks such as Latte, Mocha, Cappuccino, or Frappuccino.) NONE (GO TO QUESTION 138)
per day 136a. Each time you ate eggs , how many did you usually eat? □ 1 egg □ 2 eggs □ 3 or more eggs	□ Less than 1 cup per month □ 1-3 cups per month □ 1 cup per day □ 1-3 cups per month □ 1 cup per day □ 2-3 cups per day □ 4-5 cups per day □ 2-4 cups per week □ 6 or more cups per day
136b. How often were the eggs you ate egg	137a. How often was the coffee you drank decaffeinated?
substitutes or egg whites only? Almost never or never About 1/4 of the time About 1/2 of the time About 3/4 of the time Almost always or always	☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always
136c. How often were the eggs you ate regular whole eggs ?	138. How often did you drink coffee drinks , such as Latte, Mocha, Cappuccino , or Frappuccino (including caffeinated or decaffeinated, hot or cold)?
☐ Almost never or never☐ About ¼ of the time	► □ NEVER (GO TO QUESTION 139)
☐ About ½ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ Less than 1 time per month ☐ 1 time per day ☐ 1-3 times per month ☐ 2-3 times per day ☐ 1 time per week ☐ 4-5 times per day
136d. How often were the eggs you ate cooked in oil butter , or margarine ?	☐ 2-4 times per week ☐ 6 or more times ☐ 5-6 times per week per day
☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always	138a. Each time you drank coffee drinks , how much did you usually drink? ☐ Less than 8 ounces (250 ml) ☐ 8 to 16 ounces (250 to 500 ml)
TOO SOCO A	☐ More than 16 ounces (more than 500 ml) 138b. How often were the coffee drinks you drank decaffeinated? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
▼	▼

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136e. How often were the eggs you ate part of egg



Over the past 12 months	140. How many cups of HOT tea , caffeinated or decaffeinated (including herbal), did you drink?
139. How many glasses, cans, or bottles of COLD or ICED tea , caffeinated or decaffeinated, did you drink?	NONE (GO TO QUESTION 141)
□ NONE (GO TO QUESTION 140) □ Less than 1 glass, can □ 5-6 glasses, cans or	☐ Less than 1 cup per ☐ 5-6 cups per week month ☐ 1 cup per day ☐ 1-3 cups per month ☐ 2-3 cups per day
or bottle per month bottles per week ☐ 1-3 glasses, cans or ☐ 1 glass, can or bottle bottles per month per day	☐ 1 cup per week ☐ 4-5 cups per day ☐ 2-4 cups per week ☐ 6 or more cups per day
□ 1 glass, can or bottle per week □ 2-4 glasses, cans or bottles per week □ 2-4 glasses, cans or bottles per day □ 4-5 glasses, cans or bottles per day □ 6 or more glasses, cans or bottles per day	140a. How often was the hot tea you drank herbal? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time
139a. How often was the cold or iced tea you drank decaffeinated or herbal?	☐ Almost always or always
☐ Almost never or never ☐ About ¼ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always 139b. How often was the cold or iced tea you drank	140b. How often was the hot tea you drank green tea? ☐ Almost never or never ☐ About ¼ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always
presweetened with sugar or artificial sweeteners (such as Splenda, Equal, Sweet'N Low, or others)?	140c. How often was the hot black tea and/or the green tea you drank decaffeinated ?
☐ Almost never or never (GO TO QUESTION 140) ☐ About ½ of the time ☐ About ¾ of the time ☐ About ¾ of the time ☐ Almost always or always	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
139c. What kind of sweetener was added to your presweetened cold or iced tea most of the time? ☐ Sugar or honey ☐ Artificial sweeteners (such as Splenda, Equal, Sweet'N Low, or others)	141. Over the <u>past 12 months</u> , did you add sugar , honey or other sweeteners to your tea or coffee (hot or iced)? ☐ NO (GO TO QUESTION 142) ☐ YES
	141a. How often did you add sugar or honey to your coffee or tea (hot or iced)? ☐ Almost never or never (GO TO QUESTION 141c) ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always

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Question 142 appears on the next page

Question 141c appears on the next page

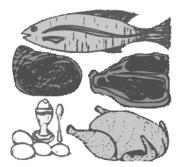
Over the past 12 months	142b. Each time non-dairy creamer was added to		
141b. Each time sugar or honey was added to your coffee or tea, how much was usually added?	your coffee or tea, how much was usually used? Less than 1 teaspoon		
☐ Less than 1 teaspoon ☐ 1 to 3 teaspoons ☐ More than 3 teaspoons	☐ 1 to 3 teaspoons ☐ More than 3 teaspoons		
141c. How often did you add artificial sweetener (such as Splenda, Equal, Sweet'N Low, or	142c. What kind of non-dairy creamer did you usually use?		
others) to your coffee or tea? Almost never or never (GO TO QUESTION 142)	☐ Regular powdered ☐ Low-fat or fat-free powdered ☐ Regular liquid		
☐ About ¼ of the time ☐ About ½ of the time	☐ Low-fat or fat-free liquid 142d. How often was cream or half and half added		
☐ About ¾ of the time ☐ Almost always or always	to your coffee or tea? Almost never or never (GO TO QUESTION 142f)		
141d. What kind of artificial sweetener did you usually use?	☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ About ¾ of the time		
☐ Equal, NutraSweet, or aspartame ☐ Sweet'N Low or cyclamate ☐ Splenda or sucralose	☐ Almost always or always		
☐ Hermesetas or saccharin ☐ Herbal sweeteners like Stevia	142e. Each time cream or half and half was added to your coffee or tea, how much was usually added?		
141e. Each time artificial sweetener was added to your coffee or tea, how much was usually added?	☐ Less than 1 tablespoon ☐ 1 to 2 tablespoons ☐ More than 2 tablespoons		
☐ Less than 1 packet or less than 1 teaspoon ☐ 1 packet or 1 teaspoon ☐ More than 1 packet or more than 1 teaspoon ■	142f. How often was milk added to your coffee or tea?		
142. Over the <u>past 12 months</u> , did you add whiteners (such as cream, milk, or non-dairy creamer) to your tea or coffee?	☐ Almost never or never (GO TO QUESTION 143) ☐ About ¼ of the time ☐ About ¾ of the time ☐ About ¾ of the time		
NO (GO TO QUESTION 143)	│		
☐ YES ↓	142g. Each time milk was added to your coffee or tea, how much was usually added?		
142a. How often was non-dairy creamer added to your coffee or tea? Almost never or never (GO TO QUESTION 142d)	☐ Less than 1 tablespoon ☐ 1 to 3 tablespoons ☐ More than 3 tablespoons		
☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	142h. What kind of milk was usually added to your coffee or tea?		
☐ Almost always or always			
▼ Question 142d appears in the next column	^¹ ↓ □ Other		
Question 143 appears on the next page	Question 143 appears on the next page 1465		

Over the past 12 months	146. Over the <u>past 12 months</u> , did you eat mayonnaise or mayonnaise-type dressing?	
143. How often was sugar or honey added to foods you ate (such as on cereal, fruit, or yogurt)? (<i>Please do not include sugar in coffee, tea, other beverages, or baked goods.)</i>	mayonnaise or mayonnaise-type dressing? NO (GO TO QUESTION 147) YES	
☐ NEVER (GO TO INTRODUCTION TO QUESTION 144)	146a. How often was the mayonnaise you ate light , low-fat or fat-free ?	
☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week ☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week ☐ 1 time per day ☐ 2 or more times per day	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	
143a. Each time sugar or honey was added to foods you ate, how much was usually added?	147. Over the past 12 months, did you eat sour cream?	
☐ Less than 1 teaspoon ☐ 1 to 2 teaspoons ☐ More than 2 teaspoons	□ NO (GO TO QUESTION 148) □ YES ↓	
The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese,	147a. How often was the sour cream you ate light , low-fat , or fat-free ?	
and salad dressing that you ate. If possible, please check the labels of these foods to help you answer.	☐ Almost never or never☐ About ¼ of the time☐ About ½ of the time	
144. Over the past 12 months, did you eat margarine?	☐ About ¾ of the time ☐ Almost always or always	
NO (GO TO QUESTION 145) YES 144a. How often was the margarine you ate light or low-fat (stick or tub)? Almost never or never About 1/4 of the time About 1/2 of the time About 3/4 of the time	▼ Allinost alliays of alliays	
☐ Almost always or always	148. Over the past 12 months, did you eat cream cheese?	
145. Over the past 12 months, did you eat butter?	☐ NO (GO TO QUESTION 149)	
☐ NO (GO TO QUESTION 146) ☐ YES 145a. How often was the butter you ate light or	☐ YES ↓ 148a. How often was the cream cheese you ate light, low-fat, or fat-free?	
low-fat? ☐ Almost never or never ☐ About 1/4 of the time ☐ About 1/2 of the time ☐ About 3/4 of the time ☐ Almost always or always	☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	

Question 146 appears in the next column

Question 149 appears on the next page

Over the past 12 months	152. Over the <u>past month</u> , which of the following foods did you eat AT LEAST THREE TIMES ?		
149. Did you eat salad dressing ?	(Mark all that apply.)		
□ NO (GO TO INTRODUCTION TO QUESTION 150) □ YES ↓ 149a How often was the salad drossing you at a light	 ☐ Avocado, guacamole ☐ Beef jerky ☐ Cheesecake ☐ Chocolate, fudge, or ☐ Game Meat (such as bison, wild goose, venison) ☐ Granola bars ☐ Hot peppers 		
149a. How often was the salad dressing you ate light, low-fat, or fat-free? ☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always	butterscotch toppings or syrups Chow mein noodles Croissants Dark chocolate Dried apricots Dried curcumin, turmeric Jell-O, gelatin Mangoes Plotives Plickles or pickled vegetables or fruit Plantains Pork neck bones, hock, head, feet		
The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.	☐ Dried oregano, rosemary, thyme ☐ Egg rolls ☐ Fresh hasil cilantro		
150. Over the past 12 months, how many servings of vegetables (not including salad or potatoes) did you eat per week or per day? ☐ Less than 1 per week ☐ 2 per day ☐ 1-2 per week ☐ 3 per day ☐ 3-4 per week ☐ 4 per day ☐ 5-6 per week ☐ 5 or more per day ☐ 1 per day ☐ 1 per day 151. Over the past 12 months, how many servings of	or parsley		
fruit (not including juices) did you eat per week or per day? Less than 1 per week	☐ YES ↓ 153a. Which of the following foods did you TOTA EXCLUDE from your diet? (Mark all that apply.) ☐ Meat (beef, pork, lamb, etc.) ☐ Poultry (chicken, turkey, duck, etc.) ☐ Fish and shellfish ☐ Eggs ☐ Dairy products (milk, cheese, etc.)		



Introduction to Question 154 appears on the next page



The next questions are about your use of vitamin pil or other supplements.	ls
154. Over the <u>past 12 months</u> , did you take any multivitamins , such as One-a-Day-, Centrum-, or Prenatal-type multivitamins (as pills, liquids, or packets)?	

· □ NO (GO TO INTRODUCTION TO QUESTION 156) r □ YES 155. How often did you take One-a-Day-, Centrum-, or Prenatal-type multivitamins? ☐ Less than 1 day per month ☐ 1-3 days per month ☐ 1-3 days per week ☐ 4-6 days per week ■ Every day 155a. Did your multivitamin usually contain minerals (such as iron, zinc, etc.)? ■ NO ☐ YES ☐ Don't know 155b. Was your multivitamin usually a Prenatal-type? □ NO ☐ YES □ Don't know 155c. For how many years have you taken multivitamins? ☐ Less than 1 year ☐ 1-4 years ☐ 5-9 years ■ 10 or more years 155d. Over the past 12 months, did you take any vitamins, minerals, or herbal supplements other than your multivitamin? **↓**□ NO Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you: . Did not skip any pages and · Crossed out the incorrect answer and circled the correct answer if you made any changes. ☐ YES (GO TO INTRODUCTION TO

These last questions are about the vitamins, minerals, or herbal supplements you took that are NOT part of a One-a-Day-, Centrum-, or Prenatal-type of multivitamin.

Over the past 12 months...

156. How often did you take Antacids that contai	n
Calcium such as Tums or Rolaids?	

	☐ NEVER (GO TO QUESTION 157)
	☐ Less than 1 day per month ☐ 1-3 days per month ☐ 1-3 days per week ☐ 4-6 days per week ☐ Every day
	156a. When you took Antacids that contain Calcium such as Tums or Rolaids, about how many tablets or lozenges did you take in one day?
	☐ Less than 1 ☐ 1 ☐ 2 ☐ 3 ☐ 4 or more ☐ Don't know
	156b. Was your Antacid usually extra strength ? ☐ NO ☐ YES ☐ Don't know
	156c. For how many years have you taken Antacids that contain Calcium such as Tums or Rolaids?
•	☐ Less than 1 year ☐ 1-4 years ☐ 5-9 years ☐ 10 or more years
	157. How often did you take Calcium (with or without Vitamin D) (NOT as part of a multivitamin in Question 155 or antacid in Question 156)?
	☐ NEVER (GO TO QUESTION 158)
	☐ Less than 1 day per month ☐ 1-3 days per month ☐ 1-3 days per week ☐ 4-6 days per week
	☐ Every day

QUESTION 156)

Introduction to Question 156 appears in the next column

Question 158 appears on the next page

Over the past 12 months	158b. For how many years have you taken Vitamin D ?
157a. When you took Calcium , about how much elemental calcium did you take in one day? (If possible, please check the label for elemental calcium.)	☐ Less than 1 year ☐ 1-4 years ☐ 5-9 years ☐ 10 or more years
☐ Less than 500 mg ☐ 500-599 mg ☐ 600-999 mg ☐ 1,000 mg or more ☐ Don't know	159. How often did you take Iron (NOT as part of a multivitamin in Question 155)? ☐ NEVER (GO TO QUESTION 160)
157b. Did your Calcium usually contain Vitamin D ? ☐ NO ☐ YES ☐ Don't know	☐ Less than 1 day per month ☐ 1-3 days per month ☐ 1-3 days per week ☐ 4-6 days per week ☐ Every day
157c. Did your Calcium usually contain Magnesium ? ☐ NO ☐ YES ☐ Don't know	159a. For how many years have you taken Iron ? ☐ Less than 1 year ☐ 1-4 years ☐ 5-9 years ☐ 10 or more years
157d. Did your Calcium usually contain Zinc? NO YES Don't know 157e. For how many years have you taken Calcium? Less than 1 year 1-4 years 5-9 years 10 or more years 158. How often did you take Vitamin D on its own or as part of a calcium supplement (NOT as part of a multivitamin in Question 155)? NEVER (GO TO QUESTION 159) Less than 1 day per month 1-3 days per week 4-6 days per week 4-6 days per week Every day 158a. When you took Vitamin D, about how much did you take in one day? Less than 400 IU 400-799 IU 800-999 IU 1,000 IU or more Don't know	160. How often did you take Folic Acid (NOT as part of a multivitamin in Question 155)? NEVER (GO TO QUESTION 161) Less than 1 day per month 1-3 days per month 1-3 days per week 4-6 days per week Every day 160a. When you took Folic Acid, about how much did you take in one day? Less than 0.4 mg 0.4-0.9 mg 1.0 mg More than 1.0 mg Don't know 160b. For how many years have you taken Folic Acid? Less than 1 year 1-4 years 5-9 years 10 or more years
Question 159 appears in the next column	Question 161 appears on the next page 1465

Question 161 appears on the next page

Over the past 12 months	The next two questions ask you about other		
161. How often did you take Vitamin C (NOT as part of a multivitamin in Question 155)? ☐ □ NEVER (GO TO QUESTION 162)	supplements you took more than once per week. 163. Please mark any of the following single supplements you took more than once per week (NOT as part of a multivitamin in Question 155):		
☐ Less than 1 day per month ☐ 1-3 days per month ☐ 1-3 days per week ☐ 4-6 days per week ☐ Every day	☐ B-6 ☐ B-complex ☐ B-12 ☐ Beta-carotene ☐ Magnesium	☐ Occu-vite/Eye health ☐ Potassium ☐ Selenium ☐ Vitamin A ☐ Zinc	
161a. When you took Vitamin C , about how much did you take in one day? □ Less than 500 mg □ 500-999 mg □ 1,000-1,499 mg □ 1,500-1,999 mg □ 2,000 mg or more □ Don't know 161b. For how many years have you taken Vitamin C ? □ Less than 1 year □ 1-4 years □ 5-9 years □ 10 or more years	164. Please mark any of the for other supplements of the formula per week. Chondroitin Coenzyme Q-10 Echinacea Energy supplements Fish oil/Omega-3's Flaxseed oil Garlic Ginger Ginkgo biloba	following herbal, botanical, you took more than once Ginseng Glucosamine Peppermint Probiotics Red clover Saw palmetto Soy supplement Sports supplements St. John's wort Other	
162. How often did you take Vitamin E (NOT as part of a multivitamin in Question 155)? NEVER (GO TO INTRODUCTION TO QUESTION 163) Less than 1 day per month 1-3 days per week 4-6 days per week Every day Less than 400 IU 400-799 IU 800-999 IU 1,000 IU or more Don't know Less than 1 year 1-4 years 5-9 years 10 or more years	Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you: Did not skip any pages and Crossed out the incorrect answer and circled the correct answer if you made any changes.		

Introduction to Question 163 appears in the next column

