# 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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# 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 (pinteraction = 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  $\leq 0.05$ ). 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  $\leq 0.06$ ). 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  $\leq 0.07$ ). 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.

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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.

# **<u>1.1 Breast Cancer</u>**

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

1

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  $\geq$  85% be achieved in ER+/PR+ and HER2- patients, and an RDI  $\geq$  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.

#### **<u>1.3 Quality of Life</u>**

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' QoL.

## 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 chemotherapyrelated 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 n-3 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 non-obese 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 moderateintensity 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  $\beta$ -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.

Variables	Total (n = 49)	<b>Placebo</b> $(n = 26)$	$\mathbf{DHA}$ (n = 23)
Age (years) <sup>1</sup>	50.8 (31-73)	51.2 (31-69)	50.4 (32-73)
<b>BMI</b> $[kg/m^2]^2$	$28.8\pm6.7$	$27.5\pm6.0$	$30.3\pm7.3$
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 <sup>3</sup>			
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 <sup>3</sup>			
No	27 (55.1%)	13 (50.0%)	14 (60.9%)
Yes	22 (44.9%)	13 (50.0%)	9 (39.1%)
Age at menarche (years) <sup>2</sup>	$12.8 \pm 1.5$	$12.7 \pm 1.7$	$12.8 \pm 1.3$
Missing values	4 (8.2%)	2 (7.7%)	2 (8.7%)
Diabetes <sup>3</sup>			
No	47 (95.9%)	26 (100.0%)	21 (91.3%)
Yes	2 (4.1%)	0 (0%)	2 (8.7%)
Ethanol abuse <sup>3</sup>			
No	48 (98.0%)	26 (100.0%)	22 (95.7%)
Yes	1 (2.0%)	0 (0%)	1 (4.3%)

Table 1. DHA WIN participant demographic and clinical characteristics.

Smokers <sup>3</sup>			
No	41 (83.7%)	21 (80.8%)	20 (87.0%)
Yes	8 (16.3%)	5 (19.2%)	3 (13.0%)
Histology <sup>3,4</sup>	0 (10.070)	5 (17.270)	5 (15.070)
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 <sup>3</sup>	2 (4.170)	1 (5.670)	1 (4.370)
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 <sup>3</sup>			()
T1	1 (2.0%)	1 (3.8%)	0 (0.0%)
T2	26 (53.1%)	14 (53.8%)	12 (52.2%)
T3	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 <sup>3</sup>	0 (12.270)	5 (11.570)	5 (15.070)
N0	12 (24.5%)	6 (23.1%)	6 (26.1%)
N0 N1	20 (40.8%)	10 (38.5%)	10 (43.5%)
N1 N2	5 (10.2%)	3 (11.5%)	2 (8.7%)
N2 N3	2 (4.1%)	1 (3.9%)	2 (8.776) 1 (4.4%)
Unknown	10 (20.4%)	6 (23.1%)	4 (17.4%)
ECOG <sup>3,5</sup>	10 (20.470)	0 (23.170)	4 (17.470)
Baseline			
0	11 (00 00/)	24(02,20/)	20(97.00/)
	44 (89.8%)	24 (92.3%)	20 (87.0%)
] Unimerum	2(4.1%)	2 (7.7%)	0 (0.0%)
Unknown End of treatment	3 (6.1%)	0 (0.0%)	3 (13.0%)
0	25(71.40/)	22(94(0))	12 (56 50/)
0	35 (71.4%)	22 (84.6%)	13 (56.5%)
2	10(20.4%)	2 (7.7%)	8 (34.8%)
	2(4.1%)	1(3.8%)	1 (4.3%)
Unknown Total recervited (n)	2 (4.1%)	1 (3.8%)	1 (4.3%)
Total recruited (n)	76	39	37
<b>Overall compliance</b> <sup>2</sup>	$83.9\pm20.0$	$81.3\pm22.5$	$86.3 \pm 17.7$
Missing values <sup>3</sup>	13 (26.5%)	9 (34.6%)	4 (17.4%)

# Pathological complete response<sup>3</sup>

No	32 (65.3%)	19 (73.1%)	13 (56.5%)
Yes	17 (34.7%)	7 (26.9%)	10 (43.5%)
<sup>1</sup> Mean (range); <sup>2</sup> Mean	$\pm$ SD; <sup>3</sup> Count (percentage of total of	or given treatment g	group); <sup>4</sup> HER2+

(ER-, PR-, HER2+), TNBC (ER-, PR-, HER2-), Luminal A (ER+ and/or PR+, HER2-), Luminal B (ER+ and/or PR+, HER2+);  ${}^{5}0$  = 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  $\leq 0.05$ . 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 ( $\geq 150$  minutes/week) over time.

	≥ 150 minute aerobic ez		
	Yes	No	p-value
<b>Week 0</b> $(n = 46)$			
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%)	
<b>Week 3</b> $(n = 45)$			
DHA	5 (23.8%)	16 (76.2%)	0.53
Placebo	8 (33.3%)	16 (66.7%)	0.55
Total	13 (28.9%)	32 (71.1%)	
<b>Week 6</b> $(n = 47)$			
DHA	5 (22.7%)	17 (77.3%)	0.23
Placebo	10 (40.0%)	15 (60.0%)	0.25
Total	15 (31.9%)	32 (68.1%)	
<b>Week 9</b> $(n = 47)$			
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%)	
<b>Week 12</b> $(n = 47)$			
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%)	

<b>Week 15</b> $(n = 45)$			
DHA	4 (20.0%)	16 (80.0%)	0.73
Placebo	7 (28.0%)	18 (72.0%)	0.75
Total	11 (24.4%)	34 (75.6%)	
<b>Week 18</b> (n = 42)			
DHA	4 (21.1%)	15 (78.9%)	0.73
Placebo	7 (30.4%)	16 (69.6%)	0.75
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 ( $\geq 2$  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).

	≥ 2 times/week training o			
	Yes	No	p-value	
<b>Week 0</b> $(n = 47)$				
DHA	5 (22.7%)	17 (77.3%)	0.36	
Placebo	9 (36.0%)	16 (64.0%)	0.30	
Total	14 (29.8%)	33 (70.2%)		
<b>Week 3</b> $(n = 45)$				
DHA	4 (19.0%)	17 (81.0%)	1.00	
Placebo	5 (20.8%)	19 (79.2%)	1.00	
Total	9 (20.0%)	36 (80.0%)		
<b>Week 6</b> $(n = 47)$				
DHA	5 (22.7%)	17 (77.3%)	0.26	
Placebo	9 (36.0%)	16 (64.0%)	0.36	
Total	14 (29.8%)	33 (70.2%)		
<b>Week 9</b> $(n = 47)$				
DHA	5 (22.7%)	17 (77.3%)	0.52	
Placebo	8 (32.0%)	17 (68.0%)	0.53	
Total	13 (27.7%)	34 (72.3%)		
<b>Week 12</b> $(n = 47)$				
DHA	3 (13.6%)	19 (86.4%)	0.47	
Placebo	6 (24.0%)	19 (76.0%)	0.47	
Total	9 (19.1%)	38 (80.9%)		

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

<b>Week 15</b> $(n = 45)$			
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%)	
<b>Week 18</b> (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 ( $\geq 2$  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).

	$\mathbf{DHA}$ (n = 22)	<b>Placebo</b> $(n = 24)$	p-value
Energy (kcal)	$1684\pm568$	$1821\pm1255$	0.64
% from carbohydrate	$48.7\pm10.0$	$48.0\pm9.5$	0.82
% from fat	$34.3\pm 6.9$	$36.4\pm7.3$	0.32
% from protein	$17.1\pm3.6$	$16.8\pm3.6$	0.79
% from alcohol	$2.0\pm3.1$	$1.5 \pm 2.2$	0.57
Carbohydrate (g)	$212\pm109$	$218\pm156$	0.90
Protein (g)	$69.8\pm21.7$	$78.2\pm58.6$	0.53
Total fat (g)	$62.2\pm19.5$	$74.1\pm54.6$	0.34
Total monounsaturated fatty acids (g)	$25.1\pm8.1$	$29.6\pm22.1$	0.37
Total polyunsaturated fatty acids (g)	$10.5\pm3.4$	$14.8 \pm 14.7$	0.19
PUFA 18:2 (Octadecadienoic acid) (g)	$8.3\pm2.9$	$12.1\pm12.5$	0.17
PUFA 18:3 (Octadecatrienoic acid) (g)	$1.8\pm0.7$	$2.2\pm1.8$	0.32
Total saturated fatty acids (g)	$20.8\pm8.3$	$23.1\pm17.0$	0.56
Cholesterol (mg)	$233\pm79$	$249\pm156$	0.67
Sodium (mg)	$2492\pm934$	$2880\pm2237$	0.45
Sugar (g)	$103\pm80$	$93\pm77$	0.65
Dietary fiber (g)	$18.3\pm8.9$	$22.7\pm19.4$	0.33

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

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  $20.6 \pm 15.3$  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%

<sup>1</sup>AMDR 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  $p \le 0.05$ ).

	<b>DHA WIN</b> $(n = 46)$	<b>CCHS</b> (n = 696)	p-value
Energy (kcal/day)	$1755\pm980$	$1575\pm923$	0.20
% from carbohydrate	$48.3\pm9.7$	$47.6\pm13.2$	0.71
% from fat	$35.4\pm7.1$	$33.0\pm10.6$	0.14
% from protein	$16.9\pm3.6$	$16.7\pm5.3$	0.76
Carbohydrate (g/day)	$215\pm135$	$188\pm132$	0.18
Protein (g/day)	$74.2\pm44.6$	$65.0\pm26.4$	0.03
Total fat (g/day)	$68.4\pm41.7$	$60.0\pm26.4$	0.05
Total monounsaturated fatty acids (g/day)	$27.4\pm16.9$	$21.9\pm13.2$	0.01
Total polyunsaturated fatty acids (g/day)	$12.8\pm11.0$	$12.3\pm7.9$	0.71
Total saturated fatty acids (g/day)	$22.0\pm13.5$	$19.8\pm13.2$	0.27
Cholesterol (mg/day)	$241\pm124$	$218\pm185$	0.40
Sodium (mg/day)	$2695\pm1733$	$2206\pm1398$	0.02
Total sugar (g/day)	$97.8\pm77.8$	$77.0\pm79.1$	0.08
Dietary fiber (g/day)	$20.6\pm15.3$	$14.9\pm10.6$	<0.001

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

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 > 0.05).

				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	$88.9 \pm 14.0$	$82.2\pm17.0$	-6.7 (-16.0 to 2.7)	0.82	0.44	<0.001	0.65	0.36	<0.001
Placebo	$85.2 \pm 14.1$	$79.4\pm16.0$	-5.9 (-14.9 to 3.1)	0.82	0.44	~0.001	0.05	0.30	~0.001
Physical WB									
DHA	$24.6\pm4.4$	$21.8\pm5.0$	-2.8 (-5.6 to 0.0)	0.69	0.70	<0.001	0.95	0.46	<0.001
Placebo	$24.5\pm4.4$	$21.1 \pm 6.8$	-3.4 (-6.7 to 0.1)	0.69	0.79	<0.001	0.85	0.46	<0.001
Social WB									
DHA	$24.8\pm4.3$	$23.2\pm4.8$	-1.6 (-4.3 to 1.1)	0.87	0.26	<0.001	0.72	0.14	<0.001
Placebo	$23.3 \pm 5.1$	$21.6 \pm 5.4$	-1.7 (-4.7 to 1.3)	0.87 0.26	~0.001	0.72	0.14	<b>\0.001</b>	
<b>Emotional WB</b>									
DHA	$17.6 \pm 4.8$	$18.8\pm4.2$	+1.2 (-1.5 to 3.9)	0.57	0.02	0.01	0.65	0.97	0.01
Placebo	$17.1 \pm 5.1$	$19.1 \pm 3.9$	+2.0 (-0.5 to 4.6)	0.57	0.83	0.01	0.65	0.87	0.01
Functional									
WB									
DHA	$21.9\pm5.9$	$18.4\pm5.8$	-3.5 (-7.0 to 0.0)	0.33	0.43	<0.001	0.35	0.52	<0.001
Placebo	$20.1\pm5.1$	$18.0\pm5.2$	-2.1 (-5.0 to 0.8)	0.55	0.45	~0.001	0.35	0.32	~0.001
FACT-B total									
score									
DHA	$118.6\pm17.0$	$108.5\pm21.8$	-10.2 (-21.9 to 1.6)	0.86	0.73	<0.001	0.75	0.64	<0.001
Placebo	$115.7\pm18.0$	$106.9\pm19.9$	-8.8 (-19.8 to 2.2)	0.00	0.75	-0.001	0.75	0.04	-0.001
FACT-B TOI									
DHA	$76.2\pm12.5$	$66.5\pm15.0$	-9.8 (-18.0 to -1.5)	0.91	1.00	<0.001	0.83	0.95	<0.001
Placebo	$75.8\pm11.2$	$66.3\pm13.7$	-9.5 (-16.6 to -2.3)	0.71	1.00	~0.001	0.05	0.25	~0.001

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

BC subscale									
score									
DHA	$29.7\pm5.9$	$26.2\pm6.7$	-3.5 (-7.3 to 0.3)	0.88	0.24	<0.001	0.93	0.11	<0.001
Placebo	$31.2\pm4.4$	$27.8\pm5.5$	-3.3 (-6.1 to -0.5)	0.00	0.24	<b>~0.001</b>	0.75	0.11	-0.001
FACT-Taxane									
total score									
DHA	$150.2\pm18.4$	$136.9\pm21.4$	-13.3 (-25.3 to -1.3)	0.95	0.72	<0.001	0.84	0.73	<0.001
Placebo	$147.8\pm15.1$	$135.1\pm21.4$	-12.7 (-23.6 to -1.8)	0.75	0.72	-0.001	0.04	0.75	-0.001
FACT-Taxane									
ΤΟΙ									
DHA	$107.8\pm14.8$	$94.8\pm14.8$	-12.9 (-21.8 to -4.1)	0.75	0.87	<0.001	0.74	0.97	<0.001
Placebo	$105.9\pm12.2$	$94.5\pm17.3$	-11.3 (-20.0 to -2.6)	0.75	0.07	-0.001	0.71	0.97	-0.001
Taxane									
subscale score									
DHA	$61.3\pm6.0$	$54.6\pm7.1$	-6.6 (-10.6 to -2.7)	0.47	0.73	<0.001	0.46	0.12	<0.001
Placebo	$60.9\pm6.5$	$56.0\pm9.3$	-4.9 (-9.5 to -0.3)	0.47	0.75	~0.001	0.40	0.12	<b>\0.001</b>
FACT-ES total									
score									
DHA	$154.9\pm21.5$	$145.7\pm22.9$	-9.2 (-22.5 to 4.2)	0.62	0.95	<0.001	0.68	0.96	<0.001
Placebo	$155.3\pm17.0$	$144.6\pm21.1$	-10.7 (-22.0 to 0.6)	0.02	0.95	~0.001	0.08	0.90	~0.001
ES subscale									
score									
DHA	$66.0\pm9.4$	$63.5 \pm 8.1$	-2.5 (-7.7 to 2.8)	0.51	0.11	0.01	0.44	0.05	0.03
Placebo	$69.6\pm4.9$	$65.4 \pm 7.7$	-4.2 (-7.8 to -0.5)	0.31	0.11	0.01	0.44	0.05	0.03
Fatigue									
subscale score									
DHA	$44.3 \pm 11.1$	$38.0\pm10.7$	-6.3 (-12.9 to 0.3)	0.66	0.82	<0.001	0.70	0.66	<0.001
Placebo	$43.1 \pm 8.2$	$38.0\pm10.9$	-5.2 (-10.6 to 0.2)	0.66	0.82	<0.001	0.70	0.66	<0.001
<b>PSS score</b>									
DHA	$19.7 \pm 7.2$	$18.0 \pm 9.2$	-1.7 (-6.6 to 3.2)	0.04	0.50	0.00	0.02	0.00	0.00
Placebo	$20.2\pm8.5$	$19.2 \pm 8.7$	-1.0 (-5.9 to 3.8)	0.84	0.72	0.22	0.92	0.80	0.29

<b>CES-D</b> score									
DHA	$7.0 \pm 3.2$	$7.3\pm4.0$	+0.3 (-1.9 to 2.4)	0.78	0.69	0.38	0.84	0.96	0.37
Placebo	$7.3\pm4.3$	$7.8\pm3.9$	+0.5 (-1.8 to 2.8)	0.78	0.09	0.38	0.64	0.90	0.37
STAI score									
DHA	$20.4\pm7.0$	$18.7\pm6.6$	-1.7 (-5.8 to 2.4)	0.89	0.86	0.04	0.79	0.88	0.01
Placebo	$20.8\pm 6.1$	$18.9\pm 6.0$	-1.9 (-5.3 to 1.5)	0.89	0.80	0.04	0.79	0.88	0.01
Fordyce									
Emotions									
Combination									
score									
DHA	$59.4\pm24.3$	$63.5\pm21.8$	+4.1 (-10.2 to 18.5)	0.16	0.60	0.01	0.14	0.36	0.03
Placebo	$57.6\pm22.4$	$68.1 \pm 17.4$	+10.5 (-1.2 to 22.2)	0.10	0.00	0.01	0.14	0.50	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).

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#### 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  $\leq 0.06$ ), except emotional well-being, which increased in all groups (p-time  $\leq 0.06$ ) (Tables 8-11). Anxiety decreased over time in all groups (p-time  $\leq 0.03$ ) while the happiness measure increased over time (p-time  $\leq 0.07$ ).

# 5.1.2.1 Aerobic Exercise Classification at Baseline and QoL

On average, participants that reported  $\geq 150$  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 ± 3.9 versus 60.1 ± 7.2) and end of treatment (56.3 ± 10.7 versus 55.0 ± 7.2) (p-recommendation < 0.002) and a greater happiness

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

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				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									
$\geq$ 150 min/week	$85.4 \pm 15.6$	$80.1 \pm 15.2$	-5.4 (-17.1 to 6.4)	0.12	0.64	~0.001	0.05	0.61	<0.001
< 150 min/week	$87.2 \pm 13.5$	$79.7 \pm 16.7$	-7.4 (-15.6 to 0.7)	0.12	0.04	<0.001	0.05	0.61	<0.001
Physical WB									
$\geq$ 150 min/week	$24.4\pm5.4$	$21.2 \pm 7.3$	-3.2 (-7.9 to 1.6)	0.86	0.96	<0.001	0.78	0.56	<0.001
< 150 min/week	$24.6\pm3.9$	$21.3 \pm 5.5$	-3.3 (-5.8 to -0.9)	0.80	0.90	<0.001	0.78	0.30	<0.001
Social WB									
$\geq$ 150 min/week	$24.4\pm6.0$	$22.4\pm6.4$	-2.0 (-6.6 to 2.6)	0.76	0.83	<0.001	0.82	0.82	<0.001
< 150 min/week	$23.9\pm4.2$	$22.2\pm4.6$	-1.6 (-3.9 to 0.6)			<0.001			<0.001
<b>Emotional WB</b>									
$\geq$ 150 min/week	$14.9\pm5.5$	$18.2\pm3.0$	+3.3 (0.1 to 6.6)	0.05	0.07	<0.001	0.05	0.18	<0.001
< 150 min/week	$18.1 \pm 4.2$	$19.0\pm4.3$	+0.9 (-1.3 to 3.1)	0.05		<0.001	0.05	0.18	<0.001
<b>Functional WB</b>									
$\geq$ 150 min/week	$20.1\pm4.7$	$18.9\pm4.9$	-1.2 (-4.7 to 2.3)	0.10	0.76	<0.002	0.09	0.82	~0.001
< 150 min/week	$21.0\pm5.9$	$17.2 \pm 5.3$	-3.8 (-6.7 to -0.8)	0.10	0.70	<b>\0.002</b>	0.09	0.82	<0.001
FACT-B total score									
$\geq$ 150 min/week	$114.6\pm21.2$	$106.2\pm19.8$	-8.4 (-23.8 to 7.0)	0.44	0.70	<0.001	0.41	0.65	~0.001
< 150 min/week	$117.6\pm15.5$	$106.8\pm20.8$	-10.9 (-20.6 to -1.2)	0.44	0.70	~0.001	0.41	0.05	<0.001
FACT-B TOI									
$\geq$ 150 min/week	$75.4\pm13.6$	$65.8\pm13.9$	-9.5 (-19.8 to 0.7)	0.68	0.99	~0.001	0.69	0.02	~0.001
< 150 min/week	$75.9 \pm 11.1$	$65.5\pm14.1$	-10.3 (-17.0 to -3.7)	0.08	0.99	.99 <0.001	0.68	0.93	<0.001
BC subscale score									
$\geq$ 150 min/week	$30.9\pm6.2$	$26.8\pm 6.5$	-4.1 (-8.8 to 0.6)	0.73	0 00	<0.001	0.75	0.71	<0.001
< 150 min/week	$30.3\pm4.9$	$27.0\pm5.9$	-3.2 (-6.1 to -0.4)	0.73	0.88		0.75	0.71	~0.001

 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.</th>

ITTOI TURANC COUNT									
score									
$\geq$ 150 min/week	$148.0\pm17.5$	$135.9\pm24.1$	-12.1 (-28.0 to 3.9)	0.59	0.99	<0.001	0.52	0.77	<0.001
< 150 min/week	$148.5\pm16.9$	$134.7\pm19.9$	-13.8 (-23.5 to -4.0)	0.39	0.99	~0.001	0.52	0.77	~0.001
FACT-Taxane TOI									
$\geq$ 150 min/week	$107.8\pm12.7$	$95.5\pm20.2$	-12.2 (-25.0 to 0.5)	0.94	0.61	<0.001	0.95	0.07	<0.001
< 150 min/week	$105.6\pm14.3$	$93.4 \pm 14.0$	-12.1 (-19.5 to -4.7)	0.94	0.01	~0.001	0.95	0.07	~0.001
Taxane subscale									
score									
$\geq$ 150 min/week	$62.5\pm3.9$	$56.3\pm10.7$	-6.2 (-12.2 to -0.2)	0.65	0.32	<0.001	0.73	<0.002	<0.001
< 150 min/week	$60.1\pm7.2$	$55.0\pm7.2$	-5.2 (-8.9 to -1.4)	0.05	0.52	~0.001	0.75	~0.002	~0.001
FACT-ES total									
score									
$\geq$ 150 min/week	$154.6\pm19.0$	$143.4\pm20.8$	-11.1 (-26.3 to 4.0)	0.97	0.88	<0.001	0.98	0.71	<0.001
< 150 min/week	$154.3 \pm 19.7$	$144.5\pm22.3$	-9.9 (-21.0 to 1.3)	0.97		~0.001	0.98	0.71	~0.001
ES subscale score									
$\geq$ 150 min/week	$69.1\pm4.9$	$63.8\pm8.6$	-5.4 (-10.6 to -0.1)	0.26	0.72	0.01	0.31	0.78	0.01
< 150 min/week	$67.1\pm8.7$	$64.7\pm7.8$	-2.3 (-6.6 to 2.0)	0.20	0.72	0.01	0.51	0.78	0.01
Fatigue subscale									
score									
$\geq$ 150 min/week	$44.3\pm9.6$	$40.1\pm13.1$	-4.2 (-12.6 to 4.2)	0.30	0.38	<0.001	0.33	0.09	<0.001
< 150 min/week	$43.0\pm10.1$	$36.4\pm9.5$	-6.6 (-11.7 to -1.5)	0.50	0.50	~0.001	0.55	0.09	~0.001
PSS score									
$\geq$ 150 min/week	$21.6\pm8.8$	$17.5\pm8.4$	-4.0 (-10.4 to 2.3)	0.01	0.98	0.02	0.01	0.13	0.02
< 150 min/week	$19.4\pm7.1$	$19.7\pm8.7$	+0.3 (-3.8 to 4.4)	0.01	0.98	0.02	0.01	0.15	0.02
<b>CES-D</b> score									
$\geq$ 150 min/week	$8.1\pm5.1$	$7.5\pm4.2$	-0.6 (-4.0 to 2.9)	0.10	0.73	0.66	0.09	0.94	0.64
< 150 min/week	$6.9\pm3.0$	$7.9\pm3.7$	+1.0 (-0.7 to 2.8)	0.10	0.75	0.00	0.09	0.94	0.04
STAI score									
$\geq$ 150 min/week	$22.3\pm 6.9$	$17.5 \pm 6.1$	-4.7 (-9.5 to 0.1)	0.01	0.00	<0.003	0.01	0.46	~0.001
< 150 min/week	$20.0\pm 6.3$	$19.8\pm6.2$	-0.2 (-3.4 to 3.0)	0.01	0.98	~0.003	0.01	0.46	<0.001

**FACT-Taxane total** 

Fordyce Emotions Combination score									
$\geq$ 150 min/week	$60.5\pm21.0$	$72.4\pm13.3$	+12.0 (-1.1 to 25.0)	0.19	0.16	0.01	0.21	0.02	0.01
< 150 min/week	$57.2\pm24.7$	$60.5\pm20.9$	+3.3 (-9.1 to 15.7)	0.19	0.10	0.01	0.21	0.03	0.01

16 participants reported  $\geq$  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).

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**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), precommendation (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.

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			-	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									
$\geq$ 150 min/week	$87.7\pm16.7$	$85.7\pm13.9$	-2.1 (-16.0 to 11.9)	0.01	0.59	<0.001	0.01	0.65	<0.001
< 150 min/week	$88.3 \pm 14.6$	$79.4 \pm 18.0$	-8.9 (-17.5 to -0.3)	0.01	0.39	~0.001	0.01	0.03	<b>\0.001</b>
Physical WB									
$\geq$ 150 min/week	$25.3\pm2.5$	$22.9\pm5.7$	-2.4 (-6.3 to 1.5)	0.46	0.34	<0.001	0.35	0.87	<0.001
< 150 min/week	$24.5\pm5.1$	$21.0\pm6.5$	-3.5 (-6.5 to -0.5)		0.34	~0.001	0.55	0.87	<b>\0.001</b>
Social WB									
$\geq$ 150 min/week	$22.4\pm6.7$	$21.6\pm6.9$	-1.1 (-7.2 to 4.9)	0.57	0.36	<0.005	0.53	0.11	<0.005
< 150 min/week	$24.5\pm4.2$	$22.9\pm4.3$	-1.6 (-3.8 to 0.6)		0.50	-0.005	0.55	0.11	<0.003
<b>Emotional WB</b>									
$\geq$ 150 min/week	$17.9\pm3.7$	$19.7\pm2.5$	+1.8 (-1.0 to 4.6)	0.53	0.73	0.01	0.56	0.36	0.01
< 150 min/week	$17.9\pm5.0$	$19.0\pm4.5$	+1.1 (-1.3 to 3.6)	0.55	0.75	0.01	0.50	0.30	0.01
<b>Functional WB</b>									
$\geq$ 150 min/week	$21.8\pm5.3$	$21.8\pm2.7$	0.0 (-3.8 to 3.8)	0.01	0.05	0.01	0.01	0.98	0.01
< 150 min/week	$21.0 \pm 6.1$	$16.9\pm5.7$	-4.1 (-7.1 to -1.1)	0.01	0.03	0.01	0.01	0.98	0.01
FACT-B total score									
$\geq$ 150 min/week	$119.7\pm20.9$	$112.4\pm19.9$	-7.3 (-25.9 to 11.4)	0.14	0.56	<0.001	0.10	0.76	<0.001
< 150 min/week	$117.8\pm17.7$	$106.1 \pm 22.3$	-11.6 (-22.0 to -1.2)	0.14	0.50	~0.001	0.10	0.70	~0.001
FACT-B TOI									
$\geq$ 150 min/week	$79.2 \pm 12.1$	$71.4\pm13.1$	-7.8 (-19.3 to 3.8)	0.25	0.19	<0.001	0.20	0.81	<0.001
< 150 min/week	$75.8\pm12.5$	$64.4 \pm 15.2$	-11.4 (-18.5 to -4.3)	0.25	0.19	<b>\0.001</b>	0.20	0.81	<b>\0.001</b>
BC subscale score									
$\geq$ 150 min/week	$31.9\pm5.3$	$26.7\pm7.0$	-5.2 (-10.9 to 0.5)	0.22	0.70	<0.001	0.19	0.98	<0.001
< 150 min/week	$30.2 \pm 5.1$	$27.0\pm6.3$	-3.2 (-6.1 to -0.3)	0.22	0.70	~0.001	0.17	0.20	~0.001

 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.</th>

score										
$\geq 150$	) min/week	$151.6\pm16.7$	$140.8\pm16.6$	-10.9 (-26.1 to 4.3)	0.34	0.42	<0.001	0.31	0.51	<0.001
< 150	) min/week	$149.5\pm18.3$	$134.3\pm23.9$	-15.2 (-26.3 to -4.1)	0.54	0.42	<b>\0.001</b>	0.51	0.51	~0.001
FACT-1	<b>Faxane TOI</b>									
$\geq 150$	) min/week	$111.1 \pm 7.7$	$99.8 \pm 11.8$	-11.3 (-20.5 to -2.1)	0.73	0.08	<0.001	0.63	0.87	<0.001
< 150	) min/week	$105.8\pm15.7$	$92.5\pm17.8$	-13.3 (-22.0 to -4.7)	0.75	0.08	~0.001	0.05	0.87	~0.001
Taxane	subscale									
score										
$\geq 150$	) min/week	$63.9\pm0.3$	$55.1\pm8.5$	-8.8 (-14.6 to -3.1)	0.17	0.26	<0.001	0.18	0.48	<0.001
< 150	) min/week	$59.9\pm7.3$	$55.1\pm8.8$	-4.8 (-8.9 to -0.7)	0.17	0.20	<b>\0.001</b>	0.18	0.40	~0.001
FACT-E	ES total									
score										
$\geq 150$	) min/week	$157.1\pm17.9$	$149.8\pm22.0$	-7.3 (-25.8 to 11.1)	0.30	0.62	<0.001	0.28	0.48	<0.001
< 150	) min/week	$156.2 \pm 21.3$	$144.2\pm23.1$	-12.1 (-23.7 to -0.4)	0.30	0.02	<0.001	0.28	0.40	~0.001
ES subs	cale score									
$\geq 150$	) min/week	$70.0\pm3.6$	$64.1 \pm 10.1$	-5.9 (-12.6 to 0.9)	0.33	0.67	<0.009	0.31	0.46	0.01
< 150	) min/week	$67.5\pm9.1$	$64.9\pm7.4$	-2.6 (-6.9 to 1.6)	0.55	0.07	<b>\0.009</b>	0.51	0.40	0.01
Fatigue	subscale									
score										
$\geq 150$	) min/week	$45.6\pm7.4$	$40.9\pm12.1$	-4.8 (-13.7 to 4.2)	0.46	0.30	<0.001	0.39	0.77	<0.001
< 150	) min/week	$43.2\pm10.9$	$36.6\pm10.9$	-6.5 (-12.1 to -1.0)	0.40	0.30	<b>\0.001</b>	0.39	0.77	~0.001
PSS scor	re									
$\geq 150$	) min/week	$20.5\pm8.3$	$17.9\pm8.8$	-2.6 (-10.3 to 5.0)	0.30	0.93	0.12	0.25	0.65	0.16
< 150	) min/week	$19.3\pm8.3$	$18.7\pm9.6$	-0.5 (-5.1 to 4.0)	0.50	0.95	0.12	0.23	0.05	0.10
CES-D s	score									
$\geq 150$	) min/week	$7.2 \pm 5.3$	$6.8 \pm 4.7$	-0.4 (-4.8 to 4.0)	0.17	0.85	0.54	0.15	0.84	0.40
< 150	) min/week	$6.7 \pm 3.3$	$7.8 \pm 3.9$	+1.0 (-0.8 to 2.9)	0.17	0.85	0.54	0.15	0.84	0.49
STAI sc	ore			· · /						
≥150	) min/week	$19.5 \pm 5.8$	$16.6 \pm 6.0$	-2.9 (-8.1 to 2.3)	0.22	0.20	0.01	0.24	0.47	0.01
< 150	) min/week	$20.2\pm6.9$	$19.2 \pm 6.4$	-1.0 (-4.4 to 2.4)	0.23	0.39	0.01	0.24	0.47	0.01
				. , , ,						

**FACT-Taxane total** 

# Fordyce Emotions Combination score

$\geq$ 150 min/week	$70.0\pm15.5$	$78.4 \pm 12.0$	+8.4 (-4.4 to 21.2)	0 14 ~0 003	0.01	0.11	<0.003	0.01
<150 min/week	$58.0\pm25.3$	$61.4\pm20.8$	+3.4 (-8.8 to 15.6)	0.14 \0.003	0.01	0.11	<b>~0.002</b>	0.01

11 participants reported  $\geq$  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).

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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  $\leq$ 0.05. Abbreviations: p-interaction (p-int; p time\*recommendation), p-recommendation (p-rec), World Health Organization (WHO), Functional Assessment of Cancer Therapy-General (FACT-G), recommendation (rec), body mass index (BMI).


Week

**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 ± 7.0 versus  $20.9 \pm 6.5$ ) and at the end of chemotherapy ( $17.9 \pm 6.6$  versus  $19.3 \pm 6.1$ ) (p-recommendation = 0.02) and a greater happiness score at baseline ( $68.5 \pm 17.3$  versus  $55.0 \pm 24.4$ ) and at the end of chemotherapy ( $73.1 \pm 13.8$  versus  $61.6 \pm 20.8$ ) (p-recommendation = 0.01). These changes are shown in Table 10.

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				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	$88.8 \pm 11.6$	$85.9\pm10.2$	-2.8 (-11.3 to 5.7)	0.06	0.17	<0.001	0.04	0.44	~0.001
< 2 times/week	$86.1 \pm 15.4$	$78.0\pm18.2$	-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	$25.9\pm2.4$	$23.6\pm4.6$	-2.2 (-5.1 to 0.7)	0.39	0.03	<0.001	0.24	0.67	<0.001
< 2 times/week	$23.9\pm4.9$	$20.4\pm6.4$	-3.5 (-6.4 to -0.7)		0.03	<0.001	0.24	0.67	<0.001
Social WB									
$\geq$ 2 times/week	$24.6\pm3.3$	$23.8\pm4.2$	-0.8 (-3.7 to 2.2)	0.20	0.20	0.01	0.17	0.22	0.01
< 2 times/week	$23.9\pm5.3$	$21.8\pm5.5$	-2.2 (-4.9 to 0.5)		0.30	0.01	0.17	0.23	0.01
<b>Emotional WB</b>									
$\geq$ 2 times/week	$16.3\pm6.0$	$19.0 \pm 3.4$	+2.7 (-1.1 to 6.5)	0.01	0.72	<0.003	0.20	0.70	<0.003
< 2 times/week	$17.5 \pm 4.4$	$18.8\pm4.2$	+1.3 (-0.9 to 3.4)	0.21	0.73	<0.002	0.28	0.79	<0.002
<b>Functional WB</b>									
$\geq$ 2 times/week	$22.0\pm3.4$	$19.5\pm4.0$	-2.5 (-5.5 to 0.4)	0.78	0.11	0.11 < <b>0.001</b>	0.70	0.42	<0.001
< 2 times/week	$20.3\pm6.2$	$17.4 \pm 5.7$	-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	$119.9\pm16.9$	$114.1 \pm 15.2$	-5.8 (-18.2 to 6.7)	0.10	0.20	<0.001	0.06	0.67	<0.001
< 2 times/week	$115.7\pm18.1$	$104.4\pm22.4$	-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	$79.0\pm10.7$	$71.3 \pm 10.2$	-7.7 (-15.9 to 0.4)	0.24	0.00	<0.001	0.20	0.97	<0.001
< 2 times/week	$74.5\pm12.2$	$63.9\pm15.4$	-10.6 (-17.6 to -3.6)	0.34	0.08	<0.001	0.20	0.87	<0.001
BC subscale score									
$\geq$ 2 times/week	$31.1 \pm 6.1$	$28.1 \pm 6.1$	-3.0 (-7.7 to 1.8)	0.74	0.51	<0.001	0.64	0.49	<0.001
< 2 times/week	$30.3\pm5.0$	$26.7\pm6.2$	-3.6 (-6.4 to -0.8)	0.74	0.51	<0.001	0.64	0.48	<0.001

 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.</th>

FACT-Taxane total									
score									
$\geq$ 2 times/week	$154.1\pm8.0$	$141.9\pm13.2$	-12.3 (-21.0 to -3.5)	0.55	0.07	<0.001	0.37	0.58	<0.001
< 2 times/week	$146.4 \pm 19.2$	$133.0\pm23.8$	-13.4 (-24.4 to -2.5)	0.55	0.07	-0.001	0.57	0.50	\$0.001
FACT-Taxane TOI									
$\geq$ 2 times/week	$112.1 \pm 4.2$	$99.1\pm9.7$	-13.0 (-19.0 to -7.0)	0.68	0.02	<0.001	0.97	0.55	<0.001
< 2 times/week	$104.2\pm15.4$	$92.5\pm18.1$	-11.7 (-20.2 to -3.3)	0.08	0.02	~0.001	0.97	0.55	-0.001
Taxane subscale									
score									
$\geq$ 2 times/week	$63.1 \pm 1.8$	$55.9\pm7.4$	-7.1 (-11.5 to -2.8)	0.32	0.21	<0.001	0.32	0.78	<0.001
< 2 times/week	$60.1 \pm 7.2$	$55.3\pm8.8$	-4.9 (-8.9 to -0.9)	0.52	0.21	~0.001	0.52	0.78	-0.001
FACT-ES total									
score									
$\geq$ 2 times/week	$161.1 \pm 10.1$	$151.1 \pm 17.6$	-10.0 (-21.5 to 1.5)	0.72	0.09	<0.001	0.56	0.76	<0.001
< 2 times/week	$152.3 \pm 21.7$	$142.1 \pm 23.3$	-10.3 (-21.7 to 1.2)	0.72	0.07	<b>~0.001</b>	0.50	0.70	-0.001
ES subscale score									
$\geq$ 2 times/week	$70.1\pm3.5$	$65.2\pm8.8$	-4.9 (-10.3 to 0.5)	0.41	0.24	0.01	0.47	0.64	0.01
< 2 times/week	$67.0\pm8.6$	$64.2\pm7.6$	-2.8 (-6.8 to 1.3)	0.41	0.24	0.01	0.47	0.04	0.01
Fatigue subscale									
score									
$\geq$ 2 times/week	$46.5 \pm 7.1$	$42.9\pm9.9$	-3.6 (-10.3 to 3.0)	0.29	0.03	<0.001	0.28	0.64	<0.001
< 2 times/week	$42.3 \pm 10.5$	$35.7\pm10.7$	-6.5 (-11.8 to -1.3)	0.27	0.05	<b>~0.001</b>	0.20	0.04	-0.001
PSS score									
$\geq$ 2 times/week	$20.7\pm7.6$	$18.1 \pm 7.4$	-2.6 (-8.5 to 3.2)	0.30	0.93	0.06	0.25	0.73	0.09
< 2 times/week	$19.6\pm8.0$	$18.8\pm9.6$	-0.8 (-5.2 to 3.6)	0.50	0.75	0.00	0.25	0.75	0.07
<b>CES-D</b> score									
$\geq$ 2 times/week	$6.5\pm3.5$	$7.1 \pm 3.7$	+0.6 (-2.2 to 3.4)	0.86	0.33	0.40	0.91	0.59	0.37
< 2 times/week	$7.6\pm4.0$	$8.0\pm4.0$	+0.4 (-1.6 to 2.4)	0.80	0.55	0.40	0.91	0.39	0.37
STAI score									
$\geq$ 2 times/week	$19.8\pm7.0$	$17.9\pm6.6$	-1.9 (-7.2 to 3.4)	0.84	0.47	0.05	0.96	0.02	0.03
< 2 times/week	$20.9\pm6.5$	$19.3 \pm 6.1$	-1.7 (-4.8 to 1.5)	0.04	0.4/	0.03	0.90	0.02	0.03

Fordyce Emotions Combination score									
$\geq$ 2 times/week	$68.5\pm17.3$	$73.1\pm13.8$	+4.7 (-7.7 to 17.0)	0.80	0.01	0.04	0.00	0.01	0.04
< 2 times/week	$55.0\pm24.4$	$61.6\pm20.8$	+6.6 (-5.1 to 18.3)	0.80	0.01	0.04	0.90	0.01	0.04

14 participants reported resistance training exercise  $\geq 2$  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.

			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	$88.0\pm16.1$	$84.6\pm12.7$	-3.4 (-19.5 to 12.7)	0.44	0.58	<0.003	0.44	0.93	<0.002	
< 2 times/week	$88.2\pm14.9$	$80.3\pm18.0$	-8.0 (-16.2 to 0.3)	0.44	0.38	~0.003	0.44	0.95	<b>~0.002</b>	
Physical WB										
$\geq$ 2 times/week	$25.5\pm3.0$	$22.5\pm5.6$	-3.0 (-7.8 to 1.8)	0.01	0.42	<0.002	0.81	0.61	~0.007	
< 2 times/week	$24.5\pm4.8$	$21.2\pm6.5$	-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	$24.3\pm3.3$	$22.1 \pm 5.1$	-2.2 (-6.8 to 2.4)	0.41	0.97	<0.001	0.44	0.41	<0.001	
< 2 times/week	$23.8\pm5.3$	$22.5\pm5.2$	-1.3 (-3.9 to 1.3)	0.41	0.97	~0.001	0.44	0.41	<0.001	
<b>Emotional WB</b>										
$\geq$ 2 times/week	$17.6\pm6.8$	$19.5\pm4.0$	+1.9 (-4.1 to 7.9)	0.67	0.98	0.06	0.69	0.70	0.06	
< 2 times/week	$17.9\pm4.1$	$19.1\pm4.1$	+1.2 (-0.8 to 3.2)	0.07	0.98	0.00	0.09	0.70	0.00	
<b>Functional WB</b>										
$\geq$ 2 times/week	$21.0\pm4.8$	$20.5\pm4.1$	-0.5 (-5.3 to 4.3)	0.08	0.41	0.02	0.07	0.68	0.02	
< 2 times/week	$21.3\pm6.1$	$17.7 \pm 5.7$	-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	$117.5\pm20.6$	$112.4\pm18.9$	-5.1 (-27.1 to 16.9)	0.30	0.63	<0.001	0.25	0.60	<0.001	
< 2 times/week	$118.4\pm18.1$	$106.8\pm22.4$	-11.6 (-21.7 to -1.6)	0.30	0.03	-0.001	0.25	0.00	~0.001	
FACT-B TOI										
$\geq$ 2 times/week	$76.9 \pm 11.5$	$70.8\pm12.0$	-6.2 (-18.8 to 6.5)	0.11	0.40	<0.001	0.06	0.51	<0.001	
< 2 times/week	$76.5\pm12.7$	$65.2 \pm 15.5$	-11.3 (-18.3 to -4.4)	0.11	0.49	<b>\0.001</b>	0.06	0.51	~0.001	
BC subscale score										
$\geq$ 2 times/week	$30.4\pm5.5$	$27.8\pm7.4$	-2.7 (-9.7 to 4.4)	0.39	0.20 0.99	0.39 0.88 < <b>0</b>	<0.001	0.27	0.08	<0.001
< 2 times/week	$30.7\pm5.1$	$26.8\pm6.2$	-3.9 (-6.7 to -1.2)	0.39	0.00	~0.001	0.27	0.00	~0.001	

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.</p>

FACT-Taxane total									
score									
$\geq$ 2 times/week	$155.9\pm10.5$	$139.0\pm15.7$	-16.9 (-33.1 to -0.6)	0.61	0.34	<0.001	0.79	0.78	<0.001
< 2 times/week	$149.0\pm18.7$	$135.3 \pm 23.6$	-13.7 (-24.1 to -3.2)	0.01	0.51		0.79	0.70	
FACT-Taxane TOI									
$\geq$ 2 times/week	$107.3\pm14.5$	$97.4 \pm 11.1$	-9.9 (-24.2 to 4.3)	0.54	0.66	<0.001	0.39	0.40	<0.001
< 2 times/week	$107.1\pm14.4$	$93.7\pm17.7$	-13.4 (-21.3 to -5.4)	0.54	0.00	~0.001	0.39	0.40	~0.001
Taxane subscale									
score									
$\geq$ 2 times/week	$59.0\pm10.8$	$54.4\pm8.2$	-4.6 (-15.2 to 6.0)	0.78	0.62	<0.004	0.75	0.06	<0.003
< 2 times/week	$61.4\pm5.3$	$55.3\pm8.8$	-6.1 (-9.6 to -2.6)	0.78	0.02	<0.004	0.75	0.00	<0.005
FACT-ES total									
score									
$\geq$ 2 times/week	$164.7 \pm 11.5$	$150.5\pm22.9$	-14.2 (-36.5 to 8.2)	0.48	0.18	<0.001	0.58	0.76	<0.001
< 2 times/week	$155.0\pm21.3$	$144.5\pm22.9$	-10.4 (-21.3 to 0.4)	0.48	0.18	<0.001	0.38	0.70	<0.001
ES subscale score									
$\geq$ 2 times/week	$71.1 \pm 2.3$	$65.9 \pm 11.7$	-5.2 (-15.0 to 4.5)	0.50	0.25	0.04	0.72	0.04	0.00
< 2 times/week	$67.5 \pm 8.7$	$64.4 \pm 7.2$	-3.1 (-7.0 to 0.7)	0.59	0.25	0.04	0.72	0.84	0.06
Fatigue subscale									
score									
$\geq$ 2 times/week	$43.1\pm9.8$	$39.4 \pm 11.9$	-3.8 (-15.4 to 7.9)	0.20	0.00	-0.001	0.26	0.00	-0.001
< 2 times/week	$44.0 \pm 10.3$	$37.4 \pm 11.2$	-6.6 (-11.8 to -1.4)	0.30	0.88	<0.001	0.26	0.22	<0.001
PSS score			· · · · · · · · · · · · · · · · · · ·						
$\geq$ 2 times/week	$20.3\pm9.3$	$18.3 \pm 8.2$	-2.0 (-11.4 to 7.4)	0.(1	0.04	0.00	0.54	0.50	0.24
< 2 times/week	$19.4 \pm 8.1$	$18.6 \pm 9.6$	-0.8 (-5.1 to 3.5)	0.61	0.94	0.20	0.54	0.56	0.24
<b>CES-D</b> score									
$\geq$ 2 times/week	$6.6 \pm 3.2$	$7.5 \pm 4.8$	+0.9 (-3.5 to 5.3)	<b>.</b>	0.01				
< 2 times/week	$6.9 \pm 4.0$	$7.5 \pm 4.0$	+0.6 (-1.4 to 2.6)	0.85	0.91	0.32	0.88	0.76	0.30
STAI score		,							
$\geq$ 2 times/week	$20.8\pm6.0$	$19.0 \pm 8.1$	-1.8 (-9.5 to 5.8)						
< 2 times/week	$19.9 \pm 6.8$	$19.0 \pm 0.1$ $18.4 \pm 6.0$	-1.4 (-4.5 to 1.7)	0.80	0.75	0.03	0.81	0.62	0.03
· 2 thirds/ week	$17.7 \pm 0.0$	$10.7 \pm 0.0$	1.7 ( 4.2 to 1.7)						

Fordyce Emotions									
<b>Combination score</b>									
$\geq$ 2 times/week	$64.7\pm20.1$	$74.3\pm15.8$	+9.6 (-9.8 to 28.9)	0.39	0.20	0.07	0.39	0.49	0.07
< 2 times/week	$60.4\pm24.5$	$63.5\pm20.9$	+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  $\geq 2$  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).



**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).

	Α	chieved a pCR	
	Yes	No	p-value
≥150 min/week			
<b>Week 0</b> (n = 46)			
Yes	7 (43.8%)	9 (56.3%)	0.52
No	9 (30.0%)	21 (70.0%)	0.32
Total	16 (34.8%)	30 (65.2%)	
<b>Week 3</b> $(n = 45)$			
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%)	
<b>Week 6</b> $(n = 47)$			
Yes	6 (40.0%)	9 (60.0%)	0.75
No	11 (34.4%)	21 (65.6%)	0.75
Total	17 (36.2%)	30 (63.9%)	
<b>Week 9</b> $(n = 47)$			
Yes	4 (26.7%)	11 (73.3%)	0.52
No	13 (40.6%)	19 (59.4%)	0.52
Total	17 (36.2%)	30 (63.8%)	
<b>Week 12</b> $(n = 47)$			
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%)	
<b>Week 15</b> $(n = 45)$		·	
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%)	
<b>Week 18</b> (n = 42)			
Yes	3 (27.3%)	8 (72.7%)	0.40
No	14 (45.2%)	17 (54.8%)	0.48
Total	17 (40.5%)	25 (59.5%)	

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

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).

	A	Achieved a pCR	
	Yes	No	p-value
$\geq$ 2 times/week			
<b>Week 0</b> (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%)	
<b>Week 3</b> $(n = 45)$			
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%)	
<b>Week 6</b> $(n = 47)$			
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%)	
<b>Week 9</b> $(n = 47)$			
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%)	
<b>Week 12</b> $(n = 47)$			
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%)	
<b>Week 15</b> $(n = 45)$			
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%)	
<b>Week 18</b> (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%)	

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

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

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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.  $\geq$  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 nonmetastatic breast cancer [19]. The DHA intervention was minimally invasive, and selfadministered 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].

## **<u>6.5 Final Conclusions</u>**

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**

Date: \_\_\_\_\_

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

# 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

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## 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 <u>right now</u>, 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</u> <u>days</u> by circling the appropriate number using the following scale.

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

	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
<ol> <li>I feel close to my partner (or the person who is my main support)</li> </ol>	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	s 0	1	2	3	4

### During the **PAST WEEK**:

10.0

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

### **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

C

	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>:

C

### **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					
1. 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
<ol><li>felt confident about your ability to handle your personal problems</li></ol>	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	4				
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</u> <u>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 PAST WEEK:

The percentage of time I felt <u>happy</u> was:		%
The percentage of time I felt <u>unhappy</u> 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.

	0 or noneof the time	1 Some of the time		2 Much of the	time	3 Most or all of the
time	(< 1 day)	(1-2 days)		(3-4 day	ys)	(5-7 days)
During	g the <u>PAST WEEK</u> :					
1. I fe	lt depressed.		0	1	2	3
2. I fe	It that everything I did wa	as an effort.	0	1	2	3
3. My	sleep was restless.		0	1	2	3
4. I wa	as happy.		0	1	2	3
5. I fel	it lonely.		0	1	2	3
6.Peop	ple were unfriendly.		0	1	2	3
7. I en	joyed life.		0	1	2	3
8. I fel	lt sad.		0	1	2	3
9. I fe	It that people disliked me	2.	0	1	2	3
10. I c	ould not get "going".		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> weeks. 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> exercise (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 <b>AEROBIC</b> EXERCISE (HEART BEATS RAPIDLY, SWEATING) (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).		
b. MODERATE INTENSITY <b>AEROBIC</b> EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) (e.g., fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).		
c. LIGHT INTENSITY <b>AEROBIC</b> EXERCISE (MINIMAL EFFORT, NO PERSPIRATION) (e.g., easy walking, yoga, bowling, lawn bowling, shuffleboard).		
d. <b>STRENGTH/RESISTANCE</b> 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



#### **GENERAL INSTRUCTIONS**

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- 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 fluid ounce = 30ml 1 teaspoon = 5ml 1 tablespoon = 15ml Weight 1 ounce = 30g

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:	In what you bor ☐ Jan ☐ Feb	month were n? Ul Aug	In what year were you born?	Are you male or female? Male Female
month day year	Mar Apr May	Cot	BAR CODE L	ABEL OR SUBJECT ID
	Jun			nexe
DHQ II PastYear				1465

<ul> <li>1. Over the <u>past 12 months</u>, how often did you drink tomato juice?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit j you drank calcium-fortified?</li> <li>3b. How often was the orange juice or grapefruit juice or grapefruit juice or grapefruit juice</li> </ul>	uice
□ 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 per day         □ 5-6 times per week       □ 4 or the time         □ 4.5       □ 4.5         □ 5-6 times per week       □ 4.5         □ 4.       Over the past 12 months, how often did you drink	
1a.       Each time you drank tomato juice, how much did you usually drink?       mixtures (such as apple, grape, pineapple, or others)?	
<ul> <li>Less than ½ cup (4 ounces)</li> <li>½ to 1¼ cups (4 to 10 ounces)</li> <li>More than 1¼ cups (10 ounces)</li> <li>Over the past 12 months, how often did you drink</li> <li>Over the past 12 months, how often did you drink</li> <li>I time per month or less</li> <li>I time per month</li> <li>I time per day</li> <li>I time per day</li> <li>I time per day</li> <li>I time per month</li> <li>I time per day</li> </ul>	
other vegetable juice? (Please do not include tomato juice.)          □ 3-4 times per week □ 5-6 times per week day         day	
Image: NEVER (GO TO QUESTION 3)       4a. Each time you drank other 100% fruit juice or 100% fruit juice mixtures, how much did you usually drink?         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 per day         5-6 times per week       day         Image: Marked times per week       11/2 cups (6 to 12 ounces)         Image: Marked times per week       More than 11/2 cups (12 ounces)	
<ul> <li>2a. Each time you drank other vegetable juice, how much did you usually drink?</li> <li> Less than ¾ cup (6 ounces) ¾ to 1¼ cups (6 to 10 ounces) More than 1¼ cups (10 ounces) </li> </ul>	
▼ ■ NEVER (GO TO QUESTION 6)	
3. Over the past 12 months, how often did you drink 100% orange juice or grapefruit juice?       □ 1 time per month or less       □ 1 time per day         □ 2-3 times per month       □ 2-3 times per month       □ 2-3 times per day         □ 1 vertice       □ 1 time per month or less       □ 1 time per day         □ 1 vertice       □ 1 time per month or less       □ 1 time per day         □ 2-3 times per week       □ 4-5 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         3-4 times per week       6 or more times per day         3-4 times per week       6 or more times per day         5-6 times per week       6 or more times per day         5-6 times per week       6 or more times per day	
3a. Each time you drank 100% <b>orange juice</b> or <b>grapefruit juice</b> , 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)	
V     V       Question 4 appears in the next column     Question 6 appears on the next page     1465	



Over the <u>past 12 months</u>	7a. Each time you drank <b>chocolate milk</b> or <b>hot</b> <b>chocolate</b> , how much did you usually drink?
5a. Each time you drank <b>other fruit drinks</b> , how much did you usually drink?	Less than 1 cup (8 ounces)
☐ Less than 1 cup (8 ounces) ☐ 1 to 2 cups (8 to 16 ounces) ☐ More than 2 cups (16 ounces)	☐ 1 to 2 cups (8 to 16 ounces) ☐ More than 2 cups (16 ounces)
5b. How often were your other fruit drinks <b>diet</b> or <b>low calorie</b> ?	7b. How often was the chocolate milk or hot chocolate you drank <b>reduced-fat</b> or <b>fat-free</b> ?
<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>
6 How often did you dripk milk or milk substitutes	8. How often did you drink <b>milkshakes</b> ?
<ol> <li>How often did you drink milk or milk substitutes as a beverage (NOT in coffee, NOT in cereal)?</li> </ol>	□ NEVER (GO TO QUESTION 9)
(Please do not include chocolate milk, hot chocolate, and milk in milkshakes or meal replacement beverages.)	□ 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 per         □ 5-6 times per week       □ day
<ul> <li>1 time per month or less</li> <li>1 time per day</li> <li>2-3 times per month</li> <li>2-3 times per day</li> <li>1-2 times per week</li> <li>4-5 times per day</li> <li>3-4 times per week</li> <li>6 or more times per</li> <li>5-6 times per week</li> <li>6a. Each time you drank milk or milk substitutes as a beverage, how much did you usually</li> </ul>	<ul> <li>5-6 times per week day</li> <li>8a. Each time you drank milkshakes, how much did you usually drink?</li> <li>Less than 1 cup (8 ounces)</li> <li>1 to 2 cups (8 to 16 ounces)</li> <li>More than 2 cups (16 ounces)</li> </ul>
drink?	↓
☐ Less than 1 cup (8 ounces) ☐ 1 to 1½ cups (8 to 12 ounces) ☐ More than 1½ cups (12 ounces)	<ol> <li>How often did you drink meal replacement or high-protein beverages (such as Boost, Breakfast Essential, Ensure, Slimfast or others)?</li> </ol>
6b. What kind of <b>milk</b> or <b>milk substitutes</b> did you usually drink?	NEVER (GO TO QUESTION 10)
<ul> <li>☐ Whole milk</li> <li>☐ 2% fat milk</li> <li>☐ 1% fat milk</li> <li>☐ Skim, nonfat, or 0.5% fat milk</li> <li>☐ Soy milk</li> <li>☐ Rice milk</li> <li>☐ Almond milk</li> </ul>	□ 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 per day         □ 5-6 times per week       □ 4 or more times per day
↓ Other	9a. Each time you drank meal replacement or high-protein beverages, how much did you usually drink?
<ol> <li>How often did you drink chocolate milk or hot chocolate?</li> </ol>	Less than 1 cup (8 ounces)
	$\square$ 1 to 1½ cups (8 to 12 ounces) $\square$ More than 1½ cups (12 ounces)
□ 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 per day         □ 5-6 times per week       □ day	

Question 8 appears in the next column

3

Question 10 appears on the next page



Over the <u>past 12 months</u>	11b. How often did you drink <b>sports drinks DU</b> THE REST OF THE YEAR?		
10. How often did you drink <b>soft drinks</b> or <b>pop?</b>			
□ NEVER (GO TO QUESTION 11)	☐ 1 time per month or less ☐ 1 time 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 weekper 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		
10a. Each time you drank <b>soft drinks</b> or <b>pop</b> , how much did you usually drink?	11c. Each time you drank <b>sports drinks</b> , how much did you usually drink?		
□ Less than 12 ounces or less than 1 regular size can or bottle (355 ml)	<ul> <li>Less than 1½ cups (12 ounces)</li> <li>1½ to 3 cups (12 to 24 ounces)</li> <li>More than 3 cups (24 ounces)</li> </ul>		
<ul> <li>12 to 16 ounces or 1 regular size can or bottle (355 ml)</li> <li>More than 16 ounces or more than 1 regular size can or bottle (355 ml)</li> </ul>	12. How often did you drink <b>energy drinks</b> (such as Red Bull, Rock Star, Full Throttle, or Monster)?		
10b. How often were your soft drinks or pop <b>diet</b> or <b>calorie-free</b> ?	□ NEVER (GO TO QUESTION 13) □ 1 time per month or less □ 1 time per day		
<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	□       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		
10c. How often were your soft drinks or pop caffeine-free?	12a. Each time you drank <b>energy drinks</b> , how much did you usually drink?		
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time ☐ About ⅔ of the time	□ Less than 1 cup (8 ounces) □ 1 to 2 cups (8 to 16 ounces) □ More than 2 cups (16 ounces)		
Almost always or always	13. How often did you drink <b>beer</b> ?		
<ul> <li>In the past 12 months, did you drink sports</li> </ul>	■ NEVER (GO TO QUESTION 14) □ 1 time per month or less □ 1 time per day		
drinks (such as PowerAde or Gatorade)?	□ 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 <b>beer</b> , how much did you usually drink?		
	<ul> <li>Less than 1 regular size can or bottle (341 ml)</li> <li>1 to 3 regular size cans or bottles</li> <li>More than 3 regular size cans or bottles</li> </ul>		
□ 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 weekper day			
$\downarrow$			

Question 12 appears in the next column

4

Question 14 appears on the next page



ver the <u>past 12 months</u>	15. How often did you drink <b>wine</b> ?
Aver the past 12 months         4. How often did you drink water (including tap, bottled, carbonated, flavoured, or vitamin added water)?           NEVER (GO TO QUESTION 15)           1 time per month or less         1 time per day         2-3 times per month       2-3 times per day           -2 times per week         -5 times per day           -2 times per week         -6 or more times           -4 times per week         -6 or more times           -5 d times per week         -6 or more times           -4 cups (8 to 32 ounces)         -1 to 4 cups (8 to 32 ounces)           -1 to 4 cups (8 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (4 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (32 ounces)           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (3 to 32 ounces)           -1 to 4 cups (4 to time         -1 About ½ of the time           -1 to 4 cups (3 to 32 ounces)         -1 to 4 cups (3 to 32 ounces)           -1 to 4 cups (3 to the time         -1 Almost always or always         14c.       How ofte	15. How often did you drink wine?         NEVER (GO TO QUESTION 16)         1 time per month or less       1 time per day         2-3 times per week       2-3 times per day         1-2 times per week       6 or more times         5-6 times per week       6 or more times         15a. Each time you drank wine, how much did you usually drink?         Less than 1 glass (5 ounces)         1 to 2 glasses (5 to 12 ounces)         More than 2 glasses (12 ounces)         15b. How often was the wine you drank red wine?         Almost never or never         About ¼ of the time         About ¼ of the time         About ¼ of the time         Almost always or always         16. How often did you drink liquor or mixed drinks?         NEVER (GO TO QUESTION 17)         1 time per month or less       1 time per day         2-3 times per week       6 or more times         2-3 times per week       6 or more times         1-2 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 <t< td=""></t<>
uestion 15 appears in the next column	Question 17 appears on the next page 1465

Over the <u>past 12 months</u>			17e. Was <b>milk</b> added to y Wheat, Red River, o			
	id you eat oatmeal, Cream	of Wheat, Red River,	_			
0	r other cooked cereal?				,	
	NO (GO TO QUESTION 18)			↓ 17f. What kind of milk was	habhe vileusu se	2
]				Whole milk		
17	a. How often did you eat of Wheat, Red River, or of THE WINTER?			☐ 2% fat milk ☐ 1% fat milk ☐ Skim, nonfat, or 0.5 <sup>r</sup> ☐ Soy milk	% fat milk	
	□ NEVER			Rice milk		
	<ul> <li>1-6 times per winter</li> <li>7-11 times per winter</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times</li> </ul>		<ul> <li>Almond milk</li> <li>Other</li> <li>17g. Each time milk was Cream of Wheat, Recereal, how much was</li> </ul>	ed River, or other	r cooked
17	b. How often did you eat or Wheat, Red River, or of DURING THE REST OF	ther cooked cereal		Less than ½ cup ½ to 1 cup More than 1 cup	as usually added	ŗ
		THE TEAR?	▼ 18.	How often did you eat <b>c</b>	old cereal?	
	☐ 1-6 times per year	□ 2 times per week	_			
	<ul> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>		<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	☐ 2 times pe ☐ 3-4 times ☐ 5-6 times ☐ 1 time per ☐ 2 or more	per week per week ˈday
17	c. Each time you ate <b>oatme</b> <b>Red River</b> , or <b>other coo</b> did you usually eat?			18a. Each time you ate <b>c</b> o you usually eat?	per day <b>old cereal</b> , how r	nuch did
	☐ Less than ¾ cup ☐ ¾ to 1¼ cups ☐ More than 1¼ cups			☐ Less than 1 cup ☐ 1 to 2½ cups ☐ More than 2½ cups		
17	d. How often was <b>butter</b> or your oatmeal, Cream of other cooked cereal?			18b. How often was the c PC Force Active?	old cereal you at	e Vector or
	<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>			<ul> <li>☐ Almost never or nev</li> <li>☐ About ¼ of the time</li> <li>☐ About ¼ of the time</li> <li>☐ About ¼ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or al</li> </ul>	: :	
				18c. How often was the c Bran, Fibre 1, Fibre All-Bran Buds?		
				<ul> <li>☐ Almost never or nev</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or al</li> </ul>	: :	
	n 18 appears in the next column		<b>▼</b>	stion 19 appears on the next pag	1e	1465
<i>~</i> uc300	10 appears in the next column		2005	логи то арреато от ите пели рау	~	1400



19a. Each time you ate applesauce, how much Over the past 12 months... did you usually eat? 18d. How often was the cold cereal you ate some Less than 1/4 cup other bran or fibre cereal (such as Cheerios □ ¼ to ¾ cup (regular), Shredded Wheat, Raisin Bran, Bran ☐ More than ¾ cup Flakes, Mini-Wheats, Shreddies, Honey Bunches of Oats, Oatmeal Crisp or others)? 20. How often did you eat apples? Almost never or never ■ NEVER (GO TO QUESTION 21) About 1/4 of the time About 1/2 of the time □ 1-6 times per year 2 times per week □ About ¾ of the time 7-11 times per year □ 3-4 times per week Almost always or always 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 18e. How often was the cold cereal you ate any other per day type of cold cereal (such as Corn Flakes, Rice Krispies, Frosted Flakes, Special K, Froot Loops, 20a. Each time you ate apples, how many Cap'n Crunch, Honey Nut Cheerios, did you usually eat? Honeycomb, or others)? Less than 1 apple Almost never or never 1 apple About 1/4 of the time □ More than 1 apple  $\square$  About  $\frac{1}{2}$  of the time  $\Box$  About  $\frac{3}{4}$  of the time 21. How often did you eat pears (fresh, canned, or Almost always or always frozen)? □ NEVER (GO TO QUESTION 22) 18f. Was milk added to your cold cereal? □ 1-6 times per year 2 times per week □ NO (GO TO QUESTION 19) □ 7-11 times per year □ 3-4 times per week □ YES 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 18g. What kind of milk was usually added? per day U Whole milk 2% fat milk 21a. Each time you ate pears, how many 1% fat milk did you usually eat? Skim, nonfat, or 0.5% fat milk Less than 1 pear □ Soy milk 1 pear Rice milk ☐ More than 1 pear □ Almond milk □ Other 22. How often did you eat bananas? 18h. Each time milk was added to your cold □ NEVER (GO TO QUESTION 23) cereal, how much was usually added? □ 1-6 times per year 2 times per week  $\Box$  Less than  $\frac{1}{2}$  cup □ 3-4 times per week 7-11 times per year  $\square$  ½ to 1 cup 1 time per month 5-6 times per week □ More than 1 cup 2-3 times per month 1 time per day 1 time per week 2 or more times 19. How often did you eat applesauce? per day ■ NEVER (GO TO QUESTION 20) □ 1-6 times per year 2 times per week 7-11 times per year □ 3-4 times per week □ 5-6 times per week □ 1 time per month □ 2-3 times per month 1 time per day 1 time per week 2 or more times 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
22a. Each time you ate <b>bananas</b> , how many did you usually eat? □ Less than 1 banana □ 1 banana	plums, how much 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
More than 1 banana	25. How often did you eat grapes?
<ul> <li>23. How often did you eat dried fruit (such as prunes or raisins)? (<i>Please do not include dried apricots.</i>)</li> <li>NEVER (GO TO QUESTION 24) <ul> <li>16 times per year</li> <li>21 time per month</li> <li>56 times per week</li> <li>23 times per month</li> <li>1 time per day</li> </ul> </li> <li>23a. Each time you ate dried fruit, how much did you usually eat? <ul> <li>Less than 2 tablespoons</li> <li>2 to 5 tablespoons</li> <li>2 to 5 tablespoons</li> <li>More than 5 tablespoons</li> </ul> </li> <li>24. Over the past 12 months, did you eat peaches, nectarines, or plums?</li> <li>A Over the past 12 months, did you eat peaches, nectarines or plums WHEN IN SEASON? <ul> <li>NO (GO TO QUESTION 25)</li> <li>YES</li> </ul> </li> <li>24a. How often did you eat fresh peaches, nectarines or plums WHEN IN SEASON? <ul> <li>NEVER</li> <li>16 times per season</li> <li>21 time per month</li> <li>16 times per season</li> <li>24b. How often did you eat peaches, nectarines, or plums (fresh, canned, or frozen) DURING THE REST OF THE YEAR? <ul> <li>NEVER</li> <li>1-6 times per year</li> <li>24 times per week</li> <li>25 times per month</li> <li>1 time per month</li> <li>2 times per week</li> <li>2 times per week</li> <li>2 or more times per day</li> </ul> </li> </ul></li></ul>	<ul> <li>NEVER (GO TO QUESTION 26)</li> <li>☐ 1-6 times per year</li> <li>☐ 1 time per month</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> <li>☐ 2 or more times per day</li> <li>25a. Each time you ate grapes, how much did you usually eat?</li> <li>☐ Less than ½ cup or less than 10 grapes</li> <li>☐ More than 1 cup or more than 30 grapes</li> <li>☐ More than 1 cup or more than 30 grapes</li> <li>☐ More than 1 cup or more than 30 grapes</li> <li>☐ NO (GO TO QUESTION 27)</li> <li>☐ YES</li> <li>✓</li> <li>26a. How often did you eat fresh cantaloupe WHEN IN SEASON?</li> <li>☐ NEVER</li> <li>☐ 1-6 times per season</li> <li>☐ 2 times per week</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> <li>☐ 2 times per week</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> <li>☐ 2 times per week</li> <li>☐ 1 time per week</li> <li>☐ 2 times per week</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> <li>☐ 2 times per week</li> <li>☐ 1 time per week</li> <li>☐ 2 times per week</li> <li>☐ 1 time per month</li> <li>☐ 1 time per year</li> <li>☐ 2 times per week</li> <li>☐ 1 time per month</li> <li>☐ 1 time per month</li> <li>☐ 2 times per week</li> <li>☐ 1 time per month</li> <li>☐ 2 times per week</li> <li>☐ 1 time per day</li> <li>☐ 2 or more times per day</li> </ul>
	Question 27 appears on the next page   1465     8   Image



Over the <u>past 12 months</u>	28. Over the <u>past 12 months</u> , did you eat <b>strawberries</b> ?		
<ul> <li>26c. Each time you ate cantaloupe, how much did you usually eat?</li> <li>Less than ¼ melon or less than ½ cup</li> <li>¼ melon or ½ to 1 cup</li> <li>More than ¼ melon or more than 1 cup</li> </ul> 27. Over the past 12 months, did you eat melon, other	28. How often did you eat fresh strawberries WHEN IN SEASON? □ NEVER		
<pre>than cantaloupe (such as watermelon or honeydew)?</pre>	<ul> <li>1-6 times per season</li> <li>7-11 times per season</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>per day</li> </ul>		
<ul> <li>□ NEVER</li> <li>□ 1-6 times per season</li> <li>□ 2 times per week</li> <li>□ 7-11 times per season</li> <li>□ 3-4 times per week</li> </ul>	28b. How often did you eat <b>strawberries</b> (fresh or frozen) <b>DURING THE REST OF THE YEAR</b> ? ☐ NEVER ☐ 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	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 <b>melon other than</b> cantaloupe (fresh or frozen) DURING THE REST OF THE YEAR? □ NEVER	per day 28c. Each time you ate <b>strawberries</b> , how much did you usually eat?		
<ul> <li>☐ 1-6 times per year</li> <li>☐ 2 times per week</li> <li>☐ 7-11 times per year</li> <li>☐ 3-4 times per week</li> <li>☐ 1 time per month</li> <li>☐ 5-6 times per week</li> <li>☐ 1 time per week</li> <li>☐ 1 time per week</li> <li>☐ 2 or more times per day</li> <li>☐ 1 time per week</li> </ul>	<ul> <li>Less than ¼ cup or less than 4 berries</li> <li>¼ to ¾ cup or 4 to 10 berries</li> <li>More than ¾ cup or more than 10 berries</li> <li>29. Over the <u>past 12 months</u>, did you eat <b>blueberries</b>, raspberries, saskatoon berries or blackberries?</li> </ul>		
27c. Each time you ate <b>melon other than cantaloupe</b> , how much did you usually eat?			
<ul> <li>Less than 1 cup or 2 small wedges</li> <li>1 to 3 cups or 2 medium wedges</li> <li>More than 3 cups or 2 large wedges</li> </ul>	<ul> <li>↓</li> <li>29a. How often did you eat fresh blueberries, raspberries, saskatoon berries or blackberries WHEN IN SEASON?</li> <li>□ NEVER</li> </ul>		
	<ul> <li>1-6 times per season</li> <li>7-11 times per season</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>		
Question 28 appears in the next column	Question 30 appears on the next page     1465       Image: Image i		

Over the <u>past 12 months</u> 29b. How often did you eat <b>blueberries</b> , raspberries,		30c. Each time you ate <b>oranges</b> , <b>tangelos</b> , <b>mandarins</b> , or <b>clementines</b> , how many did		
saskatoon berries or blac frozen) DURING THE RES	kberries (fresh or	you usually eat? □ Less than 1 fruit □ 1 fruit		
		More than 1 fruit		
<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	31. Over the <u>past 12 months</u> , did you eat <b>grape</b> ☐ NO (GO TO QUESTION 32) ☐ YES ↓	⊧fruit?	
29c. Each time you ate <b>blueber</b> <b>saskatoon berries</b> or <b>blac</b> did you usually eat?		31a. How often did you eat <b>fresh grapefruit</b> IN SEASON? □ NEVER	WHEN	
☐ Less than ¼ cup ☐ ¼ to ¾ cup ☐ More than ¾ cup		□       1-6 times per season       □       2 times per         □       7-11 times per season       □       3-4 times         □       1 time per month       □       5-6 times         □       2-3 times per month       □       1 time per	per week per week r day	
30. Over the past 12 months, did yo tangelos, mandarins, or clem		1 time per week 2 or more per day	times	
		31b. How often did you eat grapefruit (fresh canned) DURING THE REST OF THE		
↓				
mandarins, or clementine SEASON?		1-6 times per year2 times p7-11 times per year3-4 times1 time per month5-6 times2-3 times per month1 time per1 time per week2 or moreper day	per week per week r day	
<ul> <li>7-11 times per season</li> <li>1 time per month</li> <li>2-3 times per month</li> </ul>		<ul> <li>31c. Each time you ate grapefruit, how muc usually eat?</li> <li>□ Less than ½ grapefruit</li> <li>□ ½ to 1 grapefruit</li> <li>□ More than 1 grapefruit</li> </ul>	h did you	
30b. How often did you eat <b>oranges</b> , <b>tangelos,</b> <b>mandarins</b> , or <b>clementines</b> (fresh or canned) <b>DURING THE REST OF THE YEAR</b> ?		▼ 32. How often did you eat <b>pineapple</b> ?		
<ul> <li>NEVER</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>	□       1-6 times per year       □       2 times per w         □       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 day         □       1 time per week       □       2 or more tim per day	week week y		
	per day	32a. Each time you ate <b>pineapple</b> , how muc you usually eat?	h did	
		<ul> <li>Less than ¼ cup or less than 1 medium s</li> <li>1¼ to ¾ cup or 1 to 2 medium slices</li> <li>More than ¾ cup or more than 2 medium</li> </ul>		
♥ Question 31 appears in the next column		▼ Question 33 appears on the next page	1465	

- Over the <u>past 12 months</u>	36. How often did you eat <b>coleslaw</b> ?
	► NEVER (GO TO QUESTION 37)
33. How often did you eat other kinds of fruit?	
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	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
<ul> <li>33a. Each time you ate other kinds of fruit, how much did you usually eat?</li> <li>□ Less than ¼ cup</li> <li>□ ¼ to ¾ cup</li> <li>□ More than ¾ cup</li> </ul>	usually eat? □ Less than ¼ cup □ ¼ to ¾ cup □ More than ¾ cup ▼ 37. How often did you eat <b>sauerkraut</b> or <b>cabbage</b>
<ul> <li>★</li> <li>34. How often did you eat COOKED greens (such as spinach, turnip greens, collard, mustard greens, chard, or kale)?</li> <li></li></ul>	(other than coleslaw)? □ NEVER (GO TO QUESTION 38) □ 1-6 times per year □ 2 times per week □ 7-11 times per year □ 3-4 times per week
□       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         □       1 time per week       □       2 or more times	<ul> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>37a. Each time you ate sauerkraut or cabbage, how much did you usually eat?</li> </ul>
<ul> <li>34a. Each time you ate COOKED greens, how much did you usually eat?</li> <li>□ Less than ½ cup</li> <li>□ ½ to 1 cup</li> <li>□ More than 1 cup</li> </ul>	<ul> <li>□ Less than ¼ cup</li> <li>□ ¼ to 1 cup</li> <li>□ More than 1 cup</li> <li>38. How often did you eat carrots (fresh, canned, or frozen)?</li> </ul>
<ul> <li>35. How often did you eat RAW greens (such as spinach, chard, or kale)? (We will ask about lettuce later.)</li> <li>NEVER (GO TO QUESTION 36)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times</li> </ul>	<ul> <li>NEVER (GO TO QUESTION 39)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>38a. Each time you ate carrots, how much did you usually eat?</li> </ul>
per day 35a. Each time you ate <b>RAW greens</b> , how much did you usually eat? Less than 1½ cups 1½ to 3 cups More than 3 cups	<ul> <li>Less than ¼ cup or less than 2 baby carrots</li> <li>I¼ to ¾ cup or 2 to 8 baby carrots</li> <li>More than ¾ cup or more than 8 baby carrots</li> </ul>
Question 36 appears in the next column	Question 39 appears on the next page 1465

Over the <u>past 12 months</u>			41b. How often did you eat o		
39. How often did you eat string beans or green beans (fresh, canned, or frozen)?			frozen) <b>DURING THE I</b> □ NEVER	REST OF THE YEAR?	
Г	□ NEVER (GO TO QUESTION			☐ 1-6 times per year ☐ 7-11 times per year	☐ 2 times per week ☐ 3-4 times per week
	<ul> <li>☐ 1-6 times per year</li> <li>☐ 7-11 times per year</li> <li>☐ 1 time per month</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> </ul>	□ 2 times per week □ 3-4 times per week □ 5-6 times per week □ 1 time per day □ 2 or more times		<ul> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>☐ 5-6 times per week</li> <li>☐ 1 time per day</li> <li>☐ 2 or more times per day</li> </ul>
		per day		41c. Each time you ate <b>corr</b> usually eat?	n, how much did you
	39a. Each time you ate <b>strin</b> beans, how much did yo			Less than 1 ear or less $\Box$ 1 ear or $\frac{1}{2}$ to 1 cup	·
	☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup			More than 1 ear or mor	e than 1 cup
<b>▼</b> 40.	How often did you eat <b>peas</b> frozen)?				A
Γ	<ul> <li>NEVER (GO TO QUESTION</li> <li>1-6 times per year</li> </ul>	N 41) □ 2 times per week	4	2. How often did you eat broc	coli (fresh or frozen)?
	☐ 7-11 times per year ☐ 1 time per month	□ 3-4 times per week □ 5-6 times per week		D NEVER (GO TO QUESTI	ON 43)
	☐ 2-3 times per month ☐ 1 time per week	<ul> <li>1 time per day</li> <li>2 or more times per day</li> </ul>		☐ 1-6 times per year ☐ 7-11 times per year ☐ 1 time per month	$\square$ 2 times per week $\square$ 3-4 times per week $\square$ 5-6 times per week
4	40a. Each time you ate <b>peas</b> usually eat?	, how much did you		☐ 2-3 times per month ☐ 1 time per week	<ul> <li>☐ 1 time per day</li> <li>☐ 2 or more times per day</li> </ul>
	☐ Less than ¼ cup ☐ ¼ to ½ cup ☐ More than ½ cup			42a. Each time you ate <b>broo</b> usually eat?	c <b>coli</b> , how much did you
<ul> <li>✓</li> <li>41. Over the <u>past 12 months</u>, did you eat corn?</li> <li>☐ NO (GO TO QUESTION 42)</li> </ul>			☐ Less than ¼ cup ☐ ¼ to 1 cup ☐ More than 1 cup		
		)	4:	<b>7</b> 3. How often did you eat <b>caul</b>	iflower (fresh or frozen)?
↓ 41a. How often did you eat fresh corn WHEN IN SEASON?			🗆 NEVER (GO TO QUESTI	ON 44)	
				☐ 1-6 times per year ☐ 7-11 times per year	☐ 2 times per week ☐ 3-4 times per week
	□ 7-11 times per season □ 3-4 times per v □ 1 time per month □ 5-6 times per v	<ul> <li>☐ 2 times per week</li> <li>☐ 3-4 times per week</li> <li>☐ 5-6 times per week</li> <li>☐ 1 time per day</li> </ul>		<ul> <li>☐ 1 time per month</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per week</li> </ul>	<ul> <li>☐ 5-6 times per week</li> <li>☐ 1 time per day</li> <li>☐ 2 or more times per day</li> </ul>
				43a. Each time you ate <b>cau</b> l you usually eat?	liflower, how much did
				☐ Less than ¼ cup ☐ ¼ to 1 cup ☐ More than 1 cup	
▼ Ques	tion 42 appears in the next column			, uestion 44 appears on the next page	1465
			12		

Over the <u>past 12 months</u>	47. How often did you eat <b>mixed vegetables</b> (such as vegetable stir fry, frozen or canned mixed			
44. How often did you eat <b>Brussels sprouts</b> (fresh or frozen)?	vegetables)?			
P INEVER (GO TO QUESTION 45)				
□ 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 timesper day	<ul> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>47a. Each time you ate mixed vegetables, how</li> </ul>			
44a. Each time you ate <b>Brussels sprouts</b> , how much did you usually eat?	much did you usually eat? □ Less than ½ cup			
Less than 4 Brussels sprouts or less than $\frac{1}{2}$ cup 4 to 7 Brussels sprouts or $\frac{1}{2}$ to 1 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 <b>onions</b> ?			
45. How often did you eat <b>asparagus</b> (fresh or frozen)?	□ NEVER (GO TO QUESTION 49)			
NEVER (GO TO QUESTION 46)     1-6 times per year	□       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			
I time per month       5-6 times per week         2-3 times per month       1 time per day         I time per week       2 or more times         per day       1 time per week	<ul> <li>1 time per week</li> <li>2 or more times per day</li> <li>48a. Each time you ate <b>onions</b>, how much did you usually eat?</li> </ul>			
45a. Each time you ate <b>asparagus</b> , how much did you usually eat?	<ul> <li>□ Less than 1 slice or less than 1 tablespoon</li> <li>□ 1 to 5 slices or 1 to 4 tablespoons</li> <li>□ More than 5 slices or more than 4 tablespoons</li> </ul>			
<ul> <li>☐ Less than 5 spears or less than ½ cup</li> <li>☐ 5 to 9 spears or ½ to ¾ cup</li> <li>☐ More than 9 spears or more than ¾ cup</li> </ul>	49. Now think about all the cooked vegetables you ate in the past 12 months and how they were prepared. How often were your vegetables COOKED WITH some sort of fat, including oil			
46. How often did you eat <b>winter squash</b> (such as pumpkin, butternut, or acorn)?	spray? (Please do not include potatoes.)			
P D NEVER (GO TO QUESTION 47)				
□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 timesper day□2 or more times	□       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       □       □       □			
46a. Each time you ate <b>winter squash,</b> how much did you usually eat?				
☐ Less than ¼ cup ☐ ¼ to 1 cup ☐ More than 1 cup				
Question 47 appears in the next column	Question 50 appears on the next page 1465			
1				

Over the <u>past 12 months</u>	51. How often did you eat <b>sweet peppers</b> (green, red, or yellow)?		
<ul> <li>49a. Which fats were usually added to your vegetables DURING COOKING? (<i>Please do not include potatoes.</i> Mark all that apply.)</li> <li>Margarine     <ul> <li>(including light)</li> <li>Butter     <ul> <li>(including light)</li> <li>Lard, fatback, or bacon fat</li> <li>Olive oil</li> </ul> </li> <li>50. Now, thinking again about all the cooked vegetables you ate in the past 12 months, how often was some sort of fat, sauce, or dressing</li> </ul></li></ul>			
added AFTER COOKING OR AT THE TABLE? (Please do not include potatoes.) NEVER (GO TO QUESTION 51) 1-6 times per year 3-4 times per week 7-11 times per year 5-6 times per week 1 time per month 1 time per day 2-3 times per week 3 or more times per day	<ul> <li>52. Over the <u>past 12 months</u>, did you eat fresh tomatoes (including those in salads)?</li> <li>□ NO (GO TO QUESTION 53)</li> <li>□ YES</li> <li>↓</li> <li>52a. How often did you eat fresh tomatoes (including those in salads) WHEN IN SEASON?</li> <li>□ NEVER</li> </ul>		
<ul> <li>50a. Which fats, sauces, or dressings were usually added AFTER COOKING OR AT THE TABLE? (Please do not include potatoes. Mark all that apply.)</li> <li>Margarine</li></ul>	<ul> <li>☐ 1-6 times per season</li> <li>☐ 2 times per week</li> <li>☐ 7-11 times per season</li> <li>☐ 3-4 times per week</li> <li>☐ 1 time per month</li> <li>☐ 5-6 times per week</li> <li>☐ 2-3 times per month</li> <li>☐ 1 time per day</li> <li>☐ 1 time per week</li> <li>☐ 2 or more times per day</li> <li>52b. How often did you eat fresh tomatoes (including those in salads) DURING THE REST OF THE YEAR?</li> </ul>		
<ul> <li>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?</li> <li>Did not usually add these</li> <li>Less than 1 teaspoon</li> <li>1 to 3 teaspoons</li> <li>More than 3 teaspoons</li> </ul> 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? <ul> <li>Did not usually add these</li> <li>Less than 1 tablespoon</li> <li>1 to 3 tablespoons</li> <li>More than 3 tablespoons</li> </ul>	<ul> <li>NEVER</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul> 52c. Each time you ate <b>fresh tomatoes</b> , how much did you usually eat? <ul> <li>Less than ¼ tomato</li> <li>¼ to 1 tomato</li> <li>More than 1 tomato</li> </ul>		
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 <b>sweet potatoes</b> or <b>yams</b> , how much did you usually eat?			
53. How often did you eat <b>lettuce salads</b> (with or without other vegetables)?				☐ 1 small potato or less than ½ cup ☐ 1 medium potato or ½ to 1 cup		
	ER (GO TO QUESTION	N 54)	□ 1 large potato or more than 1 cup			
□ 7-11	imes per year times per year e per month	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> </ul>	<ul> <li>56. How often did you eat French fries, home fries, hash browned potatoes, or tater tots?</li> <li> □ NEVER (GO TO QUESTION 57) </li> </ul>			
	imes per month e per week	<ul> <li>1 time per day</li> <li>2 or more times per day</li> </ul>		□ 7· □ 1	-6 times per year -11 times per year time per month	☐ 2 times per week ☐ 3-4 times per week ☐ 5-6 times per week
	ch time you ate <b>lettu</b> u usually eat?	<b>ce salads</b> , how much did			-3 times per month time per week	<ul> <li>1 time per day</li> <li>2 or more times per day</li> </ul>
	Less than ¼ cup ¼ to 1½ cups More than 1½ cups				Each time you ate <b>Fren</b> hash browned potatoe much did you usually ea	ch fries, home fries, es, or tater tots how
	53b. How often did the lettuce salads you ate include dark green lettuce?			[ [	Less than 10 fries or les 10 to 25 fries or $\frac{1}{2}$ to 1 of Marce than 25 fries or $\frac{1}{2}$ to 1	cup
	Almost never or never About ¼ of the time About ½ of the time About ¾ of the time Almost always or always	S		56b.	☐ More than 25 fries or mo How often did the Frenc browned potatoes, or ta <b>poutine (with gravy a</b> r	ch fries, home fries, hash ter tots you ate include
<ul> <li>54. How often did you eat salad dressing (including low-fat) on salads?</li> </ul>			] [	Almost never or never About ¼ of the time About ½ of the time About ¾ of the time		
□ NEVER (GO TO QUESTION 55)				Almost always or always	5	
☐ 7-11 ☐ 1 tim ☐ 2-3 t	imes per year times per year le per month imes per month le per week	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	5	N    1.    7.	w often did you eat <b>pota</b> EVER (GO TO QUESTION -6 times per year -11 times per year time per month	
	ch time you ate <b>salad</b> w much did you usua	ate <b>salad dressing on salads</b> , you usually eat?		☐ 2-3 times per month ☐ 1 time per week	<ul> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	
	ess than 2 tablespoon 2 to 4 tablespoons More than 4 tablespoon				Each time you ate <b>pota</b> you usually eat?	
<ul><li>↓</li><li>55. How o</li></ul>	ften did you eat <b>swee</b>	et potatoes or yams?		] [	☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup	
■ NEVER (GO TO QUESTION 56)		5		v often did you eat <b>bake</b> atoes?	d, boiled, or mashed	
7-11	☐ 1-6 times per year ☐ 7-11 times per year	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>		-	EVER (GO TO QUESTION	N 59)
🗖 2-3 t	e per month imes per month e per week			□ 7· □ 1 □ 2·	-6 times per year -11 times per year time per month -3 times per month time per week	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times</li> </ul>
♥ Question 56 appears in the next column			0	) Duestion 5	9 appears on the next page	per day 1465
_			15 15			

Over the <u>past 12 months</u>	58h. Each time <b>cheese</b> or <b>cheese sauce</b> was added to your potatoes, how much was usually added?			
<ul> <li>58a. Each time you ate baked, boiled, or mashed potatoes, how much did you usually eat?</li> <li>1 small potato or less than ½ cup</li> <li>1 medium potato or ½ to 1 cup</li> <li>1 large potato or more than 1 cup</li> </ul>	<ul> <li>Less than 1 tablespoon</li> <li>1 to 3 tablespoons</li> <li>More than 3 tablespoons</li> </ul>			
58b. How often was <b>sour cream</b> (including low-fat)	59. How often did you eat <b>salsa</b> ?			
<ul> <li>58b. How often was sour cream (including low-fat) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?</li> <li>Almost never or never (GO TO QUESTION 58d)</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>58c. Each time sour cream was added to your potatoes, how much was usually added?</li> <li>Less than 1 tablespoon</li> <li>1 to 4 tablespoons</li> <li>More than 4 tablespoons</li> <li>58d. How often was margarine (including light) added to your potatoes, EITHER IN COOKING OR AT THE TABLE?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>NEVER (GO TO QUESTION 60)</li> <li>1-6 times per year</li> <li>2-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul> 59a. Each time you ate salsa, how much did you usually eat? <ul> <li>Less than 2 tablespoons</li> <li>2 tablespoons to ½ cup</li> <li>More than ½ cup</li> </ul> 60. How often did you eat ketchup? <ul> <li>NEVER (GO TO QUESTION 61)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>3-4 times per week</li> <li>2 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2 tablespoons to ½ cup</li> <li>More than ½ cup</li> </ul> 60. How often did you eat ketchup? <ul> <li>60. How often did you eat ketchup?</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>1 time per month</li> <li>2 times per week</li> <li>2 times per week</li> <li>2 times per year</li> <li>3-4 times per week</li> <li>2 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2 times per week</li> <li>3-4 times per week</li> <li>4 time per day</li> <li>4 time per day</li> <li>4 time per day</li> <li>6 times per week</li> <li>2 times per week</li> <li>3 time per day</li> <li>6 time per week</li> <li>2 times per week</li> <li>4 time per day</li> <li>6 time per week</li> <li>2 times per week</li> <li>2 times per week</li> <li>3 time per day</li> </ul>			
<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ⅓ of the time</li> <li>Almost always or always</li> <li>58f. Each time margarine or butter was added to your potatoes, how much was usually added?</li> <li>Never added</li> <li>Less than 1 teaspoon</li> <li>1 to 3 teaspoons</li> <li>More than 3 teaspoons</li> <li>58g. How often was cheese or cheese sauce added to your potatoes, EITHER IN COOKING OR AT THE TABLE?</li> <li>Almost never or never (GO TO QUESTION 59)</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>2 to 6 teaspoons</li> <li>More than 6 teaspoons</li> <li>61. How often did you eat stuffing, dressing, or dumplings?</li> <li>C NEVER (GO TO QUESTION 62)</li> <li>C 1-6 times per year</li> <li>C 2-11 times per year</li> <li>C 3-4 times per week</li> <li>C 7-11 time per month</li> <li>C 5-6 times per week</li> <li>C 2-3 times per month</li> <li>C 1 time per week</li> <li>C 2 or more times per day</li> <li>61a. Each time you ate stuffing, dressing, or dumplings, how much did you usually eat?</li> <li>C Less than ½ cup</li> <li>C ½ to 1 cup</li> <li>More than 1 cup</li> </ul>			
<i>Question 59 appears in the next column</i>	Question 62 appears on the next page 1465			

Over the <u>past 12 months</u>	65. How often did you eat <b>other cooked dried beans</b> (such as pintos, kidney, black-eyed peas, lima,			
62. How often did you eat <b>chili</b> ?	lentils, soybeans, or refried beans)? ( <i>Please do not include bean, pea or lentil soups, or chili.</i> )			
	$\square$ NEVER (GO TO QUESTION 66)			
□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□1 time per week□2 or more times□1 time per day□1 times	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 week       1 time per week         1 time per week       2 or more times per day         1 time per week       2 or more times per day			
62a. Each time you ate <b>chili</b> , how much did you usually eat?	65a. Each time you ate <b>other beans</b> , how much did you usually eat?			
<ul> <li>☐ Less than 1 cup</li> <li>☐ 1 to 1¾ cups</li> <li>☐ More than 1¾ cups</li> </ul>	☐ Less than ¼ cup ☐ ¼ to ¾ cup ☐ More than ¾ cup			
63. How often did you eat <b>Mexican foods</b> (such as tacos, tostados, burritos, tamales, fajitas, enchiladas, quesadillas, or chimichangas)?	65b. How often were the other beans you ate <b>refried</b> <b>beans</b> , <b>beans prepared with any type of fat</b> , or <b>with meat added</b> ?			
<ul> <li>NEVER (GO TO QUESTION 64)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>	<ul> <li>Almost never or never</li> <li>About <sup>1</sup>/<sub>4</sub> of the time</li> <li>About <sup>1</sup>/<sub>2</sub> of the time</li> <li>About <sup>3</sup>/<sub>4</sub> of the time</li> <li>Almost always or always</li> </ul> 66. How often did you eat other kinds of vegetables?			
<ul> <li>63a. Each time you ate Mexican foods, how much did you usually eat?</li> <li>Less than 1 taco, burrito, etc.</li> <li>1 to 2 tacos, burritos, etc.</li> <li>More than 2 tacos, burritos, etc.</li> </ul> 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64. How often did you eat baked beans? ( <i>Please include canned, ready-made, or homemade.</i> ) 64a. Each time per week <ul> <li>2 times per week</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>64a. Each time you ate baked beans, how much did you usually eat?</li> <li>Less than ½ cup</li> <li>½ to 1 cup</li> <li>More than 1 cup</li> </ul>	<ul> <li>NEVER (GO TO QUESTION 67)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>66a. Each time you ate other kinds of vegetables, how much did you usually eat?</li> <li>Less than ¼ cup</li> <li>1/4 to ½ cup</li> <li>More than ½ cup</li> </ul> 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 67. How often did you eat rice or other cooked grains (such as bulgur, cracked wheat, or millet)? 9. Or not times per week 1. time per week 1. time per day 1. time per day 2. or more times per day 9. day			
Question 65 appears in the next column	Question 68 appears on the next page 1465			



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Over the <u>past 12 months</u> 67a. Each time you ate <b>rice</b> or <b>other cooked grains</b> , how much did you usually eat? ☐ Less than ½ cup ☐ ½ to 1½ cups ☐ More than 1½ cups	<ul> <li>68d. Each time margarine or butter was added to your pancakes, waffles, or French toast, how much was usually added?</li> <li>Never added</li> <li>Less than 1 teaspoon</li> <li>1 to 3 teaspoons</li> <li>More than 3 teaspoons</li> <li>68e. How often was syrup added to your pancakes, waffles, or French toast?</li> <li>Almost never or never (GO TO QUESTION 69)</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>68f. Each time syrup was added to your pancakes, waffles, or French toast, how much was usually added?</li> </ul>		
<ul> <li>67b. How often was butter, margarine, or oil added to your rice or other cooked grains IN COOKING OR AT THE TABLE?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul> 68. How often did you eat pancakes, waffles, or French toast?			
Image: Prench toast?         Image: NEVER (GO TO QUESTION 69)         Image: 1-6 times per year         Image: 1-6 times per week         Image: 1-6 times per week	<ul> <li>Less than 1 tablespoon         <ul> <li>1 to 3 tablespoons</li> <li>More than 3 tablespoons</li> </ul> </li> <li>69. How often did you eat lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini? (<i>Please do not include spaghetti or other pasta.</i>)</li> <li>NEVER (GO TO QUESTION 70)</li> </ul>		
<ul> <li>68a. Each time you ate pancakes, waffles, or French toast, how much did you usually eat?</li> <li>Less than 1 medium piece</li> <li>1 to 3 medium pieces</li> <li>More than 3 medium pieces</li> <li>68b. How often was margarine (including light) added to your pancakes, waffles, or French toast AFTER COOKING OR AT THE TABLE?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> </ul>	<ul> <li>☐ 1-6 times per year</li> <li>☐ 2 times per week</li> <li>☐ 7-11 times per year</li> <li>☐ 3-4 times per week</li> <li>☐ 1 time per month</li> <li>☐ 5-6 times per week</li> <li>☐ 2 or more times per day</li> <li>☐ 1 time per week</li> <li>☐ 2 or more times per day</li> <li>69a. Each time you ate lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini, how much did you usually eat?</li> <li>☐ Less than 1 cup</li> </ul>		
	<ul> <li>1 to 2 cups</li> <li>More than 2 cups</li> <li>70. How often did you eat macaroni and cheese?</li> <li>70. How often did you eat macaroni and cheese?</li> <li>71. How often did you eat macaroni and cheese?</li> <li>1.6 times per year</li> <li>2.1 times per year</li> <li>3.4 times per week</li> <li>7.11 times per year</li> <li>3.4 times per week</li> <li>2.3 times per month</li> <li>5.6 times per week</li> <li>2.3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>70a. Each time you ate macaroni and cheese, how much did you usually eat?</li> </ul>		
▼ Question 69 appears in the next column	Less than 1 cup 1 to 1½ cups More than 1½ cups Question 71 appears on the next page 1465		

#### C

	I
Over the <u>past 12 months</u>	72d.
71. How often did you eat <b>pasta salad</b> or <b>macaroni salad</b> ?	
□ NEVER (GO TO QUESTION 72)	
□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 timesper day□per day	73. Но
71a. Each time you ate <b>pasta salad</b> or <b>macaroni</b> <b>salad</b> , how much did you usually eat?	
☐ Less than ½ cup ☐ ½ to 1 cup ☐ More than 1 cup	
▼ 72. Other than the pastas listed in Questions 69, 70, and 71, how often did you eat pasta, spaghetti, or other noodles?	73a.
□       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	73b.
72a. Each time you ate <b>pasta</b> , <b>spaghetti</b> , or <b>other noodles</b> , how much did you usually eat?	73c.
☐ Less than 1 cup ☐ 1 to 3 cups ☐ More than 3 cups	
<ul> <li>72b. How often did you eat your pasta, spaghetti, or other noodles with tomato sauce or spaghetti sauce made WITH meat?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> </ul>	73d.
<ul> <li>Almost always or always</li> <li>72c. How often did you eat your pasta, spaghetti, or</li> </ul>	
other noodles with <b>tomato sauce</b> or <b>spaghetti sauce made WITHOUT meat</b> ?  Almost never or never	73e.
<ul> <li>Almost never of never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	
↓ Question 73 appears in the next column	Introducti

	72d. How often did you eat your pasta, spaghetti, or other noodles with margarine, butter, oil, or cream sauce?		
	<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>		
7	3. How often did you eat <b>bagels</b> or <b>English muffins</b> ?		
	□ NEVER (GO TO INTRODUCTION TO QUESTION 74)		
	<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 times per day</li> <li>2 or more times per day</li> </ul>		
	73a. How often were the bagels or English muffins you ate <b>whole wheat</b> ?		
	<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>		
	73b. Each time you ate <b>bagels</b> or <b>English muffins</b> , how many did you usually eat?		
	<ul> <li>☐ Less than 1 bagel or English muffin</li> <li>☐ 1 bagel or English muffin</li> <li>☐ More than 1 bagel or English muffin</li> </ul>		
	73c. How often was <b>margarine</b> (including light) added to your bagels or English muffins?		
	<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>		
	73d. How often was <b>butter</b> (including light) added to your bagels or English muffins?		
	<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>		
	73e. Each time <b>margarine</b> or <b>butter</b> was added to your bagels or English muffins, how much was usually added?		
	☐ Never added ☐ Less than 1 teaspoon		

- I to 2 teaspoons
  More than 2 teaspoons

ion to Question 74 appears on the next page



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



<ul> <li>Over the past 12 months</li> <li>75a. Each time you ate breads, dinner rolls or flatbreads, NOT AS PART OF SANDWICHES, how much did you usually eat?</li> <li>1 slice or 1 dinner roll or ½ flatbread</li> <li>2 slices or 2 dinner rolls or 1 flatbread</li> <li>More than 2 slices or dinner rolls or more than 1 flatbread</li> <li>75b. How often were the breads, rolls or flatbreads you ate white?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ⅔ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>75g. Each time cream cheese was added to your breads, rolls or flatbreads, how much was usually added?</li> <li>Less than 1 tablespoon</li> <li>1 to 2 tablespoons</li> <li>More than 2 tablespoons</li> </ul> 76. How often did you eat jam, jelly, or honey on bagels, muffins, bread, rolls, or crackers? 76. NEVER (GO TO QUESTION 77) <ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>2 times per week</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>
<ul> <li>75c. How often was margarine (including light) added to your breads, rolls or flatbreads?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>75d. How often was butter (including light) added to your breads, rolls or flatbreads?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul> 75e. Each time margarine or butter was added to your breads, rolls or flatbreads, how much was usually added? <ul> <li>Never added</li> <li>Less than 1 teaspoon</li> <li>1 to 2 teaspoons</li> <li>More than 2 teaspoons</li> </ul> 75f. How often was cream cheese (including low-fat) added to your breads, rolls or flatbreads? <ul> <li>Almost never or never (GO TO QUESTION 76)</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul>	76a. Each time you ate jam, jelly, or honey, how much did you usually eat?         Less than 2 teaspoons         2 to 4 teaspoons         More than 4 teaspoons         77. How often did you eat peanut butter or other nut butter?         NEVER (GO TO QUESTION 78)         1-6 times per year         2.1 time per month         2.3 times per month         1 time per week         2.3 times per week         1 time per week         2.3 times per week         1 time per week         1 time per week         2.3 times per month         1 time per week         2.3 times per week         1 time per week         1 time per week         2.3 times per month         1 time per week         1 to 2 tablespoons         More than 2 tablespoons         1 to 2 tablespoons         More than 2 tablespoons         78. How often did you eat roast beef or steak IN sANDWICHES?         NEVER (GO TO QUESTION 79)         1-6 times per year       3-4 times per week         1 time per day       2 or more times per week         2-3 time
Vuestion 76 appears in the next column	♦ Question 79 appears on the next page 1465



Over the <u>past 12 months</u> 78a. Each time you ate <b>roast beef</b> or <b>steak IN</b>	81. How often did you eat <b>other cold cuts</b> or <b>luncheon</b> <b>meats</b> (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? ( <i>Please do</i>		
<ul> <li>SANDWICHES, how much did you usually eat?</li> <li>Less than 1 slice or less than 2 ounces</li> <li>1 to 2 slices or 2 to 4 ounces</li> <li>More than 2 slices or more than 4 ounces</li> </ul> 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.) I NEVER (GO TO QUESTION 80) <ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul> 79a. Each time you ate turkey or chicken COLD CUTS, how much did you usually eat? <ul> <li>Less than 1 slice</li> <li>1 to 3 slices</li> <li>More than 3 slices</li> </ul>	Pastrann, of others, including tow-fat)? (Please do not include ham, turkey, or chicken cold cuts.)         Image: NEVER (GO TO QUESTION 82)         Image: 1-6 times per year       2 times per week         Image: 7-11 times per year       3-4 times per week         Image: 1 time per month       5-6 times per week         Image: 2-3 times per month       1 time per day         Image: 1 time per week       2 or more times per day         Image: 1 time per week       2 or more times per day         81a. Each time you ate other cold cuts or luncheon meats, how much did you usually eat?         Image: Less than 1 slice         Image: 1 to 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 ¼ of the time         About ¾ of the time         Almost always or always		
<ul> <li>80. How often did you eat luncheon or deli-style ham? (We will ask about other ham later.)</li> <li>INEVER (GO TO QUESTION 81)</li> <li>A 6 time and a start of the s</li></ul>	<ul> <li>82. How often did you eat canned tuna (including in salads, sandwiches, or casseroles)?</li> </ul>		
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         80a. Each time you ate luncheon or deli-style ham,	<ul> <li>NEVER (GO TO QUESTION 83)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>		
<ul> <li>book Lash and you use tarterior of a child of the ham, how much did you usually eat?</li> <li>Less than 1 slice</li> <li>1 to 3 slices</li> <li>More than 3 slices</li> <li>80b. How often was the luncheon or deli-style ham you ate light, low-fat, or fat-free?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>82a. Each time you ate canned tuna, how much did you usually eat?</li> <li>Less than ¼ cup or less than 2 ounces</li> <li>1/4 to ½ cup or 2 to 3 ounces</li> <li>More than ½ cup or more than 3 ounces</li> <li>82b. How often was the canned tuna you ate water-packed?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>About ¾ of the time</li> </ul>		
▼ Question 81 appears in the next column	Question 83 appears on the next page 1465		

<ul> <li>Over the past 12 months</li> <li>82c. How often was the canned tuna you ate prepared with mayonnaise or other dressing (including low-fat)?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>83. How often did you eat GROUND chicken or</li> </ul>	<ul> <li>84b. Each time you ate beef hamburgers or cheeseburgers from a FAST FOOD or OTHER RESTAURANT, how much did you usually eat?</li> <li>Less than 1 burger</li> <li>1 burger</li> <li>More than 1 burger</li> <li>84c. How often did you have cheeseburgers rather than hamburgers from a FAST FOOD or OTHER RESTAURANT?</li> <li>Almost never or never</li> </ul>		
<b>turkey</b> ? (We will ask about other chicken and turkey later.)	☐ 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         □       1 time per week       □       2 or more times per day	<ul> <li>85. How often did you eat beef hamburgers or cheeseburgers that were NOT from a FAST FOOD or OTHER RESTAURANT?</li> <li> INEVER (GO TO QUESTION 86) </li> </ul>		
<ul> <li>83a. Each time you ate GROUND chicken or turkey, how much did you usually eat?</li> <li>Less than 2 ounces or less than ½ cup</li> <li>2 to 4 ounces or ½ to 1 cup</li> <li>More than 4 ounces or more than 1 cup</li> </ul> 84. How often did you eat beef hamburgers or chapter burgers from a EAST FOOD or OTUER	<ul> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>85a. Each time you ate beef hamburgers or cheeseburgers that were NOT from a FAST FOOD or OTHER RESTAURANT, how much</li> </ul>		
cheeseburgers from a FAST FOOD or OTHER RESTAURANT?	did you usually eat?		
<ul> <li>NEVER (GO TO QUESTION 85)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul> 84a. Each time you ate beef hamburgers or cheeseburgers from a FAST FOOD or OTHER RESTAURANT, what size did you usually eat? <ul> <li>Small hamburger (such as a regular Burger King or McDonald's Hamburger)</li> <li>Medium (such as McDonald's or Burger King Double Burger or Cheeseburger)</li> <li>Large (such as Burger King Whopper or Double Whopper or a McDonald's Double</li> </ul>	<ul> <li>Less than 1 patty or less than 2 ounces</li> <li>1 patty or 2 to 4 ounces</li> <li>More than 1 patty or more than 4 ounces</li> <li>85b. How often were these beef hamburgers or cheeseburgers made with lean or extra lean ground beef?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>86. How often did you eat ground beef in mixtures (such as meatballs, casseroles, chili, or meatloaf)?</li> <li>NEVER (GO TO QUESTION 87)</li> <li>1 6 times per year</li> </ul>		
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         2-3 times per month       1 time per day         1 time per week       2 or more times per day         Question 87 appears on the next page       1465		
	1		
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Over the <u>past 12 months</u> 86a. Each time you ate <b>ground beef in mixtures</b> ,	89. How often did you eat <b>roast beef</b> or <b>pot roast</b> ? ( <i>Please do not include roast beef or pot roast in sandwiches.</i> )		
how much did you usually eat?			
<ul> <li>☐ Less than 3 ounces or less than ½ cup</li> <li>☐ 3 to 8 ounces or ½ to 1 cup</li> <li>☐ More than 8 ounces or more than 1 cup</li> </ul>	□       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		
<ol> <li>How often did you eat hot dogs, wieners or frankfurters? (Please do not include sausages or vegetarian hot dogs.)</li> </ol>	☐ 1 time per week ☐ 2 or more times per day		
	89a. Each time you ate <b>roast beef</b> or <b>pot roast</b> , 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	<ul> <li>Less than 2 ounces</li> <li>2 to 6 ounces</li> <li>More than 6 ounces</li> <li>90. How often did you eat steak (beef)? (<i>Please do not</i></li> </ul>		
per day	include steak in sandwiches)		
87a. Each time you ate <b>hot dogs, wieners,</b> or <b>frankfurters</b> , how many did you usually eat?			
<ul> <li>Less than 1 hot dog</li> <li>1 to 2 hot dogs</li> <li>More than 2 hot dogs</li> <li>87b. How often were the hot dogs, wieners, or frankfurters you ate light or low-fat?</li> </ul>	1-6 times per year2 times per week7-11 times per year3-4 times per week1 time per month5-6 times per week2-3 times per month1 time per day1 time per week2 or more timesper dayper day		
<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>90a. Each time you ate steak (beef), how much did you usually eat?</li> <li>□ Less than 3 ounces</li> <li>□ 3 to 7 ounces</li> <li>□ More than 7 ounces</li> </ul>		
<ul> <li>88. How often did you eat beef mixtures (such as beef stew, beef curry, beef pot pie, beef and noodles, or beef and vegetables)?</li> <li>NEVER (GO TO QUESTION 89)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2 times per day</li> </ul>	<ul> <li>90b. How often was the steak you ate lean steak?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>91. How often did you eat pork or beef spareribs?</li> </ul>		
□ 1 time per week □ 2 or more times per day			
88a. Each time you ate <b>beef mixtures</b> , how much did you usually eat? Less than ½ cup ½ to 1½ cups More than 1½ cups	□       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		
▼ Question 89 appears in the next column	Question 92 appears on the next page 1465		

-		1				
Over the <u>past 12 months</u>		9	94. How often did you eat <b>baked</b> , <b>broiled</b> , <b>roasted</b> , <b>stewed</b> , or <b>fried chicken</b> (including nuggets)? ( <i>Please do not include chicken in mixtures.</i> )			
91a. Each time you ate <b>pork</b> or <b>beef spareribs</b> , how much did you usually eat? □ Less than 4 ribs						
		[	- NEVER (GO TO QUE	STION	95)	
4 to 12 ribs			<ul> <li>☐ 1-6 times per year</li> <li>☐ 7-11 times per year</li> <li>☐ 1 time per month</li> </ul>		<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> </ul>	
			<ul> <li>2-3 times per month</li> <li>1 time per week</li> </ul>		□ 1 time per day □ 2 or more times	
92. How often did you eat roast cutlets, or turkey nuggets sandwiches)?					per day	
	1 93)			hicke	<b>n</b> (including nuggets),	
<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> </ul>		how much did you	sticks c	or wings, less than	
2-3 times per month	□ 1 time per day □ 2 or more times		<ul> <li>1 breast or thigh, or less than 4 nuggets</li> <li>□ 2 drumsticks or wings, 1 breast or thigh, or 4 to</li> </ul>			
	per day		8 nuggets More than 2 drum 1 breast or thigh, o			
92a. Each time you ate <b>roast</b> or <b>turkey nuggets</b> , how			i breast or thigh,		e man o nuggets	
eat? (Please note: 4 to ounces.)					en you ate <b>fried chicken</b> chicken nuggets?	
Less than 2 ounces			Almost never or n	ever		
□ 2 to 5 ounces □ More than 5 ounces			About ¼ of the tim			
▼ _			About ¾ of the tim	пе		
93. How often did you eat <b>chick</b> salads, sandwiches, casser			Almost always or a			
stews, or other mixtures)?			94c. How often was the	e chick	en you ate WHITE meat?	
	194)		☐ Almost never or ne ☐ About ¼ of the tim			
☐ 1-6 times per year	2 times per week		About $\frac{1}{2}$ of the tim About $\frac{3}{4}$ of the tim			
<ul> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> </ul>	□ 3-4 times per week □ 5-6 times per week □ 1 time per day		Almost always or a			
☐ 1 time per week	2 or more times per day		94d. How often did you		nicken <b>WITH skin</b> ?	
93a. Each time you ate <b>chic</b> l	<b>en mixtures</b> how much		☐ Almost never or ne ☐ About ¼ of the tim			
did you usually eat?			About ½ of the tim	ne		
Less than $\frac{1}{2}$ cup $\frac{1}{2}$ to $\frac{1}{2}$ cups			☐ About ¾ of the tim ☐ Almost always or a			
More than 1½ cups		9	, 5. How often did you eat			
			- INEVER (GO TO QUE			
			☐ 1-6 times per year		2 times per week	
			☐ 7-11 times per year ☐ 1 time per month		<ul> <li>☐ 3-4 times per week</li> <li>☐ 5-6 times per week</li> </ul>	
			2-3 times per month		□ 1 time per day	
			1 time per week		□ 2 or more times per day	
↓ ↓		' ]				
Question 94 appears in the next column		Q	, uestion 96 appears on the next µ	page	1465	
	:	25				

Over the past 12 months	98a. Each time you ate <b>liver</b> or <b>liverwurst</b> , how
<ul> <li>95a. Each time you ate baked ham or ham steak, how much did you usually eat?</li> <li>Less than 1 ounce</li> <li>1 to 3 ounces</li> <li>More than 3 ounces</li> </ul>	<ul> <li>But the you use inverse inverse and its for the second state inverse inverse</li></ul>
<ul> <li>96. How often did you eat pork (including chops, roasts, and in mixed dishes)? (Please do not include ham, ham steak, or sausage.)</li> <li>NEVER (GO TO QUESTION 97)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> <li>96a. Each time you ate pork, how much did you usually eat?</li> <li>Less than 2 ounces or less than 1 chop</li> <li>2 to 5 ounces or 1 chop</li> <li>More than 5 ounces or more than 1 chop</li> </ul>	<ul> <li>NEVER (GO TO QUESTION 100)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>7-11 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>2 or more times per day</li> <li>99a. Each time you ate bacon, how much did you usually eat?</li> <li>Fewer than 2 slices</li> <li>2 to 4 slices</li> <li>More than 4 slices</li> <li>99b. How often was the bacon you ate light, low-fat, or lean?</li> <li>Almost never or never</li> </ul>
<ul> <li>97. How often did you eat gravy on meat, chicken, potatoes (NOT including poutine), rice, etc.?</li> <li>NEVER (GO TO QUESTION 98)</li> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> </ul>	<ul> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul> 100. How often did you eat sausage (including low-fat)? INEVER (GO TO QUESTION 101)
<ul> <li>97a. Each time you ate gravy on meat, chicken, potatoes, rice, etc., how much did you usually eat?</li> <li>Less than ¼ cup</li> <li>¼ to ½ cup</li> <li>More than ½ cup</li> </ul> 98. How often did you eat liver (all kinds) or liverwurst?	<ul> <li>1-6 times per year</li> <li>2 times per week</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>100a. Each time you ate sausage, how much did you usually eat?</li> <li>Less than 2 small links or less than 1 large link</li> <li>2 to 5 small links or 1 to 2 large links</li> <li>Mere them 5 mere times 2 large links</li> </ul>
<ul> <li>NEVER (GO TO QUESTION 99)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	<ul> <li>More than 5 small links or more than 2 large links</li> <li>100b. How often was the sausage you ate light, low-fat, or lean?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>
Question 99 appears in the next column	Question 101 appears on the next page   1465     26   1465

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

Over the <u>past 12 months</u>		109. How often did you eat <b>soy burgers</b> or <b>soy</b>		
106a. Which of the following <b>fats</b> were regularly used to prepare your meat, poultry, or fish?		meat-substitutes?		
(Mark all that apply.)  Margarine (including light) Butter (including light) Lard, fatback, or bacon fat Olive oil	<ul> <li>Corn oil</li> <li>Canola or rapeseed oil</li> <li>Oil spray, such as Pam or others</li> <li>Other kinds of oils</li> <li>None of the above</li> </ul>		1-6 times per year 7-11 times per year 1 time per month 2-3 times per month 1 time per week Each time you ate <b>soy b</b>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> <li>per day</li> </ul> Ourgers or soy much did you usually eat?
107. Thinking about the <b>MEAT</b> was it cooked by <b>broiling</b> , or <b>pan-frying</b> ? (Do not inc	grilling, barbecuing,		□ Less than ¼ cup or less □ ¼ to 1 cup or 2 to 8 oun □ More than 1 cup or more	than 2 ounces ces
MEVER (GO TO QUESTIO	N 108)	▼ 110. Ov	er the past 12 months, die	d you eat <b>soups</b> ?
<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	↓	NO (GO TO QUESTION 11 YES How often did you eat so NEVER	
107a. Each time you ate me broiling, grilling, barbe was the <b>outside appe</b> Light brown Medium brown Heavily browned or bl	ecuing, or pan-frying, what earance of the meat?		<ul> <li>1-6 times per winter</li> <li>7-11 times per winter</li> <li>1 time per month</li> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>
was the <b>inside appea</b> Red (rare) Pink (medium) Brown (well-done)	ecuing, or pan-frying, what arance of the meat?	110b.	How often did you eat so OF THE YEAR? NEVER 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
108. How often did you eat <b>tofu</b> → □ NEVER (GO TO QUESTIO			☐ 2-3 times per month ☐ 1 time per week	☐ 1 time per day ☐ 2 or more times per day
<ul> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2-3 times per week</li> </ul>	<ul> <li>2 times per week</li> <li>3-4 times per week</li> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul>	110c.	Each time you ate <b>soup</b> usually eat? Less than 1 cup 1 to 2 cups More than 2 cups	
108a. Each time you ate <b>tof</b> u usually eat?				
☐ Less than ¼ cup or le ☐ ¼ to ¾ cup or 2 to 6 c ☐ More than ¾ cup or m	ounces			
♥ Question 109 appears in the next column	1	▼ Question	111 appears on the next page	1465
	2	28		

Over the past 12 months	112. How often did you eat <b>crackers</b> ?			
110d. How often were the soups you ate <b>bean, pea</b> ,	► ■ NEVER (GO TO QUESTION 113)			
<ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>	Image: 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			
<ul> <li>Almost always or always</li> <li>110e. How often were the soups you ate cream soups (including chowders)?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul> 110f. How often were the soups you ate tomato or vegetable soups (NOT cream soups)? <ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul> 110g. How often were the soups you ate broth soups (including chicken) with or without noodles or rice? <ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>Bout ¼ of the time</li> <li>Context always or always</li> </ul>				
<ul> <li>usually eat?</li> <li>Less than 1 slice or less than 1 mini pizza</li> <li>1 to 3 slices or 1 to 2 mini pizzas</li> <li>More than 3 slices or more than 2 mini pizzas</li> </ul> 111b. How often did you eat pizza with pepperoni, sausage, or other meat? <ul> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul>	<ul> <li>114a. Each time you ate baking powder biscuits including scones or tea biscuits, how many did you usually eat?</li> <li>□ Fewer than 1 biscuit</li> <li>□ 1 to 2 biscuits</li> <li>□ More than 2 biscuits</li> </ul>			
<i>Question 112 appears in the next column</i>	Question 115 appears on the next page   1465     29   1465			

Over the <u>past 12 months</u>		1	18. How often did you e	eat <b>pretz</b>	zels?	
115. How often did you eat <b>potato chips</b> (including		г	┍━━ □ NEVER (GO TO QUESTION 119)			
low-fat, baked, or low-salt)?			☐ 1-6 times per year		2 times per week	
■ NEVER (GO TO QUESTION	2 times per week		☐ 7-11 times per yea ☐ 1 time per month ☐ 2-3 times per mont ☐ 1 time per week		□ 3-4 times per week □ 5-6 times per week □ 1 time per day □ 2 or more times	
7-11 times per year3-4 times per week1 time per month5-6 times per week2-3 times per month1 time per day			ate <b>nretz</b>	per day		
☐ 1 time per week	□ 2 or more times per day		usually eat?	-		
115a. Each time you ate <b>potat</b> you usually eat?	t <b>o chips</b> , how much did		☐ 7 to 20 average ☐ More than 20 a	e twists		
<ul> <li>☐ Fewer than 10 chips or I</li> <li>☐ 10 to 25 chips or 1 to 2 d</li> <li>☐ More than 25 chips or m</li> </ul>	cups	1	119. How often did you eat peanuts, walnuts, almonds, or other nuts?			
<b>↓</b>		١r	- DNEVER (GO TO Q	UESTION	J 120)	
116. How often did you eat <b>corn</b> (including low-fat, baked, or			☐ 1-6 times per year ☐ 7-11 times per yea	r	☐ 2 times per week ☐ 3-4 times per week	
NEVER (GO TO QUESTION     1-6 times per year	I 117) □ 2 times per week		<ul> <li>☐ 1 time per month</li> <li>☐ 2-3 times per mont</li> <li>☐ 1 time per week</li> </ul>	h	<ul> <li>5-6 times per week</li> <li>1 time per day</li> <li>2 or more times</li> </ul>	
7-11 times per year	3-4 times per week				per day	
☐ 1 time per month ☐ 2-3 times per month ☐ 1 time per week	<ul> <li>☐ 5-6 times per week</li> <li>☐ 1 time per day</li> <li>☐ 2 or more times</li> </ul>		119a. Each time you ate <b>peanuts</b> , <b>walnuts</b> , <b>almor</b> or <b>other nuts</b> , how much did you usually eat			
	per day		☐ Less than ¼ cu ☐ ¼ to ½ cup	р		
116a. Each time you ate <b>corn chips</b> , how much did you usually eat?			$\square More than \frac{1}{2} ct$	qu		
☐ Fewer than 10 chips or less than 1 cup ☐ 10 to 25 chips or 1 to 2 cups			119b. How often were		s you ate <b>peanuts</b> ?	
☐ More than 25 chips or more than 2 cups			<ul> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>			
117. How often did you eat <b>popcorn</b> (including low-fat)?						
	N 118)	1	20. How often did you	eat <b>flaxs</b>	eeds?	
☐ 1-6 times per year ☐ 7-11 times per year	☐ 2 times per week ☐ 3-4 times per week	ſ	D NEVER (GO TO Q	UESTION	J 121)	
1 time per month	5-6 times per week		☐ 1-6 times per year ☐ 7-11 times per year	r	<ul> <li>2 times per week</li> <li>3-4 times per week</li> </ul>	
<ul> <li>2-3 times per month</li> <li>1 time per week</li> </ul>	☐ 1 time per day ☐ 2 or more times		□ 1 time per month □ 2-3 times per mont		□ 5-6 times per week □ 1 time per day	
	per day Each time you ate <b>popcorn</b> , how much did you		1 time per week		☐ 2 or more times per day	
usually eat? Less than 1½ cups, popped 1½ to 5 cups, popped More than 5 cups, popped			120a. Each time you a usually eat?	ate flaxs	eeds, how much did you	
			☐ Less than 1 tab ☐ 1 to 2 tablespo ☐ More than 2 tab	ons	S	
		¥				
Question 118 appears in the next column		Q 30	Duestion 121 appears on the n	lext page		
		- •				

Over the <u>past 12 months</u>	123b. How often was the <b>yogurt</b> you ate <b>low-fat</b> or <b>fat-free</b> ?		
121. How often did you eat <b>other seeds</b> , like <b>sunflower</b> or <b>pumpkin seeds</b> ?	Almost never or never		
	☐ 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         □       1 time per week       □       2 or more times per day         □       1 time per week       □       2 or more times per day	<ul> <li>Almost always or always</li> <li>124. How often did you eat cottage cheese (including low-fat)?</li> <li>NEVER (GO TO QUESTION 125)</li> </ul>		
121a. Each time you ate <b>other seeds</b> , how much did you usually eat?	□ 7-11 times per year □ 3-4 times per week		
<ul> <li>☐ Less than 2 tablespoons</li> <li>☐ 2 tablespoons to ½ cup</li> <li>☐ More than ½ cup</li> </ul>	□ 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		
122. How often did you eat energy or high-protein bars (such as Power Bars, Vector, Clif, Luna, Isoflex or others)?	<ul> <li>124a. Each time you ate cottage cheese, how much did you usually eat?</li> <li>□ Less than ¼ cup</li> </ul>		
□ NEVER (GO TO QUESTION 123)	$\square \frac{1}{4} \text{ to } \frac{3}{4} \text{ cup}$ $\square More \text{ than } \frac{3}{4} \text{ cup}$		
□       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	125. How often did you eat cheese (including low-fat; including on cheeseburgers or in sandwiches or subs, NOT including cream cheese)?		
per day	NEVER (GO TO QUESTION 126)		
<ul> <li>122a. Each time you ate energy or high-protein bars, how much did you usually eat?</li> <li>□ Less than 1 bar</li> <li>□ 1 bar</li> <li>□ More than 1 bar</li> </ul>	□       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		
123. How often did you eat <b>yogurt</b> (NOT including frozen yogurt)?	125a. Each time you ate <b>cheese</b> , how much did you usually eat?		
<ul> <li>NEVER (GO TO QUESTION 124)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>1 time per week</li> </ul>	<ul> <li>Less than ½ ounce or less than 1 slice</li> <li>½ to 2 ounces or 1 to 2 slices</li> <li>More than 2 ounces or more than 2 slices</li> <li>125b. How often was the cheese you ate low-fat?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> </ul>		
123a. Each time you ate <b>yogurt</b> , how much did you usually eat?	<ul> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul>		
<ul> <li>Less than ½ cup or less than 1 container</li> <li>½ to ¾ cup or 1 container</li> <li>More than ¾ cup or more than 1 container</li> </ul>			
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Question 124 appears in the next column	Question 126 appears on the next page146531Image: Image state		

Over the <u>past 12 months</u>	128a. Each time you ate <b>cake</b> , how much did you usually eat?		
126. How often did you eat frozen yogurt, sorbet, or ices (including low-fat or fat-free)?	Less than 1 medium piece 1 medium piece More than 1 medium piece		
□ NEVER (GO TO QUESTION 127)			
□       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	<ul> <li>129. How often did you eat cookies or brownies (including low-fat or fat-free)?</li> <li> I NEVER (GO TO QUESTION 130) </li> </ul>		
<ul> <li>126a. Each time you ate frozen yogurt, sorbet, or ices, how much did you usually eat?</li> <li>□ Less than ½ cup or less than 1 scoop</li> <li>□ ½ to 1 cup or 1 to 2 scoops</li> </ul>	□       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 1 cup or more than 2 scoops	129a. Each time you ate <b>cookies</b> or <b>brownies</b> , how much did you usually eat?		
127. How often did you eat <b>ice cream</b> or <b>ice cream bars</b> (including low-fat or fat-free)?	□ Less than 2 cookies or 1 small brownie □ 2 to 4 cookies or 1 medium brownie □ More than 4 cookies or 1 large brownie		
<ul> <li>NEVER (GO TO QUESTION 128)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2-3 times per month</li> <li>1 time per week</li> <li>2 times per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>127a. Each time you ate ice cream or ice cream bars, how much did you usually eat?</li> <li>Less than ½ cup or less than 1 scoop</li> <li>½ to 1 cup or 1 to 2 scoops</li> <li>More than 1 cup or more than 2 scoops</li> </ul>	<ul> <li>130. How often did you eat doughnuts, sweet rolls, Danish, or Pop-Tarts?</li> <li>NEVER (GO TO QUESTION 131)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>1 time per week</li> <li>2 or more times per day</li> <li>130a. Each time you ate doughnuts, sweet rolls, Danish, or Pop-Tarts, how much did you</li> </ul>		
<ul> <li>127b. How often was the ice cream you ate light, low-fat, or fat-free?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ½ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> </ul> 128. How often did you eat cake (including low-fat or fat-free)?	usually eat? Less than 1 piece 1 to 2 pieces More than 2 pieces 131. How often did you eat <b>sweet muffins</b> or <b>dessert</b> <b>breads</b> (such as banana bread, blueberry muffins, or lemon loaf, including low-fat or fat-free)? NEVER (GO TO QUESTION 132) 1-6 times per year 2 times per week		
□ NEVER (GO TO QUESTION 129)         □ 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	□       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         □       1 time per week       □       2 or more times         □       1 time per week       □       2 or more times		

Question 132 appears on the next page



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Question 129 appears in the next column

Over the <u>past 12 months</u>	133c. How often were the pies you ate cream,
<ul> <li>131a. Each time you ate sweet muffins or dessert breads, how much did you usually eat?</li> <li>Less than 1 medium piece</li> <li>1 medium piece</li> <li>More than 1 medium piece</li> </ul>	pudding, custard, or meringue pie?         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 <b>pumpkin</b> or <b>sweet potato pie</b> ?
<ul> <li>NEVER (GO TO QUESTION 133)</li> <li>1-6 times per year</li> <li>3-4 times per week</li> <li>7-11 time per month</li> <li>5-6 times per week</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>1 time per day</li> </ul> 132a. Each time you ate fruit crisp, cobbler, or strudel, how much did you usually eat? <ul> <li>Less than ½ cup</li> <li>½ to 1 cup</li> <li>More than 1 cup</li> </ul> 133. How often did you eat pie? 14-6 times per year <ul> <li>1-6 times per year</li> <li>1 time per month</li> <li>5-6 times per week</li> <li>7-11 times per year</li> <li>1 time per month</li> <li>2 times per week</li> <li>3-4 times per week</li> <li>1 time per week</li> <li>2 times per week</li> <li>1 time per day</li> <li>2 times per week</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul> 133a. Each time you ate pie, how much did you usually eat? <ul> <li>Less than ¼ of a pie</li> <li>About ¼ of a pie</li> <li>More than ¼ of a pie</li> <li>More than ¼ of a pie</li> <li>More than ¼ of a pie</li> </ul>	□ Almost never or never         □ About ½ of the time         □ About ½ of the time         □ About ¾ of the time         □ Almost always or always         133e. How often were the pies you ate pecan pie?         □ Almost never or never         □ About ¼ of the time         □ About ¼ of the time         □ About ¾ of the time         □ Almost always or always         134. How often did you eat chocolate candy?         □ 1-6 times per year       □ 3-4 times per week         □ 1 time per wonth       □ 1 time per day         □ 1 time per week       □ 2 or more times         □ 1 time per week       □ 2 or more times         □ 1 average bar or 1 to 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)         □ 1-6 times per
133b. How often were the pies you ate <b>fruit pie</b> (such as apple, blueberry, others)?	2-3 times per month       1 time per day         1 time per week       2 or more times per day         per day
<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>	<ul> <li>135a. Each time you ate other candy, how much did you usually eat?</li> <li>□ Fewer than 2 pieces</li> <li>□ 2 to 6 pieces</li> <li>□ More than 6 pieces</li> </ul>
Question 134 appears in the next column	Question 136 appears on the next page   1465     33   Image

Over the <u>past 12 months</u>	136e. How often were the eggs you ate part of <b>egg</b> salad?
136. How often did you eat <b>eggs</b> , <b>egg whites</b> , or <b>egg</b> <b>substitutes</b> (NOT counting eggs in baked goods or desserts)? ( <i>Please include eggs in salads, quiche,</i> <i>soufflés, and sandwiches.</i> )	<ul> <li>☐ Almost never or never</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>
NEVER (GO TO QUESTION 137)	
<ul> <li>NEVER (GO TO QUESTION 137)</li> <li>1-6 times per year</li> <li>7-11 times per year</li> <li>3-4 times per week</li> <li>2-3 times per month</li> <li>1 time per day</li> <li>2 or more times per day</li> </ul> 136a. Each time you ate eggs, how many did you usually eat? <ul> <li>1 egg</li> <li>2 eggs</li> <li>3 or more eggs</li> </ul> 136b. How often were the eggs you ate egg substitutes or egg whites only? <ul> <li>Almost never or never</li> <li>About ½ of the time</li> <li>About ½ of the time&lt;</li></ul>	<ul> <li>137. How many cups of coffee, caffeinated or decaffeinated, did you drink? (<i>Please do not include coffee drinks such as Latte, Mocha, Cappuccino, or Frappuccino.</i>)</li> <li>NONE (GO TO QUESTION 138)</li> <li>Less than 1 cup per</li></ul>
4 AA	☐ About ½ of the time ☐ About ¾ of the time ☐ Almost always or always
Question 137 appears in the next column	Question 139 appears on the next page 1465

Over the <u>past 12 months</u>		140. How many cups of <b>HOT tea</b> , caffeinated or decaffeinated (including herbal), did you drink?		
139. How many glasses, cans, or bottles of <b>COLD</b> or <b>ICED</b> <b>tea</b> , caffeinated or decaffeinated, did you drink?		NONE (GO TO QUESTION 141)		
		□ Less than 1 cup per □ 5-6 cups per week month □ 1 cup per day		
<ul> <li>Less than 1 glass, can or bottle per month</li> <li>1-3 glasses, cans or bottles per month</li> <li>1 glass, can or bottle per week</li> <li>2-4 glasses, cans or bottles per week</li> </ul>	<ul> <li>5-6 glasses, cans or bottles per week</li> <li>1 glass, can or bottle per day</li> <li>2-3 glasses, cans or bottles per day</li> <li>4-5 glasses, cans or bottles per day</li> <li>6 or more glasses, cans or bottles per day</li> </ul>	<ul> <li>1-3 cups per month</li> <li>2-3 cups per day</li> <li>1 cup per week</li> <li>4-5 cups per day</li> <li>2-4 cups per week</li> <li>6 or more cups per day</li> <li>140a. How often was the hot tea you drank herbal?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>About ¾ of the time</li> </ul>		
139a. How often was the cold decaffeinated or herba		☐ Almost always or always		
Low, or others)?	or iced tea you drank gar or artificial Splenda, Equal, Sweet'N GO TO QUESTION 140) 's er was added to your ced tea most of the time?	<ul> <li>140b. How often was the hot tea you drank green tea?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>About ¼ of the time</li> <li>About ¾ of the time</li> <li>About ¾ of the time</li> <li>Almost always or always</li> <li>140c. How often was the hot black tea and/or the green tea you drank decaffeinated?</li> <li>Almost never or never</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul> 141. Over the past 12 months, did you add sugar, honey or other sweeteners to your tea or coffee (hot or iced)? I NO (GO TO QUESTION 142) <ul> <li>YES</li> <li>141a. How often did you add sugar or honey to your coffee or tea (hot or iced)?</li> <li>Almost never or never (GO TO QUESTION 141c)</li> <li>About ¼ of the time</li> <li>Almost always or always</li> </ul>		
		↓		
★★ Question 140 appears in the next colum.	n	<ul> <li>♥ Question 141c appears on the next page</li> <li>Question 142 appears on the next page</li> <li>1465</li> </ul>		



Over the <u>past 12 months</u>	142b. Each time <b>non-dairy creamer</b> was added to your coffee or tea, how much was usually used?
141b. Each time <b>sugar</b> or <b>honey</b> was added to your coffee or tea, how much was usually added?	Less than 1 teaspoon
<ul> <li>Less than 1 teaspoon</li> <li>1 to 3 teaspoons</li> <li>More than 3 teaspoons</li> </ul>	More than 3 teaspoons
141c. How often did you add <b>artificial sweetener</b> (such as Splenda, Equal, Sweet'N Low, or	142c. What kind of <b>non-dairy creamer</b> did you usually use?
others) to your coffee or tea?	<ul> <li>Regular powdered</li> <li>Low-fat or fat-free powdered</li> <li>Regular liquid</li> </ul>
<ul> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> </ul>	Low-fat or fat-free liquid
<ul> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>	142d. How often was <b>cream</b> or <b>half and half</b> added to your coffee or tea? ☐ Almost never or never (GO TO QUESTION 142f)
141d. What kind of <b>artificial sweetener</b> did you usually use?	About ½ of the time About ½ of the time
<ul> <li>☐ Equal, NutraSweet, or aspartame</li> <li>☐ Sweet'N Low or cyclamate</li> <li>☐ Splenda or sucralose</li> </ul>	☐ About ¾ of the time ☐ Almost always or always
☐ Hermesetas or saccharin ☐ Herbal sweeteners like Stevia	142e. Each time <b>cream</b> or <b>half and half</b> was added to your coffee or tea, how much was usually added?
141e. Each time <b>artificial sweetener</b> was added to your coffee or tea, how much was usually added?	<ul> <li>Less than 1 tablespoon</li> <li>1 to 2 tablespoons</li> <li>More than 2 tablespoons</li> </ul>
<ul> <li>Less than 1 packet or less than 1 teaspoon</li> <li>1 packet or 1 teaspoon</li> <li>More than 1 packet or more than 1 teaspoon</li> </ul>	142f. How often was milk added to your coffee or tea?
142. Over the <u>past 12 months</u> , did you add <b>whiteners</b> (such as cream, milk, or non-dairy creamer) to your tea or coffee?	<ul> <li>☐ Almost never or never (GO TO QUESTION 143)</li> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> </ul>
□ NO (GO TO QUESTION 143) □ YES	☐ Almost always or always 142g. Each time milk was added to your coffee or
↓ 142a. How often was <b>non-dairy creamer</b> added to	tea, how much was usually added?
your coffee or tea?	☐ 1 to 3 tablespoons ☐ More than 3 tablespoons
<ul> <li>☐ About ¼ of the time</li> <li>☐ About ½ of the time</li> <li>☐ About ¾ of the time</li> </ul>	142h. What kind of <b>milk</b> was usually added to your coffee or tea?
Almost always or always	<ul> <li>☐ Whole milk</li> <li>☐ 2% milk</li> <li>☐ 1% milk</li> <li>☐ Skim, nonfat, or 0.5% fat milk</li> <li>☐ Evaporated or condensed (canned) milk</li> <li>☐ Soy milk</li> <li>☐ Rice milk</li> </ul>
↓	Almond milk
▼ Question 142d appears in the next column	★ _
<i>Question 143 appears on the next page</i>	Question 143 appears on the next page   1465     36   Image: Comparison of the next page

## Over the past 12 months ...

143. How often was **sugar** or **honey** added to foods you ate (such as on cereal, fruit, or yogurt)? (*Please do not include sugar in coffee, tea, other beverages, or baked goods.*)



The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese, and salad dressing that you ate. If possible, please check the labels of these foods to help you answer.

144. Over the past 12 months, did you eat margarine?





## er the nast 12 month

Over the <u>past 12 months</u>	152. Over the <u>past month</u> , which of the following foods did you eat <b>AT LEAST THREE TIMES</b> ?
149. Did you eat salad dressing?	(Mark all that apply.)
□ NO (GO TO INTRODUCTION TO QUESTION 150) □ YES ↓	<ul> <li>Avocado, guacamole</li> <li>Beef jerky</li> <li>Cheesecake</li> <li>Game Meat (such as bison, wild goose, venison)</li> <li>Granola bars</li> <li>Het pappers</li> </ul>
149a. How often was the salad dressing you ate <b>light low-fat,</b> or <b>fat-free</b> ?	Chocolate, fudge, or ☐ Hot peppers butterscotch ☐ Jell-O, gelatin toppings or syrups ☐ Mangoes
☐ Almost never or never ☐ About ¼ of the time ☐ About ½ of the time	□ Chow mein noodles □ Olives □ Croissants □ Pickles or pickled
<ul> <li>☐ About ¾ of the time</li> <li>☐ Almost always or always</li> </ul>	<ul> <li>☐ Dark chocolate vegetables or fruit</li> <li>☐ Dried apricots ☐ Plantains</li> </ul>
•	Dried curcumin, turmeric Drik 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.	<ul> <li>Dried oregano, rosemary, thyme</li> <li>☐ Egg rolls</li> <li>☐ Fresh basil, cilantro, or paralay</li> </ul>
150. Over the <u>past 12 months</u> , how many servings of vegetables (not including salad or potatoes) did you eat per week or per day?	Whipped cream, substitute
□ 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	□ NONE 153. For <b>ALL</b> of the <u>past 12 months</u> , have you followed any type of <b>vegetarian diet</b> ? □ NO (GO TO INTRODUCTION TO QUESTION 154)
<ul> <li>151. Over the past 12 months, how many servings of fruit (not including juices) did you eat per week or per day?</li> <li>Less than 1 per week</li> <li>1-2 per week</li> <li>3-4 per week</li> <li>5-6 per week</li> <li>5 or more per day</li> <li>1 per day</li> </ul>	<ul> <li>YES</li> <li>↓</li> <li>153a. Which of the following foods did you TOTALLY EXCLUDE from your diet? (Mark all that apply.)</li> <li>☐ Meat (beef, pork, lamb, etc.)</li> <li>☐ Poultry (chicken, turkey, duck, etc.)</li> <li>☐ Fish and shellfish</li> <li>☐ Eggs</li> <li>☐ Dairy products (milk, cheese, etc.)</li> </ul>

Introduction to Question 154 appears on the next page



<ul> <li>The next questions are about your use of vitamin pills or other supplements.</li> <li>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)?</li> </ul>	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 <u>past 12 months</u>
Prenatal-type multivitamins (as pills, liquids, or packets)? NO (GO TO INTRODUCTION TO QUESTION 156) YES 155. How often did you take <b>One-a-Day-, Centrum-,</b> or <b>Prenatal-type</b> multivitamins? Less than 1 day per month 1-3 days per week 4-6 days per week Every day 155a. Did your <b>multivitamin</b> usually contain <b>minerals</b> (such as iron, zinc, etc.)? NO YES Don't know 155b. Was your <b>multivitamin</b> usually a <b>Prenatal-type?</b> NO YES Don't know 155c. For how many years have you taken <b>multivitamins</b> ? Less than 1 year 1-4 years 5-9 years 10 or more years 155d. Over the <u>past 12 months</u> , did you take any <b>vitamins, minerals</b> , or <b>herbal supplements</b> other than your multivitamin? NO Thank you <u>very much</u> for completing this questionnaire! Because we want to be able to use all the information you have	<ul> <li>156. How often did you take Antacids that contain Calcium such as Tums or Rolaids?</li> <li>NEVER (GO TO QUESTION 157)</li> <li>Less than 1 day per month</li> <li>1-3 days per woek</li> <li>4-6 days per week</li> <li>Every day</li> <li>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?</li> <li>Less than 1</li> <li>1</li> <li>2</li> <li>3</li> <li>4 or more</li> <li>Don't know</li> </ul> 156b. Was your Antacid usually extra strength? <ul> <li>NO</li> <li>YES</li> <li>Don't know</li> </ul> 156c. For how many years have you taken Antacids that contain Calcium such as Tums or Rolaids? <ul> <li>Less than 1 year</li> <li>1-4 years</li> <li>5-9 years</li> <li>10 or more years</li> </ul> 157. How often did you take Calcium (with or without Vitamin D) (NOT as part of a multivitamin in
<ul> <li>provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:</li> <li>Did not skip any pages and</li> <li>Crossed out the incorrect answer and circled the correct answer if you made any changes.</li> </ul>	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
▼ Introduction to Question 156 appears in the next column	Question 158 appears on the next page     1465       39     39

•	
Over the <u>past 12 months</u>	158b. For how many years have you taken <b>Vitamin D</b> ?
157a. When you took <b>Calcium</b> , 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	<ul> <li>159. How often did you take Iron (NOT as part of a multivitamin in Question 155)?</li> <li>□ NEVER (GO TO QUESTION 160)</li> <li>□ Less than 1 day per month</li> </ul>
157b. Did your <b>Calcium</b> usually contain <b>Vitamin D</b> ? ☐ NO ☐ YES ☐ Don't know	<ul> <li>Less train r day per month</li> <li>1-3 days per week</li> <li>4-6 days per week</li> <li>Every day</li> </ul>
157c. Did your <b>Calcium</b> usually contain <b>Magnesium</b> ? □ NO □ YES □ Don't know	<ul> <li>159a. For how many years have you taken Iron?</li> <li>□ Less than 1 year</li> <li>□ 1-4 years</li> <li>□ 5-9 years</li> <li>□ 10 or more years</li> </ul>
157d. Did your <b>Calcium</b> usually contain <b>Zinc</b> ? ☐ NO ☐ YES ☐ Don't know	<ul> <li>160. How often did you take Folic Acid (NOT as part of a multivitamin in Question 155)?</li> <li>NEVER (GO TO QUESTION 161)</li> </ul>
<ul> <li>157e. For how many years have you taken Calcium?</li> <li>Less than 1 year</li> <li>1-4 years</li> <li>5-9 years</li> <li>10 or more years</li> </ul>	<ul> <li>Less than 1 day per month</li> <li>1-3 days per month</li> <li>1-3 days per week</li> <li>4-6 days per week</li> <li>Every day</li> </ul> 160a. When you took Folic Acid, about how much did you take in one day?
<ul> <li>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)?</li> <li> NEVER (GO TO QUESTION 159) Less than 1 day per month 1-3 days per month </li> </ul>	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 <b>Folic Acid</b> ?
<ul> <li>1-3 days per week</li> <li>4-6 days per week</li> <li>Every day</li> <li>158a. When you took Vitamin D, about how much</li> </ul>	□ Less than 1 year □ 1-4 years □ 5-9 years □ 10 or more years
did you take in one day? Less than 400 IU 400-799 IU 800-999 IU 1,000 IU or more Don't know	
Question 159 appears in the next column	Question 161 appears on the next page 1465

Over the <u>past 12 months</u>	The next two questions ask you about other supplements you took more than once per week.
<ul> <li>161. How often did you take Vitamin C (NOT as part of a multivitamin in Question 155)?</li> <li>☐ NEVER (GO TO QUESTION 162)</li> </ul>	<ul> <li>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):</li> </ul>
<ul> <li>Less than 1 day per month</li> <li>1-3 days per month</li> <li>1-3 days per week</li> <li>4-6 days per week</li> <li>Every day</li> </ul>	B-6       Occu-vite/Eye health         B-complex       Potassium         B-12       Selenium         Beta-carotene       Vitamin A         Magnesium       Zinc
<ul> <li>161a. When you took Vitamin C, about how much did you take in one day?</li> <li>Less than 500 mg</li> <li>500-999 mg</li> <li>1,000-1,499 mg</li> <li>1,500-1,999 mg</li> <li>2,000 mg or more</li> <li>Don't know</li> </ul> 161b. For how many years have you taken Vitamin C? <ul> <li>Less than 1 year</li> <li>1-4 years</li> <li>5-9 years</li> <li>10 or more years</li> </ul>	164. Please mark any of the following herbal, botanical, or other supplements you took more than once per week.            Chondroitin         Coenzyme Q-10         Glucosamine         Echinacea         Peppermint         Energy supplements         Fish oil/Omega-3's         Flaxseed oil         Garlic         Ginger         Ginger         Ginger         Ginkgo biloba         St. John's wort         Other
<ul> <li>162. How often did you take Vitamin E (NOT as part of a multivitamin in Question 155)?</li> <li>NEVER (GO TO INTRODUCTION TO QUESTION 163)</li> <li>Less than 1 day per month</li> <li>1-3 days per week</li> <li>4-6 days per week</li> <li>4-6 days per week</li> <li>Every day</li> </ul> 162a. When you took Vitamin E, about how much did you take in one day? <ul> <li>Less than 400 IU</li> <li>400-799 IU</li> <li>800-999 IU</li> <li>1,000 IU or more</li> <li>Don't know</li> </ul> 162b. For how many years have you taken Vitamin E? <ul> <li>Less than 1 year</li> <li>1-4 years</li> <li>5-9 years</li> <li>10 or more years</li> </ul>	165. Is there anything else you eat at least once a month?         Please write name of food, frequency and amount (optional).

Introduction to Question 163 appears in the next column