

Identifying distinct trajectories of health behaviors after a breast cancer diagnosis

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ABSTRACT

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Breast cancer (BC) survivors are at increased risk of cancer recurrence, a second cancer, and non-cancer comorbidities. Previous studies suggest that many women adopt a spontaneous change in lifestyle after a BC diagnosis in hope of achieving a better survival outcome. While this observation has led to the suggestion that a BC diagnosis is a “teachable moment” for improving health behaviors, other conflicting studies report that BC survivors do not make positive changes in health behaviors following a breast cancer diagnosis. Although previous studies suggest that receipt of cancer chemotherapy and hormonal therapy is associated with weight loss or weight gain, the association between post-diagnosis weight change with changes in lifestyle has not been studied in detail. The majority of prior studies of post-diagnosis changes in behavior and weight have examined the mean change between two time points, and therefore may over simplify the trajectory of change over time due to lack of more granular data. New methods are needed to examine the distribution and correlates of behavior/weight trajectories following the BC diagnosis.

In my dissertation, a systematic literature review was conducted to evaluate the evidence regarding the frequency, magnitude and pattern of post-diagnosis changes in diet [fruit/vegetable (F/V), dietary fat], physical activity [moderate to vigorous physical activity (MVPA) and sedentary behaviors], alcohol intake, and body weight among BC survivors. A total of 66 studies were included in the systematic review. These studies suggest that after a breast cancer diagnosis, women are less likely to engage in MVPA and more likely to reduce alcohol intake. Previous studies suggested that women may experience weight change after a BC diagnosis, although there were strong evidence showing both weight gain and weight loss were common. The reports of changes in diet and sedentary behavior following a BC diagnosis are limited and inconclusive about the direction of change. The results of the review suggested that there is wide variation in post-diagnosis lifestyle changes among BC survivors. However, very few studies have investigated the variability in multiple behavior trajectories following a BC diagnosis.

In this dissertation, I made use of a population of 4,505 women newly diagnosed with a BC and enrolled in the Kaiser Permanente Northern California Pathways Study. I used a combination of statistical methods, including a semi-parametric, group-based trajectory modeling and a non-parametric K-means for longitudinal data analysis, to identify latent trajectories groups that are unobserved clusters of individuals following similar trajectories of a behavior. These analyses tested the hypotheses that in the 24 months following a breast cancer diagnosis, women follow a mixture of lifestyle (F/V, dietary fat, MVPA, sedentary behavior, alcohol) and body mass index (BMI) trajectories, which can be stable, temporarily increase or temporarily decrease. My analysis identified multiple distinct trajectories of lifestyle behaviors and BMI during the first 24 months after a BC diagnosis. The trajectory analysis results suggest that the large majority of women maintained their lifestyles following a BC diagnosis. Socioeconomic status, dispositional optimism, perceived social support, and the severity of CIPN during active treatment were associated with the post-diagnosis trajectories of. Furthermore, the BMI trajectories were stable over the first 24 months following a BC diagnosis. The BMI trajectories were associated with trajectories of F/V, dietary fat intake, MVPA, sedentary behavior and alcohol intake over the same period, independent of demographic characteristics, tumor characteristics and cancer treatment received.

In summary, previous studies suggest that women may spent fewer time on MVPA and drink less alcohol after a BC diagnosis, while both weight gain and loss are common post diagnosis. In a trajectory analysis of 4505 BC survivors enrolled in the Pathways Study, I did not observe any latent trajectory of meaningful change in health behavior or BMI in the first 24 months after a BC diagnosis in the Pathways Study. Instead, my analysis suggests that most women maintained their body weight following a BC diagnosis. The BMI trajectories were strongly associated with trajectory of F/V, dietary fat intake, MVPA, sedentary behavior, and alcohol intake over the same period, independent of demographic characteristics, tumor characteristics and receipt of cancer therapies. These results suggest that there is an absence of spontaneous changes in lifestyle behaviors after BC diagnosis and the importance of maintaining a healthy lifestyle in weight management after a BC diagnosis. Future studies should examine the associations of these health behaviors and BMI trajectories and BC prognosis to better understand the effect of post-diagnosis changes in lifestyle and weight on BC-specific and all-cause mortality.

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DEDICATION

My dissertation is dedicated to my father, a strong and optimistic cancer survivor, my mother, my sister, and my girlfriend, Jiamin Han.

CHAPTER 1: INTRODUCTION

Emerging evidence suggests that a healthy diet and exercise are associated with better long-term outcomes and quality of life for breast cancer (BC) survivors.¹⁻⁶ Previous studies have suggested that BC patients may adopt healthier lifestyle changes following a cancer diagnosis, such as eating more fruit and vegetables, increasing physical activity, and reducing alcohol intake.⁷⁻¹⁰ These observations suggest that a cancer diagnosis might be a “teachable moment” for BC survivors.¹¹ However, other studies have suggested that the favorable behavior changes in response to a cancer diagnosis may not be sustainable,¹² and some studies reported unfavorable changes, such as an increase in time spent on sedentary behaviors.^{13,14} Although the reasons for unfavorable behavior change remain poorly understood, breast cancer survivors usually experience side effects of cancer treatment, which are known to disrupt lifestyle behaviors.¹⁵⁻¹⁷ Furthermore, BC survivors usually experience acute emotional distress at the time of diagnosis and early treatment, which may adversely affect lifestyle choices.¹⁸⁻²⁰

Favorable changes in health behaviors post-diagnosis are associated with BC prognosis and survival. For example, an observational study among breast cancer survivors in the Women’s Health Initiative Study and Nurses’ Health Study suggest that women who had better diet quality after diagnosis had a 26% lower all-cause mortality and 28-42% lower non-cancer mortality.^{21,22} In addition, breast cancer survivors who reported increased physical activity after diagnosis have 22% lower all-cause and 39% lower non-cancer mortality,²³ whereas women who decreased their physical activity level after a breast cancer diagnosis have 200-400% increase in all-cause mortality and two-fold increases in breast cancer mortality.^{24,25} Currently, few studies have examined the survival benefits associated with reducing smoking and alcohol intake for breast cancer survivors.

Previous studies have suggested that unfavorable changes in health behaviors after a BC diagnosis may account for post-diagnosis weight gain in breast cancer patients, which is associated with worse prognosis.²⁶ Weight gain is a common and persistent problem for many BC survivors during and after cancer treatment.²⁷ Weight gain is also known to negatively impact on quality of life and to increase the risk of developing comorbid conditions.²⁸⁻³⁰ Furthermore, unfavorable changes in body composition have been observed in BC survivors, including gain in adipose tissue and loss of lean tissue, which is

known as sarcopenic obesity.^{31,32} Loss of lean tissue, combined with gains in adipose tissue, may lead to metabolic disturbance, treatment complications, and poor survival outcomes in BC survivors.^{33,34}

The causes of weight change in the after a diagnosis of BC are not well understood. Diet and exercise patterns after diagnosis and possible treatment-related reductions in resting energy expenditure are plausible causes.^{31,32,35} However, the extent to which these individual components of energy balance contribute to weight change is not yet clear. Although poorer diet and physical inactivity have been implicated in weight gain among breast cancer survivors, there are significant gaps in knowledge, such as the longitudinal pattern of behavior change and the causes of change. The limited reports on longitudinal change in health behavior after BC diagnosis have important methodological limitations, as they failed to assess the variability of behavior change trajectories and reported mixed results regarding the direction of behavior change. Most prior studies examined the average change in behaviors and assumed all women would follow a uniform trajectory of change, thereby ignoring the variability in behavior change trajectories. In reality, women may follow a mixture of behavior change trajectories after a BC diagnosis. However, the existence of latent behavior change trajectories, where individuals can undergo trajectories that are unobserved (latent), has rarely been evaluated. Understanding latent behavior change trajectories can help identify populations engaged in unfavorable behavior trajectories who may be worthy of targeted intervention. Furthermore, few studies have evaluated the predictors of behavior change, and associations of behavior changes with the change in body weight in BC survivors. Prospective cohort studies with repeated measures of health-related behaviors and novel analytical methods that identify the latent trajectories of behavior change are needed to understand the dynamics and effects of behavior change following a cancer diagnosis.

Given these gaps in the literature, in this dissertation I examined the longitudinal trajectory of health behaviors and body mass index (BMI) among BC survivors enrolled in the Pathways Study (R01CA105274/U01CA195565, MPI: Kushi/Ambrosone). The Pathways Study is an ongoing population-based cohort of women newly diagnosed with invasive breast cancer within Kaiser Permanente Northern California (KPNC).³⁶ Recruitment began in 2006 and a total of 4,505 participants were enrolled. The Pathways Study collected longitudinal information about lifestyle factors up to 5 years after diagnosis, providing a unique opportunity to observe the natural history of behavior changes after diagnosis. This

analysis focused on health behaviors included in the American Cancer Society³⁷ and American Institute for Cancer Research³⁸ lifestyle recommendations for cancer survivors, namely, fruit/vegetable (F/V) intake, dietary fat, moderate to vigorous physical activity (MVPA), physical inactivity, alcohol intake, and BMI.

In this dissertation, Chapter Two provides a systematic review of the current literature related to changes in diet (F/V, dietary fat), physical activity (time spent on MVPA and sedentary behaviors), alcohol intake, and BMI after a BC diagnosis. Following the literature review, Chapter Three examines the trajectory of diet, physical activity, and alcohol intake from the time of diagnosis to 24 months after diagnosis among Pathways Study participants. Specifically, Chapter Three estimates the shape of latent classes of behavior trajectories after a BC diagnosis using a semi-parametric, group-based trajectory modeling (GBTM)³⁹ and the fully non-parametric method, K-means for longitudinal data (KmL).⁴⁰ I hypothesized that women would follow six different trajectories of BMI after a breast cancer diagnosis, which include: 1) maintain a healthy lifestyle, 2) make a persistently positive change, 3) make a temporarily positive change, 4) make a persistently negative change, 5) make a temporarily negative change, and 6) maintain an unhealthy lifestyle. In addition, I hypothesized that lower socioeconomic status, greater cancer treatment side effects, and worse cancer stress coping would be associated with the decline in health behaviors post-diagnosis. Using a similar trajectory analysis, Chapter Four evaluates the trajectory of BMI during the first 24 months after a BC diagnosis among Pathways Study participants, which may include: 1) maintaining a high weight, 2) losing weight persistently, 3) losing weight temporarily, also known as weight cycling, 4) gaining weight persistently, 5) gaining weight temporarily, and 6) maintaining a low weight. In Chapter Four, I also test the hypothesis that women who followed unfavorable behavior trajectories are likely to maintain a high BMI or experience weight gain.

The overall goal of my dissertation is to provide a more detailed picture of the experience and correlates of lifestyle trajectories in the first 24 months following a BC diagnosis. The use of novel statistical analysis such as GBTM and KmL may unveil important latent trajectories of behavior/BMI trajectories that are difficult to observe when using a comparison of mean changes. Results from these analyses will facilitate physicians and researchers to better understand the challenges of achieving and/or maintaining a healthy lifestyle and a healthy BMI during and after the active cancer treatment period. The

latent trajectories analysis will specifically subtype BC survivors based on their trajectories of health behaviors, which will identify subgroups of women who could be important targets for lifestyle interventions.

CHAPTER 2: A SYSTEMATIC REVIEW OF CHANGES IN HEALTH BEHAVIORS AND BODY WEIGHT FOLLOWING A BREAST CANCER DIAGNOSIS

2.1 ABSTRACT

Background: Changes in health behaviors and body weight is common among breast cancer (BC) survivors and is associated with BC prognosis. This review presents a summary of the literature on the frequency, magnitude and patterns of post-diagnosis changes in diet [fruit/vegetable (F/V), dietary fat], physical activity [sedentary and moderate to vigorous physical activity (MVPA) time], smoking, alcohol intake, and body weight among breast cancer survivors.

Methods: A systematic review was conducted by searching Pubmed, Web of Science, PsycINFO, Embase, and Medline databases through February 2017, reviewing bibliographies of eligible articles, and searching the author's personal databases using search terms for F/V, dietary fat, time spent on sedentary and MVPA, alcohol intake, and body weight. Eligible articles reported on cohort studies that included women previously diagnosed with BC, collected repeated measures of behavior data, and were published in English.

Results: A total of 2,552 publications were screened and 66 studies were included in this review. These studies suggest that there is strong evidence that women generally reduce alcohol intake following a BC diagnosis, and that women are at increased risk of both weight gain and weight loss. There is moderate evidence suggesting that there is a decrease in time spent on MVPA after a BC diagnosis. However, there is insufficient evidence to determine the change in F/V and dietary fat intake and time spent on sedentary behavior after a BC diagnosis.

Conclusion: A systematic review of the literature suggests that women are less likely to engage in MVPA and are more likely to reduce alcohol intake and gain weight after a breast cancer diagnosis. More research is needed to determine changes in diet and sedentary time among BC survivors. Future studies should aim to understand the heterogeneity and determinants of behavior change among BC survivors, which can help identify women who have difficulty meeting the health behavior guidelines and can guide the targeted interventions.

2.2 INTRODUCTION

Breast cancer is the most common cancer among women in the United States.⁴¹ With advances in early detection, and improvements in breast cancer therapies, the five-year survival rate for women with early-stage breast cancer has increased to approximately 90%, leading to a growing population of long-term breast cancer survivors.⁴² In the United States there are more than 3 million breast cancer survivors; approximately 246,660 new cases of invasive breast cancer were diagnosed in 2016.^{43,44} Despite the improvements in breast cancer survival, breast cancer survivors are often at increased risk for recurrence, secondary cancers, late effects of treatment, and other chronic conditions.^{29,44,45} While breast cancer-specific mortality has steadily decreased in recent years, deaths due to other causes account for 60%-83% of overall mortality in breast cancer survivors.^{46,47}

With a growing population of breast cancer survivors, there is considerable interest among health practitioners and breast cancer survivors to promote health and well-being. Health-related behaviors have emerged as important modifiable risk factors that play a key role in both the prevention and treatment of breast cancer. The American Cancer Society and the American Institute of Cancer Research have developed physical activity (PA), nutrition, and tobacco recommendations for cancer survivors. Specifically, the recommendations advise that cancer survivors (1) engage in at least 150 minutes of moderate-to-vigorous or 60 minutes of vigorous PA per week, (2) consume a healthy diet, with an emphasis on fruit and vegetable (F/V) intake, (3) limit alcohol drinking, (4) quit smoking, and (5) maintain a healthy body weight.^{37,48}

A cancer diagnosis has been referred to as a possible “teachable moment” when cancer survivors are likely to be motivated to make lifestyle changes to improve health outcomes^{7,11,49}, however, few cancer survivors are actually making these changes. A large cross-sectional study using the National Health Interview Survey reported that US cancer survivors are less likely to meet recommended lifestyles guidelines compared to US adults who do not have cancer.⁵⁰ Recent population-based studies in the United States have shown that up to 70% of cancer survivors are not meeting the PA recommendation, 48% to 74% are not meeting the diet recommendation and 20% to 24% continue to smoke after diagnosis.⁵¹ Lynch et al. analyzed and objectively determined that PA collected in the National Health and Nutrition Examination Survey 2003-2004, and 2005-2006 data, had demonstrated that cancer survivors

spend less than 4 minutes/day on moderate to vigorous PA. Given the conflicting reports on changes in health behaviors after a cancer diagnosis, a systematic review of literature regarding lifestyle changes among BC survivors helps determine whether there is a deficit in health behaviors in this population.

A number of observational studies have reported on post-diagnosis changes in body weight, PA, and diet in breast cancer survivors.^{10,12,14,52 53} Collectively, these findings suggest that women are likely to eat a healthier diet, quit smoking, and reduce alcohol drinking yet become more sedentary after a breast cancer diagnosis. These lifestyle factors are considered important for both cancer prevention⁵⁴ and cancer survival.³⁷ However, no systematic review has evaluated the direction and magnitude of changes in these health behaviors following a breast cancer diagnosis. As differences across studies may be due to study designs, study population, data collection methods, and analytical methods, I propose to compare and contrast these characteristics in previous studies. This chapter will systematically review literature on post-diagnosis change in lifestyle, including diet (F/V and dietary fat), physical activity (sedentary and MVPA time), smoking, alcohol intake, and body weight.

2.3 METHODS

2.3.1 Identification and selection of literature

A literature search was conducted in the major electronic bibliographic databases, including: Pubmed, Web of Science, PsycINFO, Embase, and Medline. The key words used referred to the exposure (“breast cancer” or “breast neoplasms”), the health behavior outcomes (“diet” or “fruit” or “vegetable” or “dietary fat” or “total calories” or “caloric intake” or “alcohol” or “drinking” or “physical activity” or “moderate to vigorous activity” or “sedentary activity” or “exercise” or “smoking” or “cigarette”), and the analytical methods (“change” or “longitudinal” or “difference”). The search was limited to publications in English published from inception through February 2017. In addition, the author’s personal collection of relevant previous publications was also included. These articles were identified through searches outside of the systematic database search using the structured query terms, and through the references of included studies.

Study relevance was assessed first by filtering through title and abstract. Relevant publications were then included for full text review. Studies were chosen for the systematic review based on the following inclusion criteria:

1. Use of prospective cohort design among breast cancer survivors.
2. Collected behavior and/or weight data in a longitudinal method, i.e. over at least two time intervals.
3. Reported longitudinal data on diet (fruit/vegetable and/or dietary fat intake), physical activity (time spent on moderate to vigorous activity and/or sedentary behaviors), cigarette smoking, alcohol intake, or body weight.

Studies were excluded if: 1) the study population was not restricted to breast cancer survivors or did not perform subgroup analysis in breast cancer survivors when the overall population was survivors of multiple types of cancer; 2) only used cross-sectional design, or used the control arm of a randomized controlled trial of health behavior interventions as a surrogate for a cohort study; 3) did not collect behavior data at a minimum of two time points; 4) did not assess behavior variables for the main question; 5) results were only reported in an abstract; 6) published in language other than English. The control arm of randomized controlled trials of healthy behaviors were excluded from the review because these groups usually received educational support to adopt healthier lifestyles, and therefore their behavior changes were likely driven by health education rather than the cancer diagnosis. The literature search followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.⁵⁵

2.3.2 Data extraction and quality assessment

Publications included in the systematic review were appraised based on the eligibility criteria. The following characteristics were extracted from each study: 1) study design (i.e., author, geographic location, age, follow-up period, sample size, and measurement of health behavior); 2) study findings (i.e., average change in health behaviors, percent developing positive/negative behavior change, predictors of negative behavior changes, and covariates adjusted).

Study quality was assessed using the Critical Appraisal Skills Program (CASP),⁵⁶ which has been used as a risk of bias assessment tool in previous systematic reviews of cohort studies.⁵⁷ The CASP assesses both internal and external validity by addressing seven methodological issues: 1) selection bias; 2) time from breast cancer diagnosis to behavior data collection; 3) behavior variable measurement bias; 4) accounted for confounding variables; 5) length of follow-up; 6) handling of loss to follow-up; and 7) handling of missing data. The specific questions used to assess each criterion are included in Appendix 2. Each issue was assessed and assigned a score of 1 (satisfied) or 0 (unsatisfied) based on the scoring system described by Barnett et al.⁵⁸ The assigned scores were summed to give each study a composite score ranging from 0 to 7, with each score representing a quality level: 0-2, low; 3-4, modest; and 5-7, high.

2.3.3 Level of scientific evidence

Quality assessment of included publications suggested that the studies were heterogeneous with regard to the type and measurement of health behaviors. The timing of behavior assessment, length of follow-up, and the statistical analyses varied significantly among studies that reported the same health behavior outcome. Therefore, to synthesize the methodological quality of the studies and to be able to draw conclusions regarding the direction and magnitude of health behavior change, a best-evidence synthesis was applied⁵⁹ that consists of the following three levels:

1. Strong evidence: consistent findings in ≥ 2 high-quality studies;
2. Moderate evidence: consistent findings in one high-quality studies, and at least one modest to low-quality study, or consistent findings in multiple modest to low-quality studies;
3. Insufficient evidence: only one study available or inconsistent findings in ≥ 2 studies.

Study findings were considered consistent if $\geq 75\%$ of the studies reported changes in the same direction. When two or more high-quality studies existed for a behavior outcome, the modest to low-quality studies were not considered in the best-evidence synthesis.

2.4 RESULTS

2.4.1 Search and selection

The search resulted in a total of 2,552 records (1,637 from Pubmed, 37 from Web of Science, 6 from PsycINFO, 576 from Embase, and 250 from Medline, 21 from the author's sources). The search terms and results are shown in Appendix 1. After removing duplicate publications, a total of 2,054 publications remained. After screening the titles and abstracts, 145 full papers were read. Of those, 79 were excluded because the studies did not conduct analyses separately in breast cancer survivors, did not measure the desired health behaviors, applied a cross-sectional design, had less than 2 times of behavior measures, or were only published in an abstract. Ultimately, 66 different prospective cohort studies were included in the systematic review. The literature search and selection flow diagram is presented according to the 2009 PRISMA guidelines⁵⁵ (Figure 1).

2.4.2 Study design and population characteristics

Of the 66 studies, 7 reported changes in diet, 13 reported changes in physical activity, 3 reported changes in cigarette smoking, 4 reported changes in alcohol intake, and 48 reported changes in body weight and/or BMI. The characteristics of these studies are summarized in Tables 2-5. The majority of studies used prospective cohort design to collect self-reported health behaviors and body weight, while the remaining studies collected data on weight or BMI retrospectively from electronic medical records prior to the study enrollment.⁶⁰⁻⁶⁴ The majority of studies were conducted among early stage BC survivors diagnosed at the mean age of 50-60 years in the United States, Europe and East Asia. Most studies included both premenopausal and postmenopausal women; only a few studies restricted to premenopausal^{65,66} or postmenopausal⁶⁷ women. Most studies directly recruited participants from hospitals or clinics, while the large-scale studies typically used a subsample of participants from a population-based cohort study of BC survivors [i.e., the Health, Eating, Activity, and Lifestyle (HEAL) study⁶⁸, Long Island Breast Cancer Study Project⁶⁹, Pathways Study³⁶, Shanghai Breast Cancer Survival Study⁷⁰] or a healthy population (i.e., Nurses' Health Study⁷¹, Danish Diet, Cancer and Health cohort study⁷²), or through regional and national cancer registries.

Timing of study entry relative to BC diagnosis and the course of cancer treatment varied greatly by study design. Hospital-based studies generally enrolled participants within the first 6 weeks after

diagnosis, and some specifically recruited patients either at the start⁷³⁻⁷⁵ or the end⁷⁶⁻⁷⁸ of cancer treatment to assess the effect of treatment on health behavior or weight. Population-based BC cohort studies typically recruited participants 2-6 months after diagnosis.⁷⁹⁻⁸⁵ In contrast, the behavior and weight measurement for BC patients identified from a cohort of general population were generally obtained from follow-up surveys administered before and after the diagnosis, which may span over a long period of time.⁸⁶⁻⁸⁹ The length of follow-up varied greatly as well. Most hospital-based studies followed participants up to one year after study enrollment, while population-based studies followed participants for 2-10 years after diagnosis.^{61,63,67,79,83,85,90-99}

2.4.3 Measurement of health behaviors and body weight

The included studies primarily measured diet using food frequency questionnaires (FFQs),^{65,78,84,85,100,101} and one study used a single question to assess self-reported changes after diagnosis (e.g. does the participant eat more fruits and vegetables?) at each assessment point.¹⁰² Among studies that used an FFQ, the majority used validated FFQs, such as the Women's Health Initiative FFQ,^{65,85} the FFQ used in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study,⁸⁴ and the FFQ used in the Norwegian Women and Cancer Study.¹⁰¹ However, two studies measured diet with a short FFQ that was not validated in previous research.^{78,100} These FFQs assessed the frequency and/or portion size of dietary intake of common food items in the US and Europe during the past 12 months. The FFQ used in the Norwegian Women and Cancer Study¹⁰¹ included more items on fish intake compared to other FFQs used in the US and European cohorts. Although FFQs assessed intake of specific foods, most studies only reported changes in total intake of food groups (i.e. total vegetable intake), with only two studies reporting changes in individual food items (i.e. legumes, fruit/vegetable juice).^{84,101} In analyzing changes in specific food items, only one study adjusted for the total energy intake using the nutrient density model.⁸⁴

In measuring physical activity, the majority of included studies used validated physical activity questionnaires that included the Modifiable Activity Questionnaire,¹⁰³ Godin Leisure-Time Exercise Questionnaire (LTEQ),¹⁰⁴ International Physical Activity Questionnaire (IPAQ),¹⁰⁵ Arizona Activity Frequency Questionnaire,¹⁰⁶ and the Behavioral Risk Factor Surveillance System (BRFSS) Historical

Questions.¹⁰⁷ More recent studies also assessed objectively measured physical activity using an accelerometer.^{76,108} The physical activity questionnaires measured the amount of MVPA and sedentary time by asking participants about the time and frequency of engagement in various daily activities. Based on the Compendium of Physical Activity,¹⁰⁹ each activity was classified as light, moderate and vigorous-intensity activity, and time spent on each level of activity was converted to metabolic equivalent (MET) hours.¹⁰⁹ Many studies expressed the amount of MVPA and sedentary time as hours or minutes per day or per week, while others expressed as MET-hours per day or per week. Although most studies reported data on total MVPA or sedentary time, only a few reported changes in types of MVPA or sedentary activities.^{79,82,110}

Alcohol intake and cigarette smoking were commonly assessed using questions that asked about the current use, as well as the frequency and amount of use during the past 12 months. One study assessed alcohol intake using the EPIC study FFQ.⁸⁴ Alcohol intake was analyzed as average change in number of drinks per occasion or grams of alcohol intake per day. Additionally, risky drinking behavior such as intake of >4 alcoholic beverages per occasion was also analyzed.⁹⁰ Studies of cigarette smoking often reported average number of cigarette smoked per day and percent of women who quit smoking following a BC diagnosis.

Measurement of body weight was highly dependent on study design. Hospital-based studies obtained clinically measured weight and height at each clinic visit,^{65,67,74-77,94-97,99,111,112} or utilized the electronic medical records (EMR) to retrospectively collect clinically measured weight and height pre and post-diagnosis.⁶⁰⁻⁶⁴ In contrast, large-scale population-based cohort studies often relied on self-reported weight and height,^{91-93,113-116} although a few population-based studies collected clinically measured weight and height through EMR,^{92,95,96} and some collected both self-reported and clinically measured anthropometric data.^{93,114,115} Very few studies measured body composition, only two studies assessed body composition using bioelectrical impedance analyzer (BIA).^{95,117} Only four studies collected data on waist circumference,^{92,115,117,118} and one study measured waist-to-hop ratio.¹¹⁵ In analyzing weight change, most studies reported average weight change from baseline to follow-up, and a few studies reported the average percent weight change from baseline. In addition, some studies examined the

percent of women experiencing weight gain and weight loss using 5% or 10% change in weight as cutoff values.^{64,93,95,111,113,116}

2.4.4 Statistical analysis of change in health behaviors and body weight

The majority of included studies analyzed changes in health behaviors and body weight using paired t-tests to compare the mean value at follow-up with the mean value at baseline - or to test whether the mean change was statistically different from 0. However, many studies only reported descriptive data on the percent of women who experienced change without statistical analysis.^{64,67,78,79,90,113} Only two studies used regression analyses to evaluate the non-linear trend of behavior change over time.^{99,119} Because many of the studies that had reported the changes in health behaviors and body weight after a BC diagnosis were not uniform among BC survivors, a recent study explored the heterogeneous trajectories of change in physical activity using trajectory analysis.^{119,120} However, none of the included studies assessed potential bias to the observed change in health behaviors; such as selection bias, loss to follow-up and missing data.

2.4.5 Dietary change – fruit/vegetable intake

Five prospective studies^{78,84,85,101,102} examined the change in F/V intake after a breast cancer diagnosis, of which three were of high quality^{78,84,85} (Table 2). The three high-quality studies showed inconsistent results regarding change in F/V intake. In a German cohort study (n=229), Steinhilper et al.⁷⁸ reported that BC survivors increased fruit intake by 0.4 serving/day at 1 year post-surgery, and increased the frequency of fruit and vegetable intake by 0.9 and 0.7 times/week, respectively. Women who were non-smokers were more likely to report increase in daily fruit intake. Similarly, the British DietCompLyf cohort study (n=1,560)⁸⁴ reported that BC survivors increased approximately 0.5 serving/1000 kcal/day of fruit and 0.5 serving/1000 kcal/day of vegetable at 1 year after diagnosis after adjusting for total energy intake. However, in the HEAL study (n=260), Wayne et al.⁸⁵ examined changes in F/V intake from baseline to 2 years post-diagnosis and reported no increase in daily F/V intake, although the percent of BC survivors eating 5 servings/day or more F/V increased from 20% to 24%. Although the average change in F/V intake differed by study, these studies suggested that approximately 40% to 50% BC survivors increased their F/V intake after diagnosis.^{78,85} Based on the inconsistent findings among the

prospective studies, there is insufficient evidence to conclude that F/V intake changes after a BC diagnosis - although the evidence indicated the increase in F/V is most likely short term during the first year after diagnosis.

2.4.6 Dietary change – dietary fat intake

Six studies^{65,84,85,100-102} reported the longitudinal change in dietary fat intake or percent energy intake from fat after a breast cancer diagnosis (Table 2). Of the six studies, three high-quality studies^{65,84,85} found inconsistent results regarding change in dietary fat intake. The HEAL study (n=260)⁸⁵ reported that BC survivors on average reduced 3.6 g/day of fat intake and 1% of energy from fat at 2 years post-diagnosis. The reduction in dietary fat intake was greater in women diagnosed at a younger age. Similarly, the DietCompLyf study (n=1,560)⁸⁴ reported a decrease of 4 g/1000 kcal/day in total fat intake at 1 year after diagnosis, of which 2 g/1000 kcal/day was reduced in saturated fat, and 1.2 g/1000 kcal/day was reduced in monounsaturated fat. In a study to understand energy imbalance during adjuvant chemotherapy among 53 premenopausal BC survivors,⁶⁵ there was no significant change in percent energy from fat as assessed by 2-day dietary recall and FFQ from 3 weeks to 1 year after diagnosis, although the study did not report change in total and specific type of fat intake. Based on the inconsistent findings, there is insufficient evidence to describe the change in dietary fat after a BC diagnosis. More studies are needed to understand how women change dietary fat intake in response to a BC diagnosis.

2.4.7 Physical activity change – moderate to vigorous physical activity

There were 12 studies^{73,76,78,79,81-83,98,100,108,110,119,121}, of which seven^{76,78,79,81-83,98,119} were of high quality, that reported the longitudinal change in MVPA after a BC diagnosis (Table 3). The majority of the seven studies reported decrease in MVPA over time. In the Pathways Study (n=1,696), Kwan et al. reported that MVPA decreased by 1.28 hour/week from 2 to 8 months after BC diagnosis. The decrease was primarily in household (-0.44 hour/week) and recreational (-0.74 hour/week) MVPA.⁸² Among studies that reported moderate and vigorous activities separately, a population-based cohort study of 287 Australian BC survivors showed that participants spent 17 more minutes/week on vigorous PA but 55 less minutes/week on moderate PA from 6 to 18 months after diagnosis. In contrast, a population-based cohort study of BC survivors in the US (n=315) reported that vigorous PA decreased by 5 MET-h/week

and moderate PA decreased by 2.6 MET-h/week at 12 months post-diagnosis. Both groups returned to pre-diagnosis level at around 19-30 months.⁹⁸ Only one study examined the long-term change in MVPA up to 10 years after diagnosis: the HEAL study (n=631) reported that MVPA level remained stable during the 5 years after baseline, but decreased by 4.9 MET-h/week between 5 to 10 years post-diagnosis.⁸³ In contrary to these studies indicating a decrease in MVPA following a BC diagnosis, a German study of 229 BC survivors reported that women increased 48 minutes/week of MVPA and 12% more women achieved recommended level of MVPA at 14 months after diagnosis.⁷⁸

Previous studies also suggested that the change in MVPA after a BC diagnosis is not uniform. For instance, the HEAL study (n=545) reported that, at 30 months after diagnosis, 35% women decreased time on MVPA, while 26% maintained and 39% increased time on MVPA.⁷⁹ Using a hospital sample of 199 BC patients, Brunet et al. further demonstrated that women may follow five distinct trajectories of change in MVPA during the first year after diagnosis: 5.5% of women were consistently inactive, 9.5% increased MVPA, 10.5% were inactive but increased MVPA, 25% were somewhat inactive over time, and 49% were consistently active.¹¹⁹ These studies also suggested that women who were younger at diagnosis, received chemotherapy, or had greater treatment complications were more likely to decrease their MVPA, while women who were both overweight and had healthy weight at baseline were associated with decrease in MVPA.^{82,98} Collectively, the results suggest that there is moderate evidence to conclude that women may decrease time spent on MVPA during the first 24 months following a BC diagnosis.

2.4.8 Physical activity change – sedentary activity

Only two high-quality studies examined the change in sedentary behavior following a BC diagnosis (Table 3),^{76,82} which reported inconsistent results. In the Pathways Study (n=1,696), Kwan et al. reported that BC survivors on average spent 0.83 fewer hours/week in sedentary behavior at 6 months after diagnosis.⁸² Specifically, their findings suggested that BC survivors reduced time spent on doing crafts (-0.15 hour/week), reading (-0.16 hour/week), socializing (-0.28 hour/week), and attending group events (-0.08 hour/week), but spent more time on TV watching (+0.32 hour/week). However, a study of 24 BC survivors in Ireland measured accelerometer-assessed PA data and suggested that BC survivors

spent more time on sedentary behavior and less time on light PA after treatment, and the change maintained at 1 year later.⁷⁶ Neither study identified significant predictor of change in sedentary time. Given the limited yet conflicting results, there is insufficient evidence to make any conclusions about the change in sedentary behavior following a BC diagnosis.

2.4.9 Change in alcohol intake

Four studies examined change in alcohol intake after a BC diagnosis (Table 4).^{84,86,90,102} Two of the four studies were of high quality.^{84,90} The two studies assessed alcohol intake using different methods but reported similar findings on changes in alcohol intake. Using the EPIC study FFQ, the British DietCompLyf cohort study (n=1,560) reported that BC survivors decreased an average of 0.7g/1000 kcal/day of alcohol intake at 1 year after diagnosis, which was primarily due to decrease in wine and alcoholic beverages other than beer.⁸⁴ In a large cohort study of Australian BC survivors (n=1,588), Bell et al. reported that, compared to their drinking behaviors at baseline, BC survivors were less likely to report ever consuming >4 drinks per occasion (OR=0.78, 95% CI:0.67-0.90) and less likely to report drinking >4 drinks per occasion at least weekly (OR=0.63, 95% CI: 0.49-0.81) at 2 years after diagnosis, suggesting that BC survivors may reduce the frequency and amount of alcohol intake after diagnosis.⁹⁰ It is noteworthy that the two studies employed different assessments of alcohol intake: Bell et al. assessed the frequency, amount, and occasions of alcohol intake at diagnosis and in the past 12 months at 2 years, while Veletzis et al. assessed alcohol intake using a FFQ. However, both studies asked the intake of beer, wine and other alcoholic beverages. The two studies collected data on alcohol intake during the similar time window after diagnosis: Bell et al. enrolled patients at an average of 41 weeks (10 months) after a BC diagnosis, and followed up at one year after the enrollment; the study by Veletzis recruited patients at 9-15 months post diagnosis and followed up at 24 months following the baseline visit. Because of the consistent findings in these two studies, there is sufficient evidence to conclude that BC survivors reduce alcohol intake following a BC diagnosis.

2.4.10 Change in cigarette smoking

Three studies reported change in cigarette smoking after a BC diagnosis (Table 4).^{78,86,90} Two high-quality studies^{78,90} reported the percent of women who quit smoking after a BC diagnosis. In a

German study of BC survivors (n=229), Steinhilper et al. reported that 16% of women were current smokers at baseline, of whom, only 10% quit smoking at 1 year after a BC diagnosis; the majority of women did not change smoking behavior or start smoking. However, an Australian study of 1,588 BC survivors, in which 12% were current smokers at baseline, suggested that 32% of current smokers quit smoking after diagnosis and 25% of current smokers reduced the number of cigarettes smoked per day at 2 years after diagnosis). Because of the inconsistent and relatively low smoking cessation rates reported by these studies, there is insufficient evidence to suggest that women tend to quit smoking following a BC diagnosis.

2.4.11 Weight change

A total of 48 studies assessed weight change after a BC diagnosis (Table 5).^{60-67,74,75,77,80,86-89,91-97,99,112,114-118,122-135} Of these studies, 25 high-quality studies were identified.^{60-65,67,74,76,77,80,91-97,99,112,114-116,122} Overall, approximately 19%-84% of women diagnosed with BC experienced significant weight gain during the 1-2 years after diagnosis,^{77,80,91,92,112,122} and the weight gain was maintained in 30% of BC survivors long-term.^{93,95} Four population-based cohort studies in the US and China measured self-reported weight and height among BC survivors.^{80,91,113,116} The After Breast Cancer Pooling Project (n=12,915 stage I-IV BC survivors) compared weight at 1 year prior to BC diagnosis and weight at 18-48 months post-diagnosis, and reported an average of 1.6 (SD=6.3) kg increase in body weight.⁹¹ Approximately 34.7% of women gained weight while 14.7% lost weight during this period. A recent study using data from the LACE and the Pathways Study (n=3,109 stage I-III BC survivors) reported similar findings, with 25% of women reporting weight gain and 14% reporting weight loss at 24 months after diagnosis.⁹² However, results from the Long Island Breast Cancer Study Project (n=1,436) suggested that weight gain (23%) and weight loss (22%) were equally common in BC survivors at 1 year after diagnosis.¹¹³ Few studies examined whether BC survivors followed similar trajectory of weight gain as women without BC. One study followed 345 early stage BC survivors who received chemotherapy after diagnosis and 305 healthy women over 6 years and reported that 42% of BC survivors and 32% of healthy women experienced weight gain of $\geq 5\%$ baseline weight.¹¹⁶

For studies that collected clinically measured weight and height, the average weight gain ranged from 1.0 kg to 5.9 kg during the first 24 months after diagnosis.^{61-63,74,77,93,96,99,114,115} Studies that followed participants beyond the first 24 months post-diagnosis showed that weight gain reduced over time, and the mean weight gain ranged from 0.3 kg to 2.8 kg at ≥ 3 years post-diagnosis.^{63,93,97} Among the included studies, Camoriano et al. first examined the effect of cancer treatment on weight change in a cohort of 656 BC patients undergoing treatment of chemotherapy or chemohormonal therapy or not and reported that, at 60 weeks after treatment initiation, postmenopausal women gained an average of 3.6 kg of weight and premenopausal women gained 5.9 kg. In comparison, untreated women only gained 1.8 kg during the same period.⁷⁴ A similar finding was reported in another study by Goodwin et al. among 535 locoregional BC survivors,⁷⁷ which estimated that 84% women gained weight at 1 year after surgery, and the mean weight gain was greater among those receiving chemotherapy (+2.5 kg) and hormonal therapy (+1.3 kg) than that among untreated women (+0.5 kg). Other studies that monitored weight change over the course of chemotherapy^{62,64,75,99} or hormonal therapy⁶⁷ reported similar increases in body weight. Although the a large group of BC survivors showed weight gain, 10%-52% of women experienced weight loss during the first 24 months after a BC diagnosis.^{80,91,92,95,112,122} For example, a large study of 1,002 BC survivors over 19 months of systematic treatment reported that 48% of women gained weight and 52% lost weight.¹¹² Similarly, another study that compared weight change from diagnosis to 18 months post-diagnosis among 12,590 BC survivors within the Kaiser Permanente Northern California network reported that 19% of women gained and 19% of women lost $\geq 5\%$ body weight, and the amount of weight changes were comparable between women who gained and lost weight.¹¹¹ Furthermore, in a Korean study of 260 BC survivors, Han et al. only observed a temporary weight increase of 0.3 kg during the first 3 months of adjuvant chemotherapy, and there was an overall weight loss by the end of 12 months.⁹⁴ Consistent with their findings, another study of 53 BC survivors also reported no statistically significant trend in body weight over the first year post-diagnosis.⁶⁵

Based on the included studies, except for cancer treatment, factors associated with weight gain after cancer diagnosis also include age,^{60,63,93,96,97,114} advanced disease stage,^{60,63,93,96,97,114} decreased physical activity⁹⁶ and increased energy intake.¹¹⁴ However, the evidence is limited and inconsistent. For example, both younger^{63,93,96,114} and older⁹⁷ age at diagnosis were associated with greater weight gain,

and both premenopausal^{74,114} and postmenopausal^{60,96} status were associated with weight gain. Given the large body of consistent evidence suggesting both weight gain and weight loss after a BC diagnosis across multiple BC populations, there is strong evidence that both weight gain and loss are commonly seen in women after a BC diagnosis, although the evidence that supported a weight gain outweighed the evidence that suggested weight loss.

2.5 DISCUSSION

This review aimed to systematically summarize the literature on changes in health behaviors after a BC diagnosis, taking into account the methodological quality of the studies. Based on the studies identified, there is strong evidence suggesting that women are likely to reduce alcohol intake and experience weight gain after a BC diagnosis. Further, there is moderate evidence suggesting that women spend less time on MVPA after a BC diagnosis. However, in contrast to previous studies that suggested a BC diagnosis may encourage women to seek healthier diet,^{7,11,49,53,136-138} there is insufficient evidence to conclude that BC survivors increase F/V and decrease dietary fat after diagnosis. Evidence regarding changes in cigarette smoking and sedentary behavior was scarce and inconsistent. To my knowledge, this review is the first to systematically summarize the literature regarding the change in key health behaviors following a BC diagnosis across multiple cohorts. Collectively, the results suggest that a BC diagnosis may not effectively motivate women to make positive change in health behaviors.

Amid the inconsistent reports of dietary change after a BC diagnosis, several things were noteworthy. First, the reported amount of increase in F/V intake and decrease in dietary fat intake were indeed very small. On average, the increase in F/V intake at one year after BC diagnosis was estimated to be less than 1 serving/day. That is equivalent to less than 1 medium-size apple or 1 cup of spinach. With regard to dietary fat, the reported decrease of 4 g/day is equivalent to approximately 1 teaspoon of butter, which is relatively small compared to the American Heart Association's recommended dietary fat intake of 44-78 g/day.¹³⁹ The small change in dietary fat intake could be due to the low dietary fat intake at baseline in this population (mean=37.18 g, SD=6.88 g). Second, the included studies showed that BC survivors on average consumed less than five servings/day of F/V as recommended by the ACS and

AICR.^{44,48} For instance, the HEAL study reported that BC survivors consumed approximately 3.6 servings/day of F/V at baseline.⁸⁵ Therefore, a small increase in F/V intake is unlikely to substantially change the percent of women meeting the recommended five servings per day. In fact, less than 25% of women reported consuming five servings/day of F/V in the HEAL study. Third, the comparisons may be problematic if different FFQs have inconsistent definitions of what counts as a fruit or vegetable, or used different measurement units. Among the FFQs used by the included studies, the Women's Health Initiative (WHI) and the EPIC study FFQ have more than 100 food items,^{84,85} which assessed more fruit and vegetable items than a 19-item FFQ used in a German study.⁷⁸

Unlike the mild change in diet, the observed fluctuation in MVPA was considerably large. The reported decrease in MVPA ranged from a decrease in 38-90 minutes/week, which is approximately 25%-60% of the ACS-recommended 150 minutes/week of MVPA. The amount of decrease is worrisome, given that many studies reported that BC survivors on average spent less than 150 minutes/week of MVPA at baseline.^{73,76,119} On the other hand, a number of studies reported increases in MVPA, mostly after treatment.^{73,98,110} These results suggest that the teachable moment for physical activity may come after the completion of cancer treatment, when the physical discomfort due to treatment lessens. The decreased time spent on MVPA often transferred to increases in time spent on sedentary activities. However, the two studies of changes in sedentary behaviors after a BC diagnosis reported both increases and decreases in sedentary time. Although accelerometer data suggested that women increased the time spent on sedentary activities from 6.8 hours/day to 7.6 hours/day after diagnosis,⁷⁶ data collected using the Arizona Activity Questionnaire suggested the sedentary time decreased from 17.6 hours/week to 16.8 hours/week, or from 2.5 hours/day to 2.4 hours/day.⁸² The amount of objectively measured sedentary time was comparable with that reported in BC survivors enrolled in NHANES.¹⁴⁰ It is known that the physical activity questionnaires may not accurately measure true sedentary time and even significantly under report sedentary time than accelerometer-based estimates.¹⁴¹ Although this limitation is unlikely to affect the analysis of change in sedentary time if the same questionnaire was used consistently over time, the study by Kwan et al. revealed that the overall reduction in sedentary time was primarily due to reduction in time spent on doing crafts, reading, socializing, and attending group events, but women spent statistically significantly more time on TV watching after a diagnosis.⁸² Reduction in regular social

and leisure activities and increase in TV watching in fact supports the hypothesis that BC survivors suffer from physical discomfort due to cancer treatment. Previous studies suggested that cancer treatments may disrupt health behaviors, and many cancer patients report reduction in physical activity during the phase of active treatment.^{105,106} Although cancer treatment may present barriers to the adoption of healthy behaviors, few studies formally investigated the impact of cancer treatment and treatment related side effect, such as nausea, pain and peripheral neuropathy, on changes in health behaviors in breast cancer survivors.

Although most included studies were considered to be of high quality, there are a few important methodological issues that undermine the internal validity of the estimated longitudinal changes. Although hospital-based studies generally have better control of the timing of baseline and follow-up data collection, they are generally limited by small sample sizes, short follow-up period, and limited generalizability. In contrast, large population-based cohort studies are generally limited by varying times between cancer diagnosis and baseline behavior data collection, and varying times between baseline and follow-ups. Very few studies were designed to follow a cohort of BC survivors. Even in these studies, enrollment often occurred 2 to 6-months post-diagnosis. Therefore, data collected at baseline may not reflect pre-diagnosis diet and physical activity. For studies that had relied on breast cancer survivors identified through a population-based cohort study of healthy individuals, such as the Nurses' Health Study⁸⁸ and Norwegian Women and Cancer study,¹⁰¹ the follow-up visits were scheduled based on the parent study's enrollment date, instead of time of diagnosis. As such, data were not collected regularly enough to reflect the natural history of behavior change after a BC diagnosis - especially the period immediately following diagnosis when patients were actively undergoing cancer treatment.

Another major limitation of previous studies of behavior change is the use of the overall mean change to make inference about individual behavior change, which assumed that all women would follow the same behavior change. In fact, the included studies suggested that not all women make the same behavior change. Rather, this data supports the hypothesis that there is considerable heterogeneity in women's diet changes and physical activity. However, only one study examined the heterogeneous trajectories of change in MVPA during the first year after a BC diagnosis. Furthermore, most studies

described mean changes between two time points at set interval, and therefore assume monotonic trend in behavior change over this period. Little is known about the non-linear trend in health behaviors, such as temporary decreases or increases in physical activity. Additionally, no study has examined the trajectory of dietary change or change in alcohol intake after a BC diagnosis. Future studies should give more attention to novel analytical techniques such as growth mixture modelling¹⁴² and group based trajectory modelling¹²⁰ to investigate patterns of behavior change trajectories, rather than masking these unique trajectories.

An additional methodological limitation of prior studies is that few studies considered the influence of loss to follow-up and missing data on the observed behavior change. Since most studies used paired t-tests to compare change in health behavior pre- and post-diagnosis, they implicitly restricted the analyses to participants who had complete data at baseline and follow-up. This type of analysis may overestimate the increase in beneficial health behaviors if participants who completed follow-up questionnaire were more health conscious women. Furthermore, few studies used energy adjustment in analyzing dietary change. Since many breast cancer patients experience anorexia or reduced food intake during active treatment,¹⁴³ dietary changes may occur simply as a result of lost appetite and overall reduced energy consumption. Energy-adjusted residual of dietary intake¹⁴⁴ will produce an estimate of dietary intake independent of total energy intake, and therefore is more suitable for future analysis of dietary change.

The causes of health behavior changes remain unclear. Cancer treatments may disrupt normal health behaviors. For example, cancer patients report reduction in physical activity during the phase of active treatment,^{35,145} and changes in taste sensitivity induced by chemotherapy may alter food preferences and nutritional intake.¹⁴⁶⁻¹⁴⁹ In addition, the diagnosis and treatment of cancer is a significant stressor in itself that could contribute to changes in appetite and sleep and may disrupt health behaviors and potentially increase unhealthy behaviors.^{150,151} Previous studies explained the individual differences in lifestyle choices after a breast cancer diagnosis using the stress and coping model.^{152,153} Many BC survivors live with the fear of cancer and its consequences. It is unclear how this sense of continued stress affects the adjustment in lifestyle following a BC diagnosis. The stress and coping model posits that the management of stressful feelings may influence cancer survivors' ability to make and sustain

health behavior change.¹⁵⁴ In particular, this model proposes that the use of adaptive coping to deal with cancer diagnosis stressors will be related to positive health behavior change. In breast cancer survivors, depressive symptoms are the most common stress-related symptoms.^{151,155-157} Depressive symptoms are associated with smoking and physical inactivity in general population^{158,159} and testis cancer survivors.¹⁶⁰ In contrast, greater dispositional optimism, a generalized expectancy that the future holds positive outcomes,¹⁶¹ has been associated with not smoking, moderate alcohol consumption, brisk walking, and vigorous physical activities in older women. In addition, higher perceived social support may facilitate stress coping and is linked to increased health behavior, specifically exercise, in cancer survivors.^{162,163}

The causes of weight change are also complex. Previous studies generally hypothesized that weight gain may be caused by breast cancer treatment regimens, most notably chemotherapy and hormonal therapy.^{26,27,164,165} However, the mechanism of weight gain in breast cancer survivors remains unclear. Behaviors changes that cause energy imbalance may contribute to the weight gain after a breast cancer diagnosis. The study by Chen et al. found that higher baseline dietary intake was associated with weight gain after BC diagnosis,¹¹⁴ and findings of Irwin et al. suggest that a decrease in physical activity was associated with weight gain.⁹⁶ The causal relationship between behavior change and weight change after a BC diagnosis needs further investigation.

This systematic review has several limitations. The use of quality assessment of observational study in this systematic review is controversial and may bias the conclusions of this review.^{166,167} The rationale for including study quality assessment into this systematic review was to exclude studies of low methodological quality which tend to report larger effect sizes than higher quality studies.¹⁶⁸⁻¹⁷⁰ However, some studies reported no relationship between quality score and effect size and that the quality of included study is unlikely to affect the conclusion of a systematic review.¹⁶⁶ Some suggest that the number of studies categorized as high quality or low quality depended specifically on the scale that was applied.¹⁶⁷ Therefore, the choice of scale will have a significant impact regarding what studies are eligible. Another problem with quality assessment is the lack of clear cut-off criteria for quality categories studies. This poses a significant methodological limitation to the implementation of these scales. In addition, because the type of quantitative measures of behavior change were not uniform among the included

studies, I was not able to provide a quantitative synthesis of the behavior change. Therefore, this review was only able to make conclusions on the direction of behavior change.

2.6 CONCLUSION

This review of prospective cohort studies showed strong evidence that many women reduce alcohol intake and gain weight after a BC diagnosis, and showed moderate evidence for a decrease in time spent on MVPA after a BC diagnosis. There is insufficient evidence to make any conclusion about the change in F/V, dietary fat, and time spent on sedentary behaviors after a BC diagnosis. Future studies should examine the heterogeneity of behavior change after a BC diagnosis using trajectory analysis, while accounting for potential bias due to loss to follow-up and missing data in key behavior variables. Future studies of dietary change should also use energy adjustment methods to control for change in total food intake. Finally, more studies are needed to understand the causes of change in health behaviors, and to investigate the relationship between behavior change and weight change, and how these changes ultimately affect breast cancer prognosis and survival.

2.7 FIGURES AND TABLES

Figure 1. Literature search and screen flow diagram

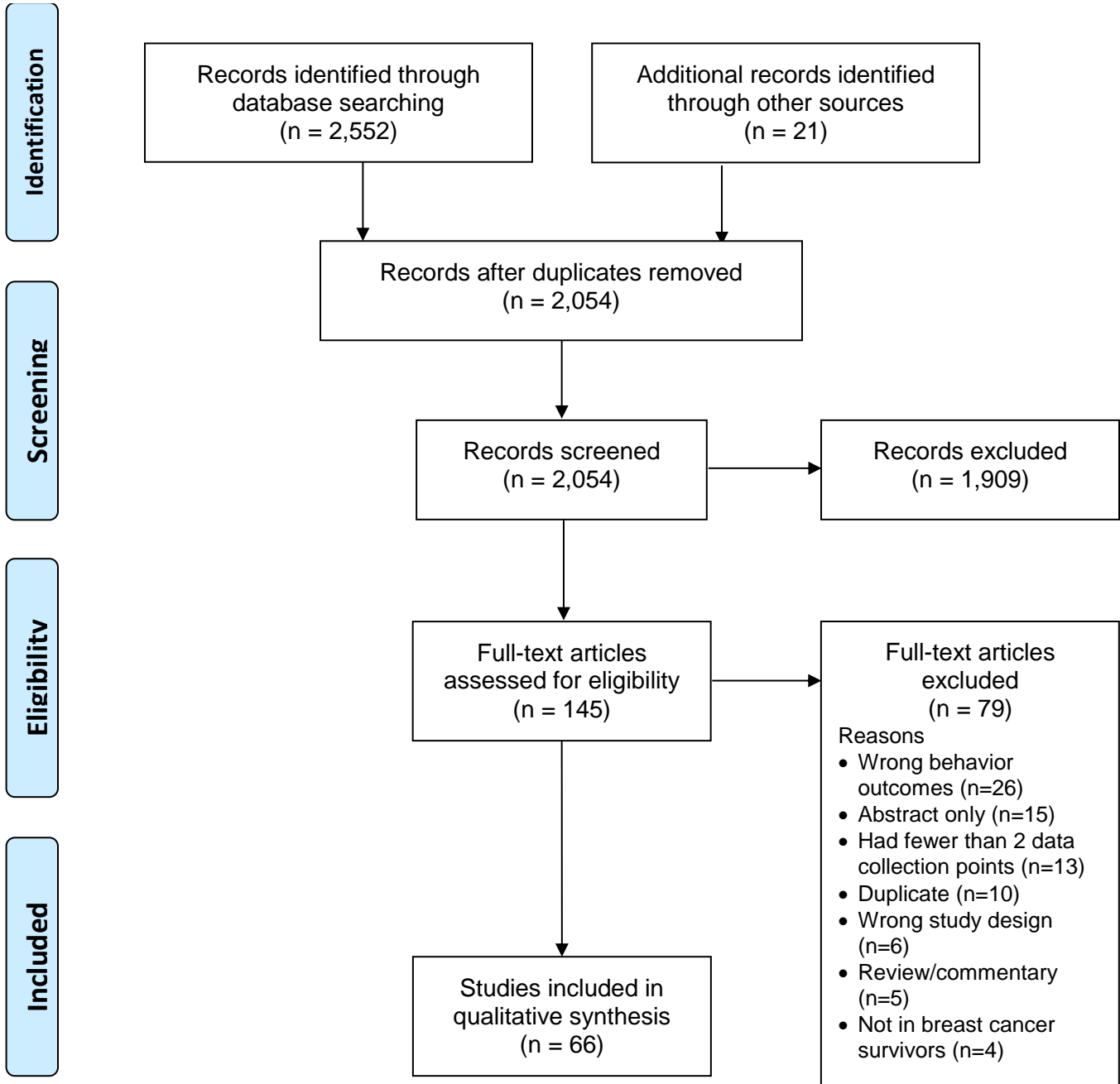


Table 1. Quality assessment of included studies based on the Critical Appraisal Skills Program (CASP)

Author Year	Was the cohort recruited in an acceptable way?	Was the follow-up regular enough to minimize bias?	Was the behavior data accurately measured to minimize bias?	Have the authors identified and taken account of the confounding factors in the design and/or analysis?	Was the follow-up of subjects complete enough?	Was the follow-up of subjects long enough?	Did the study assessed influence of missing data?	Total Score
Alfano 2007 ⁷⁹	1	1	1	0	1	1	0	5
Andrykowski 2007 ⁷³	1	1	1	0	1	0	0	4
Bell 2012 ⁹⁰	1	1	1	1	1	1	0	6
Bidstrup 2013 ⁸⁶	1	0	1	0	1	1	0	4
Bradshaw 2012 ¹¹³	1	1	0	0	1	1	1	5
Broderick 2014 ⁷⁶	1	1	1	0	1	1	0	5
Brooks 2016 ¹²³	1	0	1	0	1	1	0	4
Brunet 2013 ¹⁰⁸	1	1	1	0	1	0	0	4
Brunet 2014 ¹¹⁹	1	1	1	1	1	1	0	6
Caan 2012 ⁹¹	1	1	1	0	1	1	0	5
Camoriano 1990 ⁷⁴	1	1	1	0	1	1	0	5
Cespedes Feliciano 2017 ⁸⁰	1	1	1	0	1	1	0	5
Cespedes Feliciano 2017 ⁹²	1	1	1	0	1	1	0	5
Chaudhary 2014 ⁶⁰	1	1	1	0	1	1	0	5
Chen 2010 ¹¹⁵	1	1	1	0	1	1	0	5
Chen 2011 ¹¹⁴	1	1	1	0	1	1	0	5
Costa 2002 ¹²⁴	1	1	1	0	1	0	0	4
Costanzo 2011 ¹⁰²	1	1	0	1	1	0	0	4
Demark-Wahnefried 2001 ⁶⁵	1	1	1	1	1	1	0	6
Freedman 2004 ¹²⁵	1	1	1	0	1	0	0	4
Goodwin 1999 ⁷⁷	1	1	1	1	1	1	0	6
Gross 2015 ¹²⁶	1	0	1	0	1	1	0	4
Gu 2010 ⁹³	1	1	1	0	1	1	0	5
Harrison 2009 ⁸¹	1	1	1	0	1	1	0	5

Author Year	Was the cohort recruited in an acceptable way?	Was the follow-up regular enough to minimize bias?	Was the behavior data accurately measured to minimize bias?	Have the authors identified and taken account of the confounding factors in the design and/or analysis?	Was the follow-up of subjects complete enough?	Was the follow-up of subjects long enough?	Did the study assessed influence of missing data?	Total Score
Han 2004 ⁹⁴	1	1	1	0	1	1	0	5
Hatch 2014 ¹²⁷	1	0	1	0	1	1	0	4
Heideman 2009 ⁶¹	1	1	1	1	1	1	0	6
Huy 2012 ¹¹⁰	1	1	0	0	1	1	0	4
Imayama 2013 ⁹⁵	1	1	1	0	1	1	0	5
Ingram 2004 ⁶⁶	1	0	1	0	1	0	0	3
Irwin 2005 ⁹⁶	1	1	1	0	1	1	0	5
Jammallo 2013 ¹²⁸	1	1	1	0	1	0	0	4
Jeon 2014 ⁶²	1	1	1	0	1	1	0	5
Jernström 1999 ⁸⁷	1	0	1	0	1	1	0	4
Kogawa 2015 ¹¹²	1	1	1	0	1	1	0	5
Koo 2016 ¹²⁹	0	0	1	0	1	1	0	3
Kroenke 2005 ⁸⁸	1	0	1	0	1	1	0	4
Kumar 1997 ⁹⁷	1	1	1	0	1	1	0	5
Kwan 2012 ⁸²	1	1	1	0	1	1	0	5
Lankester 2002 ¹³⁰	1	1	1	0	1	0	0	4
Littman 2010 ⁹⁸	1	1	1	0	1	1	0	5
Liu 2014 ⁹⁹	1	1	1	0	1	1	0	5
Makari-Judson 2007 ⁶³	1	1	1	0	1	1	0	5
Mason 2013 ⁸³	1	1	1	1	1	1	0	6
Maunsell 2002 ⁵³	1	1	1	0	1	0	0	4
Nichols 2009 ⁸⁹	1	0	1	0	1	1	0	4
Nissen 2011 ¹³¹	1	1	1	0	1	0	0	4
Nyrop 2017 ⁶⁷	1	1	1	1	1	1	0	6
Pedersen 2016 ¹¹⁷	1	1	1	0	1	0	0	4

Author Year	Was the cohort recruited in an acceptable way?	Was the follow-up regular enough to minimize bias?	Was the behavior data accurately measured to minimize bias?	Have the authors identified and taken account of the confounding factors in the design and/or analysis?	Was the follow-up of subjects complete enough?	Was the follow-up of subjects long enough?	Did the study assessed influence of missing data?	Total Score
Phillips 2016 ¹²¹	1	0	1	0	1	0	0	3
Rabin 2006 ¹⁰⁰	1	1	1	0	1	0	0	4
Saquib 2007 ¹⁷¹	1	1	1	0	1	1	0	5
Sedjo 2013 ¹¹⁶	1	1	1	1	1	1	0	6
Sheppard 2013 ⁶⁴	1	1	1	0	1	1	0	5
Skeie 2009 ¹⁰¹	1	0	1	0	1	1	0	4
Steinhilper 2013 ⁷⁸	1	1	1	0	1	0	0	4
Thivat 2010 ¹³²	1	1	1	0	1	0	0	4
Trédan 2010 ⁷⁵	1	0	1	0	1	0	0	3
Vagenas 2015 ¹³³	1	1	1	0	1	0	0	4
Vargas-Meza 2016 ¹⁷²	1	1	1	0	1	0	0	4
Velentzis 2010 ⁸⁴	1	1	1	0	1	1	0	5
Wanders 2015 ¹³⁴	1	1	1	0	1	0	0	4
Wang 2014 ¹⁷³	1	1	1	0	1	0	0	4
Wayne 2004 ⁸⁵	1	1	1	0	1	1	0	5
Yaw 2010 ¹¹⁸	1	1	1	0	1	0	0	4
Young 2014 ¹³⁵	1	1	1	0	1	0	0	4

Note: Each criterion is assessed as satisfied (1) or not satisfied (0). The scores were summed to give each study a composite score ranging from 0 to 7, with each score representing a quality level: 0-2, low; 3-4, modest; and 5-7, high.

Table 2. Summary of studies on dietary change after a breast cancer diagnosis

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Time of assessment	Change in diet	Predictors of change
Fruit/vegetable								
Costanzo 2011 ¹⁰²	USA	79 stage 0-III BC survivors, mean age=55	Hospital	Chemotherapy and/or radiation	Single question assessed self-reported changes after diagnosis (e.g. does the participant eat more fruits and vegetables?)	3 weeks and 3 months after diagnosis	No significant change in F/V intake	Belief that cancer is due to diet and healthy diet could prevent recurrence is associated with increased F/V intake
Skeie 2009 ¹⁰¹	Norway	563 stage I-IV BC survivors, mean age=51	Norwegian Women and Cancer study	Hormonal therapy	A semi-quantitative FFQ with emphasis on fish intake	From 1996-1999 to 2002-2005	Increased 51g/day of F/V intake	Stage II BC survivors made larger changes compared to stage I survivors
Steinhilper 2013 ⁷⁸	Germany	229 stage I-III BC survivors, mean age=53	Hospital	Chemotherapy and/or radiotherapy	A 19-item FFQ assessed intake of food and food group	After surgery to 14 months post surgery	Increased 0.4 serv/day of fruit and 0.7 serv/day of vegetable	Nonsmokers at baseline increased more fruit intake
Velentzis 2010 ⁸⁴	UK	1,560 stage I-III BC survivors	DietComplyf cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	The European Prospective Investigation into Cancer and Nutrition (EPIC) Study FFQ	Pre-diagnosis and 1 year after diagnosis	Increased 1 serv/1000 kcal/day of F/V and decreased 172 kcal of total energy intake	Not assessed
Wayne 2004 ⁸⁵	USA	260 stage 0-IIIA BC survivors from the HEAL study, mean age=58	Health, Eating, Activity, and Lifestyle (HEAL) study	Chemotherapy and/or radiotherapy and/or hormonal therapy	The Women's Health Initiative FFQ	Pre-diagnosis and 2 years after diagnosis	No change in F/V intake; reduced 137 kcal/day energy intake	Not identified
Dietary fat								
Costanzo 2011 ¹⁰²	USA	79 stage 0-III BC survivors, mean age=55	Hospital	Chemotherapy and/or radiation	Single question assessed self-reported changes after diagnosis (e.g. does the participant eat	3 weeks and 3 months after diagnosis	No significant change in % calories from fat	Not identified

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Time of assessment	Change in diet	Predictors of change
					more fruits and vegetables?)			
Demark-Wahnefried 2001 ⁶⁵	USA	53 stage 0-III BC survivors, mean age=41	Hospital	Chemotherapy and/or radiation	2-day dietary recall and FFQ	3 weeks, 6 months, and 1 year after diagnosis	No significant change in % calories from fat	Not assessed
Rabin 2006 ¹⁰⁰	USA	61 stage 0-III BC survivors, mean age=56	Hospital	No	A 23-item FFQ assesses dietary behaviors over the past month	From completion of all treatment to 3 months post treatment	No significant change in % calories from fat	Perceived efficacy of behavior in preventing cancer was not associated with dietary change
Skeie 2009 ¹⁰¹	Norway	563 stage I-IV BC survivors, mean age=51	Norwegian Women and Cancer study	Hormonal therapy	A semi-quantitative FFQ with emphasis on fish intake	From 1996-1999 to 2002-2005	Decreased fat spread on bread, amount unclear	Stage II BC survivors made larger changes than stage I survivors
Velentzis 2010 ⁸⁴	UK	1,560 stage I-III BC survivors	DietCompLyf cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	The European Prospective Investigation into Cancer and Nutrition (EPIC) Study FFQ	Pre-diagnosis and 1 year after diagnosis	Decreased 4g/1000 kcal/day of fat	Not assessed
Wayne 2004 ⁸⁵	USA	260 stage 0-IIIA BC survivors from the HEAL study, mean age=58	Health, Eating, Activity, and Lifestyle (HEAL) study	Chemotherapy and/or radiotherapy and/or hormonal therapy	FFQ	Pre-diagnosis and 2 years after diagnosis	Reduced 3.6g/day of fat and 1% of energy from fat	Younger women reported greater decrease in total energy and dietary fat

Table 3. Summary of studies on physical activity change after a breast cancer diagnosis

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
Moderate to vigorous physical activity								
Alfano 2007 ⁷⁹	USA	545 stage I-III BC survivors, mean age=58	Health, Eating, Activity, and Lifestyle (HEAL) study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Modifiable Activity Questionnaire assessed time spent on MVPA	6 months to 29 months after diagnosis	35% patients decreased time on MVPA, while 26% maintained and 39% increased time on MVPA	Not assessed
Andrykowski 2007 ⁷³	USA	231 stage 0-II BC survivors, mean age=55	Hospital	Chemotherapy and/or radiotherapy	Godin Leisure-Time Exercise Questionnaire (LTEQ)	Before adjuvant treatment, after 1st cycle of treatment, and till 2 and 6 months after treatment	Total energy expenditure and time spent on MVPA decreased during treatment, but recovered at 6 months after treatment, with 19% patients decreased their energy expenditure and 16% increased	Not assessed
Brunet 2013 ¹⁰⁸	Canada	150 stage I-III BC survivors, mean age=54	Life After Breast Cancer: Moving On cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	GT3X accelerometer	4 months after diagnosis to 3 and 6 months after baseline	No statistically significant change in MVPA	Change in self-determination for exercise is positively associated with change in MVPA

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
Brunet 2014 ¹¹⁹	Canada	199 stage I-III BC survivors, mean age=55	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	LTEQ	3 months after diagnosis to 3, 6, 9, and 12 months after baseline	Five trajectories of change during the first 12 months after diagnosis in MVPA were identified: 5.5% were consistently inactive, 9.5% showed decreasing level, 10.5% were inactive but increased MVPA, 25% were somewhat inactive over time, and 49% were consistently active	Patients with higher depressive symptom and fatigue and lower cancer worry were less likely to maintain high MVPA over time
Harrison 2009 ⁸¹	Australia	287 BC survivors, mean age=55	Regional cancer registry	Chemotherapy and/or radiotherapy and/or hormonal therapy	Questions used in the Behavioral Risk Factor Surveillance System	6 months to 18 months after diagnosis	Patients spent 17 more minutes/week on vigorous PA and 55 less minutes/week on moderate PA	Higher baseline PA level and more treatment complications were associated with lower total PA hours/week
Huy 2012 ¹¹⁰	Germany	1,067 stage I-IV BC survivors, mean age=64	MARIE/MARIEplus cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	A short retrospective physical activity questionnaire assessed total leisure time MVPA	2 months after diagnosis to active treatment period and 1 year after surgery	Median leisure time MVPA decreased by 22 MET.h/week during therapy and recovered to prediagnosis level at 1 year after surgery	Receipt of chemo and/or radiation, presence of medical risk factors and not in rehabilitation were associated with decrease in

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
								MVPA after therapy
Kwan 2012 ⁸²	USA	1,696 stage I-IV BC survivors, mean age=60	The Pathways Study cohort	Chemotherapy and/or radiotherapy and/or hormonal therapy	Arizona Activity Frequency Questionnaire	2 months to 8 months after diagnosis	Patients reported 1.28 h/week decrease in MVPA	Being overweight or obese at baseline and receipt of chemotherapy were associated with greater decrease in MVPA
Littman 2010 ⁹⁸	USA	315 stage I-IV BC survivors, mean age=52	Regional cancer registry	Chemotherapy and/or radiotherapy	Modifiable Activity Questionnaire assessed time spent on MVPA	Baseline (median=11 months post-diagnosis) and three intervals after diagnosis (0-12, 13-18, 19-30 months)	Vigorous PA decreased by 5 MET-h/week and moderate PA decreased by 2.6 MET-h/week at 0-12 months post-diagnosis. The MVPA level returned to pre-diagnosis level at 19-30 months post-diagnosis	Women aged <40 and with BMI <25 kg/m ² at diagnosis had the greatest reduction in MVPA
Mason 2013 ⁸³	USA	631 stage 0-IIIa BC survivors, mean age=54	The Health, Eating, Activity and Lifestyle (HEAL) study	Chemotherapy and/or hormonal therapy	Modifiable Activity Questionnaire assessed time spent on MVPA	6 months after diagnosis to 2, 5, and 10 years post-diagnosis	MVPA level remained stable during the 5 years after baseline, but decreased by 4.9 MET-h/week between 5 to 10	Meeting PA guideline at baseline is associated with meeting PA guideline at 5 and 10 years

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
							years post-diagnosis	
Phillips 2016 ¹²¹	USA	1,477 stage 0-IV BC survivors, mean age=57	Army of Women	Chemotherapy and/or radiotherapy and/or hormonal therapy	Godin Leisure-Time Exercise Questionnaire (LTEQ) and Actigraph accelerometer	Baseline (median=87 months after diagnosis) to 6 months after baseline	MVPA decreased 3 min/day at 6 months	Not assessed
Rabin 2006 ¹⁰⁰	USA	61 stage 0-III BC survivors, mean age=56	Hospital	No	Paffenbarger Activity Questionnaire	From completion of all treatment to 3 months post treatment	Trend of decreased total energy expenditure	Not identified
Steinhilper 2013 ⁷⁸	Germany	229 stage I-III BC survivors, mean age=53	Hospital	Chemotherapy and/or radiotherapy	Self-reported time spent on MVPA per week	After surgery to 14 months post-surgery	Increased 0.8 h/week of MVPA, 12% more achieved recommended exercise level	Higher level job title is associated high increase in MVPA
Sedentary behavior								
Broderick 2014 ⁷⁶	Ireland	24 stage I-IIIB BC survivors, mean age=51	Hospital	Radiotherapy and/or hormonal therapy	RT3 accelerometer and International Physical Activity Questionnaire (IPAQ)	6 weeks after chemotherapy to 6 and 12 months later	Patients spent more time on sedentary behavior and less time on light PA after treatment, and the change maintained at 1 year	Not assessed
Kwan 2012 ⁸²	USA	1,696 stage I-IV BC survivors, mean age=60	The Pathways Study cohort	Chemotherapy and/or radiotherapy and/or hormonal therapy	Arizona Activity Frequency Questionnaire	2 months to 8 months after diagnosis	Patients reported 0.83 h/week decrease in sedentary behavior	Not identified

Table 4. Summary of studies on cigarette smoking and alcohol intake after a breast cancer diagnosis

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
Alcohol intake								
Bell 2012 ⁹⁰	Australia	1,588 stage I-IV BC survivors, mean age=57	Regional cancer registry	Radiotherapy	Questionnaire assessed the frequency, amount, and occasions of alcohol intake at diagnosis and in the past 12 months at 2 years	Time of diagnosis to 2 years post-diagnosis	No significant change in alcohol intake	Not assessed
Bidstrup 2013 ⁸⁶	Denmark	449 I-III BC survivors, mean age=57	Danish Dit, Cancer and Health cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Questionnaire assessed amount of alcohol consumption per day	Baseline (1993-1997) to follow-up (2000-2002)	Alcohol consumption increased by 0.6 g/day	No significant predictors
Costanzo 2011 ¹⁰²	USA	79 stage 0-III BC survivors, mean age=55	Hospital	Chemotherapy and/or radiation	Self-reported changes after diagnosis (e.g. had the participant increased her level of alcohol intake?)	3 weeks to 3 months after diagnosis	No significant change in alcohol intake	Belief that lower alcohol intake could prevent recurrence is associated with reduced alcohol intake
Velentzis 2010 ⁸⁴	UK	1,560 stage I-III BC survivors	DietCompLyf cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	FFQ	Pre-diagnosis and 1 year after diagnosis	Decreased 0.7g/1000 kcal/day of alcohol intake	Not assessed
Cigarette smoking								
Bell 2012 ⁹⁰	Australia	1,588 stage I-IV BC survivors, mean age=57	Regional cancer registry	Radiotherapy	Questionnaire assessed ever smoking at diagnosis and in the past 12 months at 2 years, and cigarettes smoked per day	Time of diagnosis to 2 years post-diagnosis	32% quit smoking after diagnosis and 25% continued smokers reduced the number of cigarettes smoked per day	Baseline number of cigarettes smoked per day is associated with continued smoking

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of behavior	Length of follow up	Change in health behaviors	Predictors of change
Bidstrup 2013 ⁸⁶	Denmark	449 I-III BC survivors, mean age=57	Danish Diet, Cancer and Health cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Questionnaire assessed amount of tobacco consumption per day	Baseline (1993-1997) to follow-up (2000-2002)	Tobacco consumption decreased 1.1g/day	No significant predictors
Steinhilper 2013 ⁷⁸	Germany	229 I-III BC survivors, mean age=53	Hospital	Chemotherapy and/or radiotherapy	Questionnaire assessed current smoking status and amount of cigarette consumption per day	After surgery to 14 months post-surgery	Only 10% quit smoking	No significant predictors

Table 5. Summary of studies on weight change after a breast cancer diagnosis

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Bidstrup 2013 ⁸⁶	Denmark	449 I-III BC survivors, mean age=57	Danish Diet, Cancer and Health cohort study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight/height	Baseline (1993-1997) to follow-up (2000-2002)	No significant change in BMI	Not identified
Bradshaw 2012 ¹¹³	USA	1,436 BC survivors, mean age=59	Long Island Breast Cancer Study Project	Chemotherapy	Self-reported weight	Baseline to 1 year after diagnosis	23% patients lost >5% weight, 55% maintained weight, and 22% increased weight at 1 year after diagnosis	Not assessed
Broderick 2014 ⁷⁶	Ireland	24 stage I-III BC survivors, mean age=51	Hospital	Radiotherapy and/or hormonal therapy	Clinically measured weight/height	6 weeks after chemotherapy to 6 and 12 months post treatment	Mean BMI increased by 1 kg/m ² at 12 months	Not assessed
Brooks 2016 ¹²³	USA	1,386 contralateral breast cancer (CBC) and 2,045 unilateral breast cancer (UBC) patients, median age =46	Women's Environmental Cancer and Radiation Epidemiology (WECARE) Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight/height and/or medical record data	From date of first BC diagnosis to the second BC diagnosis after 1 year	9%-14% survivors lost weight>3 lbs, 35%-49% survivors gained >3 lbs	Not assessed
Caan 2012 ⁹¹	USA, China	12,915 stage I-IV BC survivors, mean age=57	After Breast Cancer Pooling Project	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight	1 year before diagnosis to 18-48 months after diagnosis	Mean weight increased 1.6kg, and 34.7% women gained weight and 14.7% lost weight	Not assessed
Camoriano 1990 ⁷⁴	USA	656 BC survivors, age 20-74	Hospital	Chemotherapy and/or radiotherapy	Clinically measured weight	At the beginning of treatment and 60 weeks later	Mean weight increased 1.8 kg among postmenopausal women without treatment, 3.6 kg for treated postmenopausal women, and 5.9 kg for treated premenopausal women	Premenopausal and receipt of cancer treatment is associated with more gain in weight

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Cespedes Feliciano 2017 ⁹²	USA	3,109 stage I-III BC survivors, mean age=57	LACE and Pathways Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight	1 year before diagnosis to 24 months after diagnosis	25% women gained ≥ 10 lbs, and 14% women lost ≥ 10 lbs	Not assessed
Cespedes Feliciano 2017 ⁸⁰	USA	12,590 stage I-III BC survivors, mean age=59	Kaiser Permanente Northern California	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight/height	From 3 months around time of diagnosis to 18 months post-diagnosis	19% women lost $>5\%$ weight (mean=-18 lbs), and 19% gained $>5\%$ weight (mean=15 lbs)	Not assessed
Chaudhary 2014 ⁶⁰	USA	246 stage 0-IV BC survivors, mean age=59	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Retrospective chart review	Time of diagnosis to 12 months post-diagnosis	Mean weight increased by 0.39% at 1 year after diagnosis	Postmenopausal status and lower stage were associated with higher weight gain
Chen 2010 ¹¹⁵	China	5,042 0-IV BC survivors, mean age=54	Shanghai Breast Cancer Survival Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight before diagnosis, and clinically measured weight after diagnosis	Pre-diagnosis and post-diagnosis (mean=6 months) to 18 months after diagnosis	Mean weight increased 1.0 kg and 1.5 kg at 6 and 18 months post-diagnosis	Not assessed
Chen 2011 ¹¹⁴	China	4,516 0-IV BC survivors, mean age=54	Shanghai Breast Cancer Survival Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight before diagnosis, and clinically measured weight after diagnosis	Pre-diagnosis and post-diagnosis (mean=6 months) to 18 months after diagnosis	Mean weight increased 1.7 kg at 18 months post-diagnosis; 61% women gained weight	Higher tumor stage, younger age, premenopausal status, mixed receptor status, pre-diagnosis weight loss, higher dietary intake, and cigarette smoking were associated with greater weight gain
Costa 2002 ¹²⁴	Brazil	106 BC survivors, mean age=50	Hospital	Chemotherapy	Retrospective chart review	Every month since chemotherapy treatment for 6 months	Mean weight increased by 0.5% per month after treatment	Metastatic disease is associated with lower weight gain

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Demark-Wahnefried 2001 ⁶⁵	USA	53 stage 0-III BC survivors, mean age=41	Hospital	Chemotherapy and/or radiation	Clinically measured weight/height	3 weeks, 2 month, 6 months, and 1 year after diagnosis	No significant linear trend in body weight or BMI	Not assessed
Freedman 2004 ¹²⁵	USA	20 stage I-III BC survivors	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight and body composition	Before chemotherapy treatment and at 2 weeks and 6 months after chemotherapy	Mean weight increased 1 kg and % body fat increased 0.9% from 2 weeks to 6 months after chemotherapy	Not assessed
Goodwin 1999 ⁷⁷	USA	535 locoregional BC survivor, mean age=50	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight	Baseline (4-12 weeks after surgery) to 1 year later	84% women gained weight, with a mean weight gain of 1.6 kg. Mean weight gain was 2.5 kg for those receiving chemotherapy, 1.3 kg for those receiving tamoxifen, and 0.5 kg in untreated women	Onset of menopause and adjuvant chemotherapy was associated with greater weight gain
Gross 2015 ¹²⁶	USA	303 stage I-III BC survivors (mean age=54) and 307 cancer-free women (mean age=54)	Breast and Ovarian Surveillance Service (BOSS) Cohort Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight	Baseline to 4 years follow-up	BC survivors gained 3 lb more weight than cancer-free women	Diagnosed <5 years, ER-tumor, receipt of chemotherapy, and concurrent use of Statin with chemotherapy were associated with higher weight gain
Gu 2010 ⁹³	China	5,014 0-III BC survivors, mean age=54	Shanghai Breast Cancer Survival Study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Self-reported weight before diagnosis, and clinically measured weight after diagnosis	Pre-diagnosis and post-diagnosis (mean=6 months) to 6, 18, and 36 months after diagnosis	Median weight increased 1.0 kg, 2.0 kg, and 1.5 kg at 6, 18, and 36 months post-diagnosis; 26%, 37%, and 33% women gained ≥5% weight at 6, 18, and 36 months.	Younger age, lower baseline weight, and higher tumor stage were associated with more weight gain

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Han 2009 ⁹⁴	Korea	260 stage I-III BC survivors. Mean age=47	Hospital	Chemotherapy and/or hormonal therapy	Clinically measured weight/height	Time of diagnosis to 3, 6, 12, and 24 months post-diagnosis	Mean weight changes were 0.30 kg at 3 months, 0.16 kg at 6 months, -0.34 kg at 1 year, and -0.40 kg at 2 years	Higher baseline weight and not receiving hormone therapy were associated with more weight loss
Hatch 2014 ¹²⁷	USA	46 stage 0-IIIa BC survivors and 116 healthy controls	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Retrospective chart review	Time of diagnosis to completion of treatment	No significant weight change	Higher cancer stage and receipt of chemotherapy were associated with less weight gain
Heideman 2009 ⁶¹	Netherland	271 stage I-III BC survivors, mean age=54	Hospital	Chemotherapy and/or hormonal therapy	Retrospective chart review	Time of diagnosis to approximately 1 and 3 years post-diagnosis	Mean weight increased 2.0 kg during the first year, and 2.4 kg at 3 years post diagnosis	Receipt of systematic treatment was associated with greater weight gain
Imayama 2013 ⁹⁵	USA	483 stage 0-IIIa BC survivors, mean age=56	The Heath, Eating, Activity and Lifestyle (HEAL) study	Chemotherapy and/or radiotherapy	Clinically measured weight/height	Baseline (6 months post-diagnosis) to 30 months post-diagnosis	9% lost ≥5% weight, 64% maintained weight, and 27% gained ≥5% weight	Not assessed
Ingram 2004 ⁶⁶	Canada	76 stage I-II BC survivors, mean age=44	Hospital	Chemotherapy and/or hormonal therapy	Clinically measured weight/height and body composition	Pretreatment to completion of cycle 4 of chemotherapy	34% gained >2.5 kg weight and 10.5% lost >2.5 kg weight; mean weight increased 1.4 kg during treatment. The weight changes were primarily due to changes in fat mass	Not assessed

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Irwin 2005 ⁹⁶	USA	514 stage 0-IIIa BC survivors, mean age=56	The Health, Eating, Activity and Lifestyle (HEAL) study	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight/height and body composition	Baseline (6 months post-diagnosis) to 2 years post-diagnosis	Mean weight increased 1.7 kg and % body fat increased 2.1%	Higher tumor stage, younger age, being postmenopausal, and decrease in physical activity were associated with weight gain
Jammallo 2013 ¹²⁸	USA	787 BC survivors, mean age=56	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Clinically measured weight/height and body composition	Reoperation to 4 months post operation	Mean weight increased 3.1 lb (0.3%)	Not assessed
Jeon 2014 ⁶²	Korea	108 stage I-II BC survivors, mean age=50	Hospital	Chemotherapy and/or hormonal therapy	Retrospective chart review	Time of diagnosis to completion of chemotherapy, and to 12 and 24 months after diagnosis	Mean weight increased 3.6 kg after chemotherapy	Not assessed
Jernström 1999 ⁸⁷	USA	45 BC survivors and 393 cancer-free women, mean age=53	Rancho Bernado Study	Unclear	Clinically measured weight/height	From 1972-1974 to 1992-1994	Mean weight increased 4.4 kg in BC survivors and 1.35 kg in cancer-free women	Not assessed
Kogawa 2015 ¹¹²	USA	1,002 stage III BC survivors	Hospital	None	Clinically measure weight/height	At diagnosis before chemotherapy to the end of neoadjuvant systematic treatment (mean=19.6 months)	48% women gained weight and 52% lost weight	Lower baseline weight was associated with greater weight gain
Koo 2016 ¹²⁹	Korea	822 stage 0-IIIa BC survivors who survived >5 years, mean age=49	Hospital	Chemotherapy and/or radiotherapy and/or hormonal therapy	Retrospective chart review for baseline weight/height, and clinically measured weight/height at follow-up	Average of 8 years from baseline	Mean weight increased 0.32 kg; 21% gained >5% weight, with an mean weight gain of 5.55 kg	Lower baseline weight, younger age, and not using hormonal therapy were associated with greater weight gain

Author Year	Country	Sample characteristics	Recruitment source	Adjuvant treatment	Measurement of weight	Length of follow up	Change in weight	Predictors of change
Kroenke 2005 ⁸⁸	USA	5,204 women with invasive BC	Nurses' Health Study	Unclear	Self-reported weight/height	Before diagnosis to ≥ 12 months after diagnosis	32% women gained 0.5-2kg/m ² of BMI, and 14% gained ≥ 2 kg/m ²	Not assessed
Kumar 1997 ⁹⁷	USA	200 stage I-II BC survivors, aged 25-85 years	Hospital	Hormonal therapy and/or radiation	Clinically measured weight	From diagnosis to 3-5 years after diagnosis	Mean weight increased 1.2 kg	Age at diagnosis was positively associated with weight gain. Tamoxifen was not associated with weight gain
Lankester 2002 ¹³⁰	USA	100 stage I-II BC survivors, mean age=50	Hospital	Hormonal therapy and/or chemotherapy	Clinically measured weight	From start of chemotherapy to the end of last cycle	Mean weight increased 3.68 kg; 64% gained >2 kg, and 27% gained >5 kg	Tamoxifen was not associated with weight gain
Liu 2014 ⁹⁹	Taiwan	147 stage I-III BC survivors, mean age=47	Hospital	Hormonal therapy and/or chemotherapy	Clinically measured weight	From pre-surgery to 24 months, with monthly follow-up	Weight change followed cubic form: weight increased 2.5 kg at 8.5 months after the first chemotherapy, and reduced at 21.5 months	Weight gain was higher in women receiving cyclophosphamide, methotrexate and fluorouracil compared to those receiving anthracycline
Makari-Judson 2007 ⁶³	USA	185 stage I-IIIB BC survivors, mean age=51	Hospital	Hormonal therapy and/or chemotherapy	Retrospective chart review	Time of diagnosis to 1, 2, and 3 years post-diagnosis	Mean weight increased 1.5 kg, 2.7 kg, and 2.8 kg at 1, 2, and 3 years after diagnosis	Younger age, lower baseline weight, and adjuvant chemotherapy were associated with more weight gain
Nichols 2009 ⁸⁹	USA	3,993 BC survivors, mean age=58	Collaborative Women's Longevity Study (CWLS)	Unclear	Self-reported weight	1-2 years after diagnosis to 6 years-post diagnosis	56% women increased weight	Not assessed

CHAPTER 3: IDENTIFYING DISTINCT HEALTH BEHAVIOR TRAJECTORIES AFTER A BREAST CANCER DIAGNOSIS

3.1 ABSTRACT

Background: There is a growing interest in understanding the effect of lifestyle behaviors following a breast cancer (BC) diagnosis on BC clinical outcomes. Previous studies that examined the change in health behaviors after a BC diagnosis reported mixed results in patterns of change. This study aimed to identify distinct trajectories of change in diet, physical activity and alcohol intake following a BC diagnosis.

Methods: Data on diet [fruit/vegetable (F/V) and dietary fat intake], physical activity [moderate to vigorous physical activity (MVPA) and sedentary behavior], and alcohol intake were prospectively collected by the Pathways Study, a population-based cohort study of 4505 women newly diagnosed with a BC within the Kaiser Permanente Northern California network. The trajectory groups of health behaviors from baseline to 6 and 24 months follow-up were analyzed using a combination of a semi-parametric, group-based trajectory modeling and a non-parametric K-means for longitudinal data analysis. Predictors of behavior trajectories were tested using multinomial logistic regression.

Results: In the first 24 months following a BC diagnosis, this analysis identified three distinct trajectories of F/V intake (11% high increase-stable, 41% medium increase-stable, 48% low increase-stable), MVPA (7% high decrease-temporary, 35% medium decrease-temporary, 58% low stable) and alcohol intake (5% high decrease-stable, 16% medium decrease-temporary, and 79% low-stable), and four trajectories of dietary fat intake (14% high-stable, 35% medium high-stable, 35% medium low-stable, 17% low-stable) and sedentary behaviors (18% high-stable, 24% medium increase-stable, 27% medium decrease-stable, 31% low stable). Compared to the low increase-stable F/V group, women who were in the high or medium increase-stable F/V group had higher education and income, higher dispositional optimism and perceived social support. Compared to the low-stable group, women who were in the medium high-stable dietary fat group were more likely to experience chemotherapy-induced peripheral neuropathy at 6 months after a BC diagnosis. For MVPA, women who followed the high or medium decrease-temporary trajectory had higher education and income, higher dispositional optimism and perceived social support. Women who were in the high-stable and medium decrease-stable groups of sedentary behavior had

higher education, lower income, and reported higher perceived social support. Finally, women who follow the high or medium decrease-temporary trajectory of alcohol intake had higher education and income.

Conclusion: Overall, participants in the Pathways Study maintained their lifestyle behaviors during the first 24 months after a BC diagnosis. Socioeconomic status, dispositional optimism, perceived social support, and the severity of CIPN during active treatment may predict the post-diagnosis trajectories of health behavior.

3.2 INTRODUCTION

The overall prognosis of early stage breast cancer (BC) is good, with nearly 90% of BC survivors living beyond five years after diagnosis.^{41,43,44} The reduction in BC mortality is primarily due to advancement in cancer screening and treatment. Population screening with mammography has led to the early detection of breast cancer and reduced BC mortality by approximately 15-20%.¹⁷⁴ Chemotherapy combined with hormonal therapy may reduce the BC mortality by an additional 45%-57%.¹⁷⁵ However, for long-term BC survivors, data from the US Surveillance, Epidemiology and End Results (SEER) program and the national Swedish Cancer Database have shown that 54-70% of deaths are due to non-cancer chronic conditions, such as cardiovascular diseases, diseases of pulmonary circulation and gastrointestinal disease.¹⁷⁶⁻¹⁷⁸

Recommendations for healthy lifestyles have been made for cancer survivors to further reduce mortality due to a second cancer and non-cancer conditions among BC survivors, such as meeting certain thresholds for physical activity and dietary intake.^{37,48} These health behaviors may offer promising survival benefits for cancer survivors. For example, an observational study (n=1,490) reported that consuming 5 servings of fruit and vegetables and walking 30 minutes a day after diagnosis reduced 50% of BC mortality.¹⁷⁹ The After Breast Cancer Pooling Project, a consortium of four cohorts of 13,302 breast cancer survivors from the United States and China, suggested that engagement in at least 150 minutes of moderate to vigorous physical activities (MVPA) may reduce the all-cause mortality by 27%.¹⁸⁰ However, large population-based surveys in the US have shown that the majority of BC survivors are not meeting lifestyle behavior recommendations.^{50,51} It is unclear how women change their lifestyle in response to a BC diagnosis, and how these changes may affect overall survival.

To date, only a limited number of observational studies have examined spontaneous changes in health behaviors following a BC diagnosis. These studies suggest that women may reduce alcohol intake and reduce time spent on MVPA after a BC diagnosis.^{10,12,14,52 53} However, what aspects of diet, particularly fruit/vegetable (F/V) and dietary fat, and other health behaviors are most affected by a cancer diagnosis remain inconclusive. Furthermore, very few studies examined predictors of behavior change after a BC diagnosis. In order to improve interventions to promote adherence to lifestyle guidelines, it is important to understand the drivers of behavior change. Ultimately, understanding these drivers of

behavior change will enhance the effectiveness of targeted interventions. Previous studies have reported inconsistent associations between pre-diagnosis characteristics, such as demographic and clinical factors, and lifestyles changes after a BC diagnosis.^{60,63,93,96,97,114} Some studies have shown that receipt of chemotherapy is most consistently associated with a decrease in MVPA.^{82,110} Additionally, the decrease in MVPA is more commonly seen among women who experience treatment complications.⁸¹

There are important methodological limitations with prior studies of post-diagnosis behavior change. Previous studies of post-diagnosis change in health behavior often examined the mean change in health behaviors within the study population and therefore ignored the possibility that BC survivors follow a mixture of behavior change trajectories. The existence of latent behavior change trajectories, where individuals are captured by trajectories that are unobserved (latent), has rarely been evaluated in BC survivors. To my knowledge, only one study has examined the latent trajectory of changes in MVPA over the first year after a BC diagnosis, and identified five distinct trajectories of change in MVPA.¹¹⁹ However, the study is limited by its small sample size (n=199) and a short period of follow-up (12 months post-diagnosis). To my knowledge, no prior study has assessed the trajectory of changes in MVPA beyond the first year of BC diagnosis, or changes in other health behaviors, including diet, sedentary behavior, and alcohol intake.

This analysis fills in these research gaps by identifying distinct trajectories of changes in diet (F/V and dietary fat intake), physical activity (MVPA and sedentary behavior), and alcohol intake among BC survivors over the first 24 months after diagnosis. Based on previously reported behavior change patterns, I hypothesized that women will follow one of six trajectories after a BC diagnosis, including 1) maintain a healthy lifestyle, 2) make a persistently positive change, 3) make a temporarily positive change, 4) make a persistently negative change, 5) make a temporarily negative change, and 6) maintain an unhealthy lifestyle.. Given that lower socioeconomic status is frequently associated with unhealthy lifestyle behaviors in the general population,¹⁸¹⁻¹⁸⁵ and that higher stress and cancer treatment-related side effects may disrupt normal health behaviors in cancer survivors,^{35,145,150,151} I also evaluated the associations between behavior change trajectories with socioeconomic status (SES), psychosocial factors related to stress and coping, and cancer treatment side effect using multinomial logistic

regression, after controlling for baseline behavior level and demographic and clinical characteristics. Ultimately, the analysis will identify subgroups of women who may be good targets for behavior interventions following a breast cancer diagnosis.

3.3 METHODS

3.3.1 Study participants

The study used data from the Pathways Study,³⁶ a population-based prospective cohort of women newly diagnosed with invasive breast cancer within the Kaiser Permanente Northern California (KPNC) network from January 2006 to April 2013. Women who were at least 21 years of age at diagnosis and a current KP member, had a recent diagnosis of invasive breast cancer, had no previous history of malignant cancer, spoke English, Spanish, Cantonese, or Mandarin, and lived within a 65-mile radius of a field interviewer were eligible for recruitment. The Pathways Study recruited women using rapid case ascertainment methods. Most participants were recruited within two months (mean time = 1.8 months, range = 0.3-7.2 months) post-diagnosis. Baseline demographic and lifestyle information were collected during an in-person interview. During the follow-up, lifestyle data were collected at 6 and 24 months via mailed questionnaires, and breast cancer outcomes were identified via telephone interviews every 12 months after baseline and confirmed using KPNC electronic databases. The study protocol was approved by the institutional review board of all collaborating institutions [Kaiser Permanente Division of Research (Oakland, CA); Kaiser Permanente of Northern California; University of California at San Francisco; Georgetown University (Washington, DC); Roswell Park Cancer Institute (Buffalo, NY); the Cancer Prevention Institute of California (Fremont, CA); and Zero Breast Cancer (San Rafael, CA)]. Written informed consent was obtained from all participating subjects.

A total of 11,233 potentially eligible women were invited to participate in the study, and 4,505 enrolled. As of August 16, 2016, 416 recurrences and 549 deaths have been confirmed, with 898 experiencing either recurrence and/or death. Among the 3,579 active participants, 2,712 participants completed their 24 months behavior data collection as of August 2016, while the 72 month data collection is ongoing and is expected to finish in May 2019.

3.3.2 Baseline and follow-up data collection

Interviewers administered detailed questionnaires on diet, exercise, and psychosocial and quality-of-life measures during the baseline interview. Clinical and tumor characteristics were obtained from the KPNC Cancer Registry approximately four months post-diagnosis. At 6 and 24 months, follow-up questionnaires, phone interview, and web surveys were used to update the lifestyle information, with interviewer assistance offered if needed.

3.3.3 Measurement of health behaviors

Physical activity

Baseline physical activity data were collected using the Arizona Activity Frequency Questionnaire,¹⁸⁶ which assesses frequency and duration of daily household, recreational, transportation, and sedentary behaviors. The questionnaire is divided into four main sections: job or work-related activities, activities not related to paid or volunteer work, recreational activities, and transportation. The activities not related to paid or volunteer work are further subdivided into household chores (6 items), caregiving (5 items), and home maintenance and repairs (7 items). Recreational activities are sub-divided into sports, exercise, and dance (23 items) and sedentary recreational activities, such as reading or socializing (6 items). Four items are included under transportation. Respondents reported the frequency, duration, and intensity of each activity they engaged in at least once a month during the previous six months. Next, each activity is assigned a standard metabolic equivalent value (MET).¹⁸⁷ One MET is defined as the energy it takes to sit quietly. For the average adult, one MET is approximately one calorie per every 2.2 pounds of body weight per hour; an individual who weighs 160 pounds burns approximately 70 calories an hour while sitting or sleeping.

This analysis used data on time spent engaged in moderate-to-vigorous physical activities (MVPA) and sedentary behaviors. Moderate physical activity refers to activities equivalent in intensity to brisk walking or bicycling (3-6 METs). Vigorous physical activity produces large increases in breathing or heart rate, such as jogging, aerobic dance or bicycling uphill (>6 METs). Therefore, MVPA was defined as time spent on activities of ≥ 3 METs. Sedentary behaviors included sitting during commuting, in the

workplace, in the domestic environment, and during leisure time. Typical sedentary behaviors include TV viewing, computer use, or sitting in an automobile (1-1.5 METs).

Diet

Dietary history was collected using a 139-item modified version of the Block 2005 food frequency questionnaire (FFQ) (NutritionQuest, Berkeley, CA).¹⁸⁸⁻¹⁹⁰ The FFQ included food items selected by identifying the top population contributors of each nutrient among Whites, African Americans and Hispanics in the National Health and Nutrition Examination Survey (1999–2002). The 139 food items and additional questions were selected to be representative of a wide range of dietary factors, as well as to capture foods that are popular in Hispanic and Asian populations. Completed questionnaires were sent to NutritionQuest for scanning using a nutrient database developed primarily from the USDA Food and Nutrient Database for Dietary Studies.¹⁹¹ Nutrient intakes were then calculated via computerized software programs that multiply the reported frequency of each food by the amount of nutrient in a serving of that food according to the USA nutrition database. Total nutrient intakes were then calculated by summing all foods containing that nutrient.

The primary dietary variables include daily intakes of fruit/vegetable (F/V), percent of energy from dietary fat, dietary fibers, meat, total calories, and alcohol. The FFQ assessed a number of vegetable groups, including daily intake of dark-green vegetables, deep-yellow vegetables, tomatoes, white potatoes, fried potatoes, legumes, other starchy vegetables, avocado and similar, and other vegetables (in cups). Fruit groups included citrus fruit and fruit excluding citrus fruit (in cups). Dietary fat intakes included daily intake of total fat, saturated fat, monounsaturated fatty acids, polyunsaturated fatty acids, and trans-fats (in grams). The percent energy from fat was used as the analytical variable for trajectory analysis, which was calculated as:

$$100\% \times (\text{Dietary fat intake (grams)} \times 9) / \text{Total energy intake (kcal)}$$

Daily alcohol intake was measured by the FFQ and converted into daily ethanol intake (in grams).

3.3.4 Key variables

Sociodemographic characteristics

Baseline and follow-up questionnaires assessed sociodemographic characteristics, including age at diagnosis (<50 years, 50-59 years, and 60+ years), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and Asian), education (high school or less, some college, and college and above), and household income (<\$50,000.00, \$50,000-\$89,999, and >\$90,000.00 per year).

Clinical characteristics

Breast cancer and other clinical characteristics were obtained from the KPNC cancer registry and the EHR, including family history of breast cancer (yes, no), menopausal status (pre- and post-menopause), American Joint Committee on Cancer (AJCC) stage (I-IV)¹⁹², number of positive lymph nodes (0, 1, and 2+), tumor estrogen/progesterone receptor (ER/PR) positivity (positive, negative), human epidermal growth factor receptor 2 (HER2) positivity (positive, negative), breast cancer surgery type, and adjuvant treatment received (chemotherapy, hormonal therapy, radiation therapy).¹⁹³

Psychosocial measures

Depression. Depression during the past seven days was measured by the Center for Epidemiological Studies Depression Scale (CES-D).¹⁹⁴ The CES-D is a 20-item measure that asks caregivers to rate how often over the past week they experienced symptoms associated with depression, such as restless sleep, poor appetite, and feeling lonely. Response options range from 0 to 3 for each item (0 = rarely or none of the time, 1 = some or little of the time, 2 = moderately or much of the time, 3 = most or almost all the time). Scores range from 0 to 60, with high scores indicating greater depressive symptoms. A CES-D score of 16 or greater is considered at risk for clinical depression.

Dispositional optimism. Dispositional optimism was measured by the 12-question Life Orientation Test (LOT) scale.¹⁹⁵ Of the 12 LOT scale items, 4 items measure optimism, 4 items measure pessimism, and 4 items serve as fillers. Respondents rate each item on a 4-point scale (0 = strongly disagree, 1 = disagree, 2 = neutral, 3 = agree, and 4 = strongly agree). Scores range from 0 to 32, with high scores indicating greater optimism. A score of 24 or higher suggests optimism.

Social support. Perceived social support was measured using the Medical Outcome Study (MOS) Social Support Survey Instrument.¹⁹⁶ The 19-item MOS social support survey consists of four separate social support subscales (emotional/informational support, tangible support, positive social interaction,

and affection) and an overall functional social support index. Each of the 19 items is rated on a five-point scale ranging from “none of the time” to “all of the time”, with a high subscale and/or overall score indicating a high level of perceived social support. The overall support index ranges from 19 to 95. An MOS social support score of 57 or less has been considered as lack of support.

Cancer treatment side effects

Physical well-being (PWB). The Functional Assessment of Cancer Therapy-General (FACT-G) assessed PWB using a 7-item subscale at baseline and 6 months.¹⁹⁷ This subscale asks participants to rate themselves for symptoms related to breast cancer treatment side effect in the past 7 days, such as lack of energy, nausea, and pain. For each item, self-reported symptoms were assessed on a 0-4 scale (0, very much; 1, quite a bit; 2, somewhat; 3, a little bit; 4, not at all). The total FACT-G PWB score sums responses for each item (range 0-28), with lower scores indicating worse PWB. In these analyses, a ≥ 3 decrease in the FACT-G PWB score from baseline to 6 months will be considered a clinically meaningful decrease in PWB.¹⁹⁷

Chemotherapy-induced peripheral neuropathy (CIPN). CIPN was assessed at baseline and 6 months using the Functional Assessment of Cancer Therapy-Taxane Neurotoxicity (FACT-NTX).¹⁹⁸ For each item, self-reported symptoms were assessed in the prior 7 days using a 0-4 scale (0, very much; 1, quite a bit; 2, somewhat; 3, a little bit; 4, not at all). The total FACT-NTX score sums responses for each item (range 0-44), with lower scores indicating worse neuropathy. In previous studies, a $\geq 10\%$ decrease in the FACT-NTX score was considered a clinically meaningful increase in CIPN.^{199,200}

3.3.5 Statistical analysis

The primary goal of this study was to identify latent groups of health behavior trajectories (diet, physical activity, alcohol intake) after a breast cancer diagnosis and to identify predictors of these specific trajectories. To identify trajectory groups, the study used semi-parametric, group-based trajectory modeling (GBTM) procedures as proposed by Nagin³⁹ to identify latent classes of trajectories and estimate the parameters of trajectories. GBTM uses a single outcome variable measured at multiple time points to define a latent class model in which the latent classes correspond to different growth curve shapes for the outcome variable. Traditional growth models, such as growth curve models (GCM),²⁰¹⁻²⁰⁵

generally assume a uniform trajectory underlying a group of people. In contrast, GBTM assumes that the population is composed of a mixture of distinct groups defined by their shapes of developmental trajectory. As such, this method will estimate the shape parameters and the probability of group membership, which allows further examination of the predictors of group membership. To evaluate the influence of loss to follow-up on the identification of trajectory groups, a sensitivity analysis was performed by applying the inverse probability weight (IPW)²⁰⁶ at 24 months to GBTM. In addition, a validation analysis was conducted to identify behavior change trajectory groups using a fully non-parametric method, K-means for longitudinal data (KmL).⁴⁰ Using the best trajectory group membership derived from the three models, this analysis further evaluated the predictors of each behavior change trajectory using the multinomial logistic regression. To evaluate the impact of missing data in both predictors and behavior change trajectories, a sensitivity analysis was conducted to fill in the missing data using multiple imputations,²⁰⁷ and then evaluate the deviations between associations that are observed under the complete-case analysis and those under the multiple imputations. The analytical workflow is summarized in Figure 2 and 3, and described in detail below.

Main GBTM analysis. In this study, GBTM was used as the primary method to identify the optimal number of behavior change trajectories. The outcome variables were F/V intake, percent of energy from dietary fat, time spent on MVPA and sedentary behaviors, and alcohol intake from baseline to 6 and 24 months follow-up. For each behavior change outcome, assuming the outcome variable followed a normal distribution, a single-group model saturated with quadratic parameters was tested initially, and then one additional group was included in each successive model. The study hypothesized that six distinct trajectories would be identified, and therefore tested models composed of one to six trajectory groups to find the optimal number of trajectories. Model fit was assessed based on the Bayesian Information Criterion (BIC), whereby the model with the lower BIC was favored as lower BIC indicates better model fit. Once the number of groups was determined, participants were assigned to the trajectory group that best corresponded to their observed behavior according to the maximum posterior probability of group membership. The final model was selected based on parsimony, interpretability and prior knowledge of common behavior patterns in BC survivors.^{208 209} In analyzing F/V trajectories, total calories were used as a time-varying covariate in the trajectory analysis. Because the 2010 trans-fat ban in California (Assembly

Bill No. 97) may influence the dietary fat intake trajectory for participants who were followed before and after the passage of this bill, sensitivity analyses of dietary fat change trajectories were additionally adjusted for a time varying covariate indicating whether the trans-fat ban was passed at each follow-up.

Weighted GBTM analysis. More than 30% of women were lost to follow-up at 6 months and 40% were lost to follow-up at 24 months in the Pathways Study. To evaluate the influence of loss to follow-up on the identification of trajectory groups, a sensitivity analysis was performed by applying the inverse probability weight (IPW)²⁰⁶ at 24 months to GBTM. The IPW has been shown to be more effective in correcting for selection bias than adjustment for variables that predict loss to follow-up.²¹⁰ To calculate the IPW, the probability of loss to follow-up at the 24-month wave was estimated in a logistic regression with baseline demographic and clinical characteristics as independent variables. Women who missed the 6 month follow-up but completed the 24 month follow-up were not considered as lost to follow-up at 24 months. Baseline demographic characteristics (age, race, education, and household income), tumor characteristics (tumor stage, size, grade, hormonal receptor status, and number of positive nodes), and treatment received (surgery, chemotherapy, hormonal therapy, and radiation) that were empirically associated with loss to follow-up at 24 months were included to impute the IPW. The IPW was calculated as the reciprocal of the probability of remaining in follow-up at 24 months.

Validation analysis. To verify the efficiency and success of GBTM, the study performed a validation analysis to identify behavior change trajectory groups using a fully non-parametric method, K-means for longitudinal data (KmL).⁴⁰ The KmL is a robust classification algorithm based on the Expectation-Maximization (EM) method.²¹¹ The KmL starts by assigning each observation to a random cluster, then uses the EM algorithm to alternate between 1) computing the center of each cluster (the *Expectation* phase), and 2) assigning each observation to its nearest cluster based on its distance to the cluster center (the *Maximization* phase). The EM algorithm repeats these two phases till cluster assignments become stable. By definition, KmL is not a model-based approach, and therefore is less restricted by the normality assumption required for GBTM. However, because there are no absolute criteria for an optimal number of clusters in KmL, the optimal number of cluster identified through GBTM will be used to verify if KmL produces similar trajectory groups. As a non-parametric approach, the KmL

does not allow adjustment of total energy as a time-varying covariate. Thus the KmL was not considered as an alternative to the GBTM when analyzing F/V trajectories.

Selection of final trajectory groups. For each health behavior (F/V, % energy from fat, MVPA, sedentary behavior, and alcohol intake), the best trajectory group membership was identified through a series of pairwise comparisons among the above trajectory analyses. First, when the main GBTM and the IPW-weighted sensitivity analysis generated identical categories of trajectory groups, agreement between the two sets of group membership was measured using the Cohen's kappa, ²¹² which is a common measure of agreement between two classifications of category a finite number of subjects belong to while accounting for agreement due to chance. A Cohen's kappa >0.8 indicates good agreement between the two sets of group membership. If the two trajectory groups were of good agreement, the unweighted GBTM result was retained. On the other hand, if the two trajectory groups identified different trajectory groups or were of poor agreement (Cohen's kappa ≤ 0.8), results from the IPW-weighted GBTM were favored. In the second step, the optimal group memberships derived from GBTM were then compared with that identified via KmL using Cohen's kappa. If the two trajectory analyses produced concordant group memberships (Cohen's kappa >0.8), results from the GBTM were retained; otherwise, results from the KmL were considered a better fit. The model selection process is shown in Figure 4.

Analysis of predictors of behavior change trajectory. To investigate the predictors of behavior change trajectories, Chi-squared tests and logistic regression were used to examine if baseline socioeconomic, cancer treatment side effect and psychosocial variables were associated with behavior change trajectory group membership. Baseline demographic (age, race, menopausal status) and clinical factors (tumor stage, number of positive nodes, HER2 status, ER/PR status, receipt of surgery, chemotherapy, hormonal therapy, and radiation) associated with 1) socioeconomic status, psychosocial factors, and treatment side effects and 2) behavior change trajectories, and modified any beta coefficients for the association of predictors and behavior change trajectory by $\geq 10\%$ were considered as potential confounders. Confounders were entered simultaneously into a multivariable multinomial logistic regression model with all predictors to assess their associations with the behavior change trajectory group membership. An omnibus test of the associations between predictors and outcomes were also performed using the likelihood ratio test.

Handling of missing data. Missing data in health behavior variables and covariates were addressed in multiple steps throughout the analyses. In the trajectory identification stage, participants who completed at least two assessments of health behavior were included in the GBTM and KmL analyses. GBTM used Full Information Maximum Likelihood (FIML) method to fill in missing behavior data under the assumption that data were missing at random. The KmL analysis used an innovative imputation method known as “copy mean”, which estimated the intermittent missing value of longitudinal data by treating the last observed value before each missing data as a starting value, and refined the imputation by finding the value that gives the imputed trajectory the same shape as the population mean trajectory.²¹³ The “copy mean” method has been shown to be robust under various missing data mechanisms and is considered superior to traditional imputation methods.²¹³ In analyses of the association of hypothesized predictors with behavior change trajectory, only participants with complete covariate data and known group membership were included in the main analysis. However, I performed a sensitivity analysis to examine how missing data influenced the observed association by filling missing covariate and outcome data using multiple imputations.²⁰⁷ Logistic regression based on ten imputed datasets were then pooled to estimate the beta coefficients and 95% confidence interval using Rubin’s methods.²⁰⁷ Briefly, beta coefficients estimated in each of the ten data sets were averaged to calculate the pooled beta coefficient; the pooled confidence interval was estimated as a function of variance within each imputed dataset and between-imputation variance.

The GBTM was performed using the PROC TRAJ command in SAS.²¹⁴ The KmL was implemented in R using the “kml” package.²¹⁵ Multiple imputations of missing data in baseline characteristics and trajectory group membership was conducted using the R “mi” package.²¹⁶

3.4 RESULTS

3.4.1 Participant characteristics

Demographic, clinical and psychosocial characteristics of the 4,505 Pathways Study participants are summarized in Table 6. On average, participants were diagnosed with BC at the age of 59 years [standard deviation (SD) =12] and were enrolled within two months post-diagnosis (SD=0.8 months). At

baseline, the majority of participants were white (64%), had completed at least some college education (35% some college, 49% college or above), earned more than \$50,000 a year (67%), and were postmenopausal (70%). Most women were diagnosed with stage I-III breast cancer (54% stage I, 35% stage II, and 10% stage III), negative for human epidermal growth factor receptor 2 (HER2) (86%) and positive for estrogen receptor (ER) and/or progesterone receptor (PR) (83%). Almost all women underwent surgery, with 54% receiving a mastectomy and 45% receiving a lumpectomy. Approximately 48% women were treated with chemotherapy, 75% with hormonal therapy, and 44% with radiation. Approximately 26% of women reported high depressive symptoms and only 31% felt optimistic at baseline, although the majority (67%) reported high perceived social support.

A total of 2,874 (63.7%) participants responded to 6-month follow-up questionnaires, and 2,666 (59.1%) responded to the 24-month follow-up (Table 6). Compared to the full cohort at baseline, participants who remained in the follow-up at 6 and 24 months were older, more likely to be white, received higher education, postmenopausal, diagnosed with early stage, ER/PR positive tumor, received chemotherapy and radiation therapy, and had low depressive symptom at baseline. By six months, 23% of participants reported clinically worse physical well-being, and 34% reported clinically meaningful chemotherapy-induced peripheral neuropathy. Among factors associated with loss to follow-up, multivariable logistic regression analysis identified younger age, non-white race, lower education, higher income, higher tumor stage, receipt of breast surgery and chemotherapy at baseline as significant indicators of loss to follow-up, which were used to estimate the inverse probability weight for remaining in follow-up (data not shown).

3.4.2 Identification of behavior change trajectory groups

The GBTM tested models with one to six trajectories to find the best fit for each health behavior. The distribution of F/V, % energy from fat, MVPA, and sedentary time at each assessment approximated a normal distribution, while the distribution of alcohol intake was slightly skewed to the left. The trajectory groups and their distributions are summarized in Table 7. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable). A total of 2,791 women who completed at least two out of

three dietary assessments from baseline to 6 and 24 months follow-up were included to identify F/V, dietary fat, and alcohol intake trajectory groups; 2,995 women who completed at least two out of three physical activity questionnaires were included to identify trajectory groups of MVPA and sedentary behavior. For each health behavior, the optimal model was identified if the model 1) had the lowest BIC value (sedentary behavior), or 2) yielded trajectory groups that were parsimonious and had adequate group size (F/V intake, dietary fat intake, MVPA, and alcohol intake). A three-group model was considered optimal for F/V intake, MVPA, and alcohol intake, while a four-group model was considered optimal for dietary fat intake and sedentary behavior.

The group memberships derived from the main GBTM analysis were then compared against those identified through GBTM analysis with IPW and the validation analysis using KmL to determine the final group assignment. Trajectory groups from the three sets of analyses, as well as the final model choices, are shown in Table 8. The unweighted and IPW-weighted GBTM identified highly concordant trajectory groups (Cohen's kappa ranged from 0.96-0.99). Therefore, trajectory derived from unweighted GBTM was not likely affected by loss to follow-up, and therefore was retained. Using the number of trajectory groups identified through GBTM, the KmL analysis identified trajectory groups with similar shape as those derived from GBTM. The KmL-based trajectory groups were preferred if 1) they had different groups than the GBTM-based trajectories (sedentary behavior), or 2) the KmL- and GBTM-based trajectories identified the same groups but the two sets of group membership were discordant, as evidenced by a Cohen's kappa < 0.8 (dietary fat intake and MVPA). Because the KmL analysis of F/V was unable to adjust for energy intake as a time-varying covariate, the F/V trajectory groups identified via unweighted GBTM was retained.

Figure 4 illustrates the individual behavior trajectories color-coded by the trajectory groups (Figure 4 Column A), and the mean trajectories for each group (Figure 4 Column B). Visual assessment of the final group assignments suggested that the final models successfully isolated groups with apparently distinct behavior trajectories. Examination of change in each subcategory of F/V, dietary fat, MVPA and sedentary behaviors suggested that the F/V trajectories were largely driven by the intake of fruits, dark green vegetables, and non-legume vegetables (Appendix 12A); the dietary fat trajectories were driven by intake of monosaturated fatty acids, poly unsaturated fatty acids, and saturated fat

(Appendix 12B). The change in overall MVPA during the 24 months after a BC diagnosis was largely determined by changes in household chores and recreational activities (Appendix 13A); change in sedentary behavior was primarily due to changes in driving, reading, socializing and watching TV (Appendix 13B).

3.4.3 Mean health behavior by behavior trajectory groups

Mean baseline behavior levels and mean behavior changes were summarized for each behavior trajectory group (Table 9). Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable). Across behaviors, baseline behavior level differed significantly by trajectory group (all P for ANOVA <0.001, not shown in Table 9). Groups that were characterized by a stable trend over time generally had a small change at 6 and 24 months, although there were statistically significant but small changes in the medium high-stable and medium low-stable groups of dietary fat intake, and the low-stable MVPA group at 6 and 24 months. For groups that were classified as a temporary decrease, the mean change in health behaviors were statistically significantly different from zero at 6 months but reverted back to baseline values at 24 months, although some groups continued to report a statistically significant change at 24 months (e.g. the medium decrease-temporary MVPA group and alcohol). The groups with stable increase or decrease reported statistically significant change at both 6 and 24 months. The specific changes in each behavior trajectory are summarized below.

F/V: For F/V intake, the mean baseline F/V intake was 9.17 servings/day for the high increase-stable group (11% of women), 6.16 servings/day for the medium increase-stable group (41%), and 3.31 servings/day for the low increase-stable group (48%). The marginal change in F/V after adjusting for total energy intake suggested that there were statistically significant increases in all three groups at 6 and 24 months. However, the increases in F/V intake were relatively small; for example, the high increase-stable group reported a mean increase of 0.54 servings/day of F/V at 6 months, and an increase of 0.39 servings/day at 24 months.

Dietary fat: For dietary fat intake, the baseline mean percent energy from dietary fat was 46.5% for the high-stable group (14% of women), 40.2% for the medium high-stable group (35%), 34.1% for the

low increase-stable group (35%), and 28.4% for the low-stable group (17%). Although the dietary fat level remained largely unchanged for these groups, the medium high-stable group reported a decrease of 0.83% energy from fat at 6 months ($P<0.001$), while the medium low-stable group reported an increase of 0.67% energy from fat at 6 months ($P<0.01$) and 0.72% at 24 months ($P=0.01$).

MVPA: At baseline, the mean time spent on MVPA was 18.09 hours/week for the high decrease-temporary group (7% of women), 9.05 hours/week for the medium decrease-temporary group (35%), and 2.73 hours/week for the low -stable group (48%). Most women temporarily decreased engagement in MVPA at 6 months. The high decrease-temporary group reported a decrease of 3.03 hours/week of MVPA at 6 months ($P<0.001$); the medium decrease-temporary group decreased 2.37 hours/week of MVPA at 6 months ($P<0.001$) and decreased 0.74 hours/week at 24 months ($P<0.001$). The low-stable group also reported a slight decrease of 0.49 hours/week MVPA at 6 months ($P<0.001$).

Sedentary behavior: At baseline, the mean time spent on sedentary behavior was 27.94 hours/week for the high-stable group (18% of women), 15.41 hours/week for the medium increase-stable group (24%), 22.55 hours/week for the medium decrease-stable group (27%), and 11.29 hours/week for the low-stable group (31%). The medium increase-stable group spent 4.66 more hours/week on sedentary behaviors at 6 months and 4.64 hours/week more at 24 months (both $P<0.001$). The medium decrease-stable group decreased 6.85 hours/week of sedentary behaviors at 6 months and decreased 5.31 hours/week at the 24 months (both $P<0.001$). Moreover, the high-stable and low-stable groups also decreased a small but statistically significant amount of time spent on sedentary behavior.

Alcohol: The mean baseline alcohol intake as measured by ethanol was 41.43 grams/day for the high decrease-temporary group (5% of women), 18.81 grams/day for the medium decrease-temporary group (16% of women), and 1.95 grams/day for the low-stable group (79% of women). The high decrease-temporary group decreased ethanol intake by 6.85 grams/day at 6 months ($P<0.001$), but the decrease was not statistically significant at 24 months. The medium decrease-temporary group decreased 4.88 grams/day of ethanol at 6 months ($P<0.001$) and 2.74 grams/day at 24 months ($P<0.001$). The low-stable group also reported a small but statistically significant decrease at 6 and 24 months.

3.4.4 Characteristics of behavior trajectory groups

Women who followed different trajectories of behavior change differed in a number of demographic and clinical characteristics (Appendix 3-7). Factors associated with specific behavior change trajectories in univariable analyses are described below.

Age: In univariable analyses, women diagnosed at older age were more likely to be in the high F/V intake, high sedentary behavior and high alcohol intake groups, but were less likely to be in the high MVPA group.

Race/ethnicity: Race/ethnicity was generally associated with trajectory of F/V, MVPA, sedentary behavior, and alcohol intake, with white women being more likely to be in the high F/V intake, high MVPA, high sedentary behavior, and high alcohol intake groups, compared to other race/ethnicity groups.

Education: Women with higher education were more likely to be in the high F/V, high MVPA, high sedentary behavior, and the low alcohol intake trajectory groups.

Income: Women with a household income of \$50,000 or above were more likely to be in the high F/V, high MVPA, high sedentary behavior, and the high alcohol intake trajectory groups.

Menopausal status: Postmenopausal women were less likely to be in the high MVPA trajectory group, but more likely to be in the high sedentary behavior and alcohol intake trajectory groups.

Tumor characteristics: Among tumor characteristics, higher tumor stage was associated with the low MVPA trajectory groups, and women who were positive for ER/PR were less likely to be in the low alcohol intake trajectory group.

Cancer treatment: Women who received mastectomy were more likely to be in the low F/V, low sedentary behavior, and the low alcohol trajectory groups compared to women who received lumpectomy. Women treated with chemotherapy were likely to be in the low F/V, high sedentary behavior, and low alcohol intake trajectory groups. Receipt of hormonal therapy was also associated with the low F/V trajectory group. Finally, women who received radiation were more likely to be in the high F/V, high sedentary behavior and high alcohol intake trajectory groups.

Psychosocial factors related to stress coping: Women who had higher depressive symptom at baseline were more likely in the low F/V trajectory group. Women who were more optimistic and reported receiving higher social support at baseline were more likely to be in the high F/V, high MVPA, high sedentary behavior, and high alcohol intake trajectory group. Women who reported experiencing worse CIPN at 6 months were more likely in the high dietary fat trajectory group.

3.4.5 Predictors of behavior change trajectory groups

Multinomial logistic regression analysis examined the associations of baseline behavior level, socioeconomic status, stress coping ability, and cancer treatment side effects with group membership of behavior change trajectories. The overall associations between behavior trajectory group membership and each predictor were tested first using the omnibus likelihood ratio test. Associations between each group of behavior trajectory and the predictors were tested using multinomial logistic regression analysis. Women who were in the lowest level of each health behavior were used as the referent level. Specifically, the analysis of F/V trajectory used the “low increase-stable” group as the referent group; analysis of dietary fat, MVPA, sedentary behavior, and alcohol intake used the “low-stable” group as the referent, as the “low increase-stable” group was not identified for these behaviors. The results of the regression analyses are summarized in Tables 10-12. The study screened and tested for confounding from demographic and clinical characteristics, and identified age at diagnosis, race/ethnicity, menopausal status, tumor stage, number of positive node removed, ER/PR positivity, and receipt of surgery, chemotherapy, hormonal therapy, and radiation as potential confounders. Therefore, an unadjusted model and a fully adjusted model with all confounders were fitted to examine the adjusted odds ratio of being in each of the behavior trajectory groups.

Socioeconomic status. Table 10 shows the results for association of education and household income with behavior trajectory groups. In fully adjusted analyses, women who completed college education or above had higher odds of being in the F/V high increase-stable trajectory group (OR=2.74, 95% CI: 1.64-4.57) and the medium increase-stable trajectory of F/V (OR=2.33, 95% CI: 1.67-3.26) compared to those with a high school degree or less. Higher education was also associated with higher odds of being in the MVPA high decrease-temporary trajectory group (some college vs. high school or

less: OR=3.48, 95% CI: 1.45-8.38; college or above vs. high school or less: OR=4.36, 95% CI: 1.83, 10.35) and the MVPA medium decrease-temporary trajectory group (some college vs. high school or less: OR=1.63, 95% CI: 1.16-2.30; college or above vs. high school or less: OR=2.04, 95% CI: 1.46-2.84). However, women with a college degree or above were also more likely to be in the high-stable sedentary behavior group (OR=1.63, 95% CI: 1.16-2.30) and the medium increase-stable alcohol intake group (OR=2.21, 95% CI: 1.35-3.60).

In fully adjusted analysis, compared to women with an annual household income of less than \$50,000, women with a household income of \$50,000-\$89,000 were more likely to be in the F/V medium increase-stable trajectory group (OR=1.36, 95% CI: 1.07-1.72) and the MVPA medium decrease-temporary trajectory group (OR=1.37, 95% CI: 1.09-1.71), and were less likely to be in the sedentary behavior high-stable trajectory group (OR=0.66, 95% CI: 0.48-0.91). However, women with a household income of \$50,000-\$89,000 were more likely to be in the high decrease-temporary group (OR=2.54, 95% CI: 1.49-4.34) and the high decrease-temporary alcohol intake group (OR=1.64, 95% CI: 1.21-2.21).

Stress coping. Table 11 shows the results for association of stress coping with behavior trajectory groups. In fully adjusted analyses, higher baseline dispositional optimism was associated with greater odds of being in the F/V high increase-stable (OR=1.83, 95% CI: 1.31-2.54) and the medium increase-stable trajectory groups (OR=1.50, 95% CI: 1.19-1.89), and greater odds of being in the MVPA high decrease-stable (OR=1.85, 95% CI: 1.25-2.75) and the medium decrease-stable trajectory group (OR=1.61, 95% CI: 1.29-2.00). The omnibus test showed that higher optimism was also associated with dietary fat intake trajectory groups ($P<0.01$, not shown in table), although there was no statistically significant association between optimism and individual groups of dietary fat trajectory. Women who reported receiving higher social support at baseline were more likely to be in the F/V high increase-stable (OR=1.82, 95% CI: 1.25-2.65) and the medium decrease-temporary trajectory group (OR=1.33, 95% CI: 1.06-1.67), but also more likely to be in the sedentary behavior high-stable (OR=1.86, 95% CI: 1.34-2.57) and medium decrease-stable (OR=1.42, 95% CI: 1.08-1.87) trajectory groups.

Cancer treatment side effect. Table 12 shows the results for association of cancer treatment side effects with behavior trajectory groups. Fully adjusted analyses suggested that the worsening of CIPN

was associated with higher odds of following the medium high-stable trajectory of dietary fat intake (OR=1.48, 95% CI: 1.06-2.06).

Tumor characteristics and cancer treatment received: Appendix 8 shows the associations between tumor characteristics and cancer treatment received and behavior trajectories. In fully adjusted analyses, higher number of positive lymph nodes removed was associated with higher odds of being in the F/V high increase-stable trajectory group. Women who received surgery were less likely to maintain a high level of alcohol intake; women who received chemotherapy were more likely to be in the high decrease-stable MVPA group; women who received hormonal therapy were more likely to be in the medium low-stable dietary fat group and the medium decrease-stable MVPA group.

3.4.6 Sensitivity analyses

Sensitivity analysis with multiple imputations

Appendix 14 shows the pattern of missing data in key analytical variables. Although the baseline demographic and clinical data were almost complete for all participants, a large number of data were missing for change in PWB (40%) and CIPN (56%). Missing data was more common for behavior data, with 17% baseline dietary data and 1% baseline physical activity data were missing. Because the trajectory analyses excluded participants with less than two non-missing data points, approximately 34%-38% participants were excluded from the trajectory analyses, thus their behavior change trajectory group memberships were missing. Using the multiple imputations (MI) method under the assumption that these data were missing at random, the study imputed ten separate datasets to fill in missing data in the key analytical variables and behavior trajectory group membership. Pooled results of fully adjusted multinomial logistic regression analyses from the ten imputed datasets were compared with results based on the complete case analysis (Figure 6). Briefly, the missing data have a minor influence on the observed associations of socioeconomic status, stress coping, and cancer treatment side effects with behavior trajectories. After MI, higher education was statistically significantly associated with the medium increase-stable trajectory of F/V intake (some college vs. high school or less: OR=1.59, 95% CI: 1.21-2.10). Under the MI analysis, women with a college degree or above were less likely to be in the high-

stable dietary fat group (OR= OR=0.57, 95% CI: 0.36-0.92), but women with some college education were more likely to be in the high-stable sedentary behavior group (OR= OR=1.55, 95% CI: 1.10-2.19).

Sensitivity analysis examining exact time since diagnosis as time scale

Because participants may enter into the study at different time points after diagnosis, I examined the distribution of time since diagnosis at each data collection point and used exact time since diagnosis as the underlying time scale to perform another trajectory analysis. The results suggested that women enter the study at the median time of 8 weeks (approximately 2 months) after diagnosis, while the 6 and 24 month data were collected, respectively, at the median time of 34 weeks (8.5 months) and 111 weeks (28 months) after diagnosis. Although the exact times of data collection closely matched the scheduled data collection time, there were great variations in time since diagnosis at each wave of data collection. Comparison among participants who enrolled within 2 months, between 2-3 months, and more than 3 months after diagnosis suggested that there were no differences in demographic and clinical factors among early and late enrollees (Appendix 9). However, later enrollment appeared to be associated with lower chemotherapy initiation and fewer cancer treatment-related side effects. Trajectory analyses based on exact time since diagnosis at each data collection point identified similar trajectory groups as those identified under approximate time (i.e., baseline as an approximate for time of diagnosis, 6-month follow-up as an approximate for 6 months post diagnosis, etc.; data not shown). These results suggest that the use of approximate time instead of exact time did not affect the trajectory analyses.

Sensitivity analysis examining the influence of extreme dietary data

My initial analysis used all available dietary data from the Pathways Study. However, the complete data set may include extreme dietary recall data, which were not removed by the Pathways Study or NutritionQuest during data collection and cleaning. To examine the influence of extreme dietary data on the identification of dietary trajectory groups, I performed a sensitivity analyses by excluding all extreme dietary data from women whose daily energy intake were greater than three standard deviations above the mean energy intake at each data collection. Appendix 10 shows the cutoff values to define extreme dietary data and number of women excluded at each wave (cutoff values are: 3398.3 kcal/day at baseline, 3084.6 kcal/day at 6 months and 3175.2 kcal/day at 24 months). After exclusion of extreme diet data, a total of 2,806 women had at least two complete data for fruit/vegetables and dietary fat, and 2,734

had at least two alcohol intake data. Trajectory analyses after the exclusion of extreme dietary data generated almost identical trajectory groups (Appendix 11). Therefore, extreme dietary data were unlikely to affect the identification of dietary trajectory.

3.5 DISCUSSION

This analysis showed that the majority of breast cancer survivors in the Pathways Study maintained their lifestyles over the 24 months following a diagnosis of BC, although women generally reported slight increases in F/V intake and temporary decrease in MVPA and alcohol intake during this period. Specifically, 52% of women reported medium to high level of F/V intake at baseline, and slightly increased F/V intake by no more than 0.5 serving/day over the 24 months following a BC diagnosis. Approximately 42% women reported medium to high level MVPA at baseline, but temporarily decreased engagement in MVPA by 2-3 hours/week at 6 months after diagnosis. Approximately 24% of women increased and 27% of women decreased time spent on sedentary behaviors by 5 hours/week over the 24 months after a BC diagnosis. Finally, 21% of women reported medium to high alcohol intake at baseline and temporarily decreased alcohol intake by 5-7 grams/day at 6 months after diagnosis. This analysis also identified characteristics that were predictors of health behavior trajectories, including socioeconomic status, dispositional optimism, perceived social support, and the severity of CIPN during active treatment. Specifically, higher education and income was commonly associated with higher odds of the high/medium increase-stable groups of F/V, high/medium decrease-temporary groups of MVPA, and high/medium decrease-temporary groups of alcohol intake. However, women with higher education were more likely to be in the high-stable sedentary behavior group, while women with higher income were at lower odds of maintaining high level of sedentary behavior. Higher dispositional optimism and perceived social support were associated with higher odds of the high/medium increase-stable F/V group and the high/medium decrease-temporary of MVPA, while higher social support was also associated with higher odds of the high-stable and medium decrease-stable groups of sedentary behavior. Finally, worse CIPN at 6 months after a BC diagnosis was associated with higher odds in the medium high-stable dietary fat group.

This analysis proposed new ways to identify target populations for behavior interventions. By depicting latent trajectories of health behaviors, future studies can potentially identify and directly target patients who are at high likelihood of following unfavorable health behavior trajectories. This analysis revealed that the level of health behavior at time of diagnosis is highly predictive of subsequent health behaviors during treatment and early survivorship after a BC diagnosis. Therefore, screening for health behavior at the time of cancer diagnosis could effectively identify targets to deliver behavior interventions. When direct measure of health behavior is unavailable, the high-risk group could be identified based on a patient's demographic characteristics, such as education and household income, or based on the psychosocial response to stress due to cancer, such as depressive symptom and dispositional optimism.

Few studies have examined the longitudinal trajectories of diet, physical activity and alcohol intake among BC survivors. Traditionally, studies have reported the average population change at certain time points over the course of follow-up. Based on analyses of mean change, previous studies reported relatively small and inconsistent changes in F/V, dietary fat, MVPA and sedentary behavior after a BC diagnosis. For instance, in a German cohort study (n=229), Steinhilper et al.⁷⁸ reported that BC survivors increased fruit intake by only 0.4 serving/day at one year post-surgery, and increased the frequency of fruit and vegetable intake by 0.9 and 0.7 times/week, respectively. Similarly, the British DietCompLyf cohort study (n=1,560)⁸⁴ reported that BC survivors increased approximately 0.5 serving/1000 kcal/day of fruit and 0.5 serving/1000 kcal/day of vegetable at 1 year after diagnosis after adjusting for total energy intake. The reported changes in dietary fat intake were also small. The HEAL study (n=260)⁸⁵ reported that BC survivors on average reduced 3.6 g/day of fat intake and 1% of energy from fat at 2 years post-diagnosis. Similarly, the DietCompLyf study (n=1,560)⁸⁴ reported a decrease of 4 g/1000 kcal/day in total fat intake at 1 year after diagnosis. Reports of change in MVPA were inconclusive; however, the fluctuation of MVPA after a BC diagnosis was within 2 hours/week.^{14,81,98} In the Pathways Study (n=1,696), Kwan et al. reported that MVPA decreased by 1.28 hour/week from 2 to 8 months after BC diagnosis.¹⁴ A population-based cohort study of 287 Australian BC survivors reported that participants spent 17 more minutes/week on vigorous PA but 55 fewer minutes/week on moderate PA from 6 to 18 months after diagnosis.⁸¹ However, a population-based cohort study of BC survivors in the US (n=315) reported that vigorous PA decreased by 5 MET-h/week and moderate PA decreased by 2.6 MET-h/week

at 12 months post-diagnosis.⁹⁸ Only one study reported a mean change in sedentary behavior among BC survivors. In the Pathways Study (n=1,696), Kwan et al. reported that BC survivors on average spent 0.83 fewer hours/week in sedentary behavior at 6 months after diagnosis.⁸²

The current analysis suggests that most women maintained their health behaviors in the 24 months after diagnosis, and among women who did make changes, the changes were very modest. Among women who fell into the “increase” groups of F/V, the energy-adjusted increase in F/V was less than one serving/day. For instance, although women in the high and medium increase-stable F/V group reported a statistically significant increase in F/V intake at 6 and 24 months, the average change was less than 1 serving/day of F/V. Similarly, changes in alcohol intake was also small, with the high and medium decrease-temporary group reporting a decrease of less than 1 standard drink of alcohol, which is equivalent to 16 grams of ethanol. However, the changes in physical activity were relatively larger. For instance, women in the high decrease-temporary MVPA group reported a decrease of 3 hours/week MVPA by 6 months, and women in the medium decrease-temporary group reported a decrease of 2.47 hours/week by 6 months after diagnosis. Considering that the lifestyle guidelines recommend a minimum of 2.5 hours/week of MVPA, these decreases are worthy of attention. Based on the magnitude of change, these results suggest that a BC diagnosis may encourage women to make relatively small dietary changes, but it may also prevent women from engaging in exercise.

Very few studies reported the distribution of behavior change patterns in BC survivors. Only two studies reported the prevalence of MVPA change patterns after a BC diagnosis. The HEAL study (n=545) reported that at 30 months after a BC diagnosis, 35% of women decreased time engagement in MVPA, while 26% maintained and 39% increased engagement in MVPA.⁷⁹ The current study reported a similar distribution, with approximately 42% women reporting decreased MVPA. To my knowledge, only one previous study has examined the trajectory of change in MVPA after a BC diagnosis. Using a hospital sample of 199 BC patients in Montreal, Canada, Brunet et al. analyzed data on MVPA collected every three months during the first year after a BC diagnosis. Using GBTM analysis, they demonstrated that women may follow five distinct trajectories of change in MVPA during the first year after diagnosis: 5.5% women were consistently inactive, 9.5% showed decreasing level, 10.5% were inactive but increased

MVPA, 25% were somewhat inactive over time, and 49% were consistently active.¹¹⁹ In comparison, my analysis did not identify a group of women who followed an increasing trajectory of MVPA. In fact, my analysis indicates that the majority of women (58%) maintained a low level of MVPA, and only 7% were constantly active. The differences in the discovery and distribution of MVPA trajectories could be due to the differences in the underlying source population and the method of assessing of MVPA. The current analysis defined MVPA as the total time spent on household chores, recreational activities and transportation. In contrast, Brunet et al. only assessed leisure time MVPA, which primarily included recreational activities. As such, the amount of MVPA reported in Brunet et al.'s study was considerably lower than what was reported in this analysis. In the current analysis, the majority of women were inactive, which suggests the need for increasing physical activity after a BC diagnosis.

The trajectory analyses of four health behaviors revealed that most women in the Pathways Study maintained a stable level of health behaviors in the 24 months after diagnosis. These findings raise the question as whether a cancer diagnosis elicits a true “teachable moment” where patients take action. A “teachable moment” refers to the period immediately following a major health event that may lead patients to be receptive to uptake of health promotion information. For example, a teachable moment is thought to occur after a smoker receives a diagnosis of lung disease or suffers a heart attack.^{217,218} The worries associated with these major health events motivate patients to adopt healthy behaviors, such as smoking cessation. Previous studies have suggested that cancer diagnosis would be followed by such a teachable moment, as cancer survivors are likely to feel that their lives are threatened and may experience strong emotional distress and social withdrawal.²¹⁹⁻²²¹ However, since a cancer patient typically goes through surgery and systematic therapy that may span over as long as 24 months, a patient's readiness to adopt healthier behavior may vary depending on the duration of cancer treatment. Therefore, the timing when a “teachable moment” occurs remains unclear. A “teachable moment” could occur immediately after the cancer diagnosis, during active cancer treatment, or during recovery phase after treatment has been completed. Previous studies suggest that cancer survivors may be more ready to adopt dietary changes at a later time after diagnosis. A systematic review of health behavior interventions reported that studies targeting at cancer survivors diagnosed within four months had higher attrition rates, and studies targeting at cancer survivors between 18-48 months after diagnosis had higher

retention rates.²²² The evidence for uptake of physical activity is mixed. For example, a study asked about the most preferred period for receiving exercise counseling and beginning an exercise program among more than 300 breast, prostate, colorectal, and lung cancer survivors. Approximately 39% of these cancer survivors said they preferred a time before treatment, 19% said during treatment, and 21% said immediately after treatment.²²³ This study suggested that the promotion of physical activity may not be dependent on timing of cancer treatment among cancer survivors. Although my analysis did not have data to examine the trajectory of readiness of behavior change, data suggest that BC survivors may start to increase F/V intake and reduce MVPA at baseline, which was approximately two months after diagnosis, suggesting that BC survivors may be most motivated to improve diet and face the biggest challenges to maintain regular physical activity shortly after diagnosis.

The study also highlighted several predictors of changes in F/V and MVPA in BC survivors. Higher education and higher income strongly predicted healthier lifestyles choices in BC survivors enrolled in the Pathways Study, which is consistent with previous studies in the general population. Numerous studies suggest that the low SES groups tend to adopt unhealthy behaviors, which explains a substantial proportion of the excess mortality associated with low SES.¹⁸¹⁻¹⁸⁵ The disparity in health behaviors between high and low SES groups is explained by a number of mechanisms: 1) chronic stress associated with economic disadvantage may limit an individual's capacity to adopt healthy behaviors and may drive them to seek unhealthy behaviors that are low-cost and stress-reducing;²²⁴⁻²²⁷ 2) the lower wealth of low SES groups give them less reason to invest in future longevity and more reason to focus on the present in making decisions about healthy behaviors;²²⁸⁻²³² 3) the low SES group may lack knowledge of the harm of unhealthy behaviors and therefore have less motivation to adopt healthy behaviors;²³³⁻²³⁸ 4) low SES group may lack of education, which decreases their problem-solving skills, ability to process information, and locus of control needed to overcome obstacles to achieving healthy behaviors;^{231,239-242} 5) the low SES group lacks economic resources to overcome low education, efficacy, and agency in adopting healthy behaviors;²⁴¹⁻²⁴⁴ and 6) the low SES group may share poorer community resources and less social capital that facilitate adoption of healthy behavior, such as neighborhood built environment,²⁴⁵⁻²⁵⁰ networks of health-oriented family and friends,²⁵¹⁻²⁵⁴ and social cohesion.^{245,255-257} The association between lower SES and a higher risk of adopting unhealthy behaviors justified that more

resources should be provided to the low-income, low-education group of BC survivors. This is particularly important for BC survivors, as many women may face financial burden caused by high out-of-pocket costs associated with cancer treatment.²⁵⁸ With the financial toxicity, women may have fewer resources to support the choice of a healthier lifestyle and therefore need material assistance to help make a positive change in diet and physical activity. This finding also suggests that future behavior interventions of health behaviors targeting at BC survivors should prioritize low SES populations.

Psychosocial factors relating to stress coping may influence the lifestyle choices after a BC diagnosis, but have not been formally tested in previous studies. Specifically, higher dispositional optimism and greater social support at the time of BC diagnosis may be promoters of a healthier lifestyle, especially for F/V intake and engagement in MVPA. This finding is in line with previous studies that explained the individual differences in lifestyle choices after a breast cancer diagnosis using the stress and coping model.^{152,153} The diagnosis and treatment of cancer is a significant stressor in itself that could contribute to changes in appetite and sleep and may disrupt health behaviors and potentially increase unhealthy behaviors.^{150,151} The stress and coping model posits that the ways that cancer survivors manage stressful feelings may influence their ability to make and sustain health behavior changes.¹⁵⁴ In particular, this model proposes that the use of adaptive coping to deal with cancer diagnosis stressors will be related to positive health behavior change. In breast cancer survivors, depressive symptoms are the most common stress-related symptoms.^{151,155-157} Depressive symptoms are associated with smoking and physical inactivity in the general population^{158,159} and breast and testis cancer survivors.^{119,160} In contrast, greater dispositional optimism has been associated with not smoking, moderate alcohol consumption, brisk walking, and vigorous physical activities in older women. In addition, higher perceived social support may facilitate stress coping and is linked to increased health behavior, specifically exercise, in cancer survivors.^{162,163} However, the study only observed a marginally significant association between higher depressive symptom and greater risk of decreasing F/V intake after a BC diagnosis (OR=1.86, 95% CI: 0.98-3.54). The protective effect of social support was not observed in this study.

Cancer treatments may also disrupt health behaviors. For example, cancer patients report reduction in physical activity during the phase of active treatment,^{35,145} and changes in taste sensitivity

induced by chemotherapy may alter food preferences and nutritional intake.¹⁴⁶⁻¹⁴⁹ Although cancer treatment may present barriers to the adoption of healthy behaviors, few studies formally investigated the impact of cancer treatment and treatment-related side effects on changes in health behaviors in breast cancer survivors. However, the association between cancer treatment side effects and trajectories of health behaviors was weak in this population. Of particular note, women who experienced worse CIPN during treatment period were more likely to follow a relatively high level of dietary fat intake. However, because the dietary fat pattern and the onset of CIPN were defined in overlapping time periods, this association does not indicate that women began to follow a high-fat diet after experiencing CIPN symptoms. It is also possible that women who had a high-fat diet were at greater risk of developing CIPN during active treatment, which is worthy of further investigation.

Changing lifestyle behaviors is a complex process and previous analyses of the mean change of these behaviors within a specific population are not sufficient to understand the complexity of behavior change among BC survivors. Therefore, more advanced analytical methods that distinguish the pattern of change are required. A major advantage of these analyses is the novel use of GBTM and KmL to identify subpopulations of BC survivors with distinct behavior change trajectories. These methods are person-centered analyses, which focuses on the similarities among the participants' longitudinal data, and differ from the variable-centered cluster analysis, such as the latent class analysis or latent transition analysis that focuses on understanding relationships among variables.²⁵⁹ The goal of the variable-centered analysis is to find commonality among a number of variables. In contrast, the person-centered analysis aims to identify similarities among individuals. Unlike other members of the finite mixture model family, such as the growth mixture modeling (GMM),²⁶⁰ which identifies latent classes of growth pattern based on individual characteristics, the GBTM identifies latent classes of growth patterns based on the shape parameters of growth curves. In addition, GBTM will handle missing data using Full Information Maximum Likelihood (FIML) estimation, which is unbiased and more efficient than methods that delete observations with incomplete data.²⁶¹ As such, the GBTM is a more appropriate method to identify behavior change trajectories. The use of KmL provides another robust method to validate the trajectory found in GBTM, adding confidence to the reproducibility of our findings. Because the KmL uses the EM algorithm to find the center of trajectory groups, it is more robust compared to the GBTM even when data are not normally

distributed, or group size is small. Additionally, KmL imputes missing data using an innovative method that provides reliable imputations even when the MAR assumption is violated.

The analysis also suffers from a number of limitations. An important limitation of this analysis is the lack of an ideal comparison group which represents the health behaviors before a BC diagnosis. In this analysis, baseline behavior data, which were captured at an average of 2 months post-diagnosis, were used as a measure of pre-diagnosis behavior. As such, the analysis only estimated a surrogate of change in health behaviors before and after breast cancer diagnosis. However, since the baseline behaviors were captured within approximately two months after diagnosis, one can reasonably assume that the baseline values well approximate behaviors pre-diagnosis, although no study has specifically examined the change in health behaviors immediately after a BC diagnosis. Studies that have collected both pre- and post-diagnosis behavior data are scarce. In my search of published articles, only one study examined the changes in health behaviors before and after a cancer diagnosis.²⁶² The study by Newsom et al. used data from the Canadian National Population Health Survey (NPHS) which followed 17,276 individuals aged 12 or older in 1994-1995. Follow-ups were conducted every 24 months. The study included 5,404 participants aged 50 or older at the first cycle who initially reported no chronic condition, but who reported a new diagnosis of one of five chronic conditions in a subsequent cycle during cycles 1 to 7 (1994-1995 to 2006-2007) of study follow-up. These chronic conditions included “heart disease,” “cancer” (skin cancer excluded), “effects of stroke,” “chronic bronchitis or emphysema” (asthma excluded), and “diabetes”. The study by Newsom et al. reported significant reduction in alcohol intake and smoking following a cancer diagnosis. However, because the study was only able to compare the change in health behaviors during a two-year period around the time of diagnosis, it is difficult to ascertain the exact timing of behavior change after diagnosis. Therefore, it remains unclear whether BC survivors in the Pathways Study began to make lifestyle changes before the baseline interview and whether baseline behavior approximated pre-diagnosis behavior. Collecting timely behavior data prior to the diagnosis of cancer is difficult. For large population-based cohort study, it is not feasible to prospectively collect behavior data close to a cancer diagnosis because data collection schedules are not determined by timing of cancer diagnosis. Thus, in studies of cancer survivors, recall of health behaviors before diagnosis may suffer from significant recall bias. An alternative approach to address this limitation is to

include a comparison population without breast cancer whose behaviors were not affected by a breast cancer diagnosis (the “unexposed”). However, because breast cancer may be caused by unhealthy diet and physical inactivity, breast cancer survivors may be more likely to engage unhealthy behaviors pre-diagnosis than the general population. Therefore, the use of healthy controls may introduce selection bias, leading to overestimation of behavior changes following a breast cancer diagnosis.

Another important limitation is the self-reported behavior data, which are subject to measurement error comprised of bias and random error. Social desirability bias is a common measurement error, which refers to the tendency to over- or under-report particular behaviors in order to avoid being viewed negatively.²⁶³ Increased media coverage of the potential benefits of healthy eating and physical activity may have changed people’s awareness of their diet and accuracy of self-report. If the relationship between self-report and actual health behavior changes, trend estimates or comparisons of self-reported data across different time points will conflate true changes in health behavior with changes in reporting accuracy. As such, my findings of the general increasing trend in fruit/vegetable intake raise the question of whether the self-reported diet reflect the actual diet, or merely the increased desire to present oneself as a health-conscious individual. Social desirability bias could also occur if the response rate to fruit/vegetables items on the food frequency questionnaire increased over time, leading to differential non-response bias in estimates over time. Therefore, social desirability bias may lead to erroneous conclusions regarding the observed trend estimates in fruit/vegetable and relationships with other variables of interest. In contrast, social desirability may have lower impact on physical activity and BMI, which showed either flat or decreasing trends. Due to the lack of objective behavior data in this analysis, future studies can assess the magnitude of the social desirability on reporting accuracy by comparing trajectories derived from self-reported and objective data. Previous studies of large national surveys suggest that the increases in BMI and leisure time physical activity over the past few decades were likely to reflect the actual behavior change instead of changes in reporting accuracy.^{264,265} However, social desirability may be associated with a downward bias in reporting food intake, especially total energy and dietary fat.²⁶⁶

Although the self-reported data were unlikely to bias the trend estimate for MVPA, almost all women reported engaging in sufficient amount of MVPA as recommended by the ACS, suggesting the self-reported physical activity data may overestimate the actual MVPA level. The Pathways Study assessed physical activity using the Arizona Activity Frequency Questionnaire (AAFQ), which has been shown to be an effective and accurate tool for prediction of physical activity energy expenditure based on validation studies using doubly labeled water.^{186,267} However, based on data from two large population-based studies, LACE (Life After Cancer Epidemiology) and CMH (California Men's Health Study), respondents typically misunderstood the definitions of activity intensity in the AAFQ, which may result in over-reporting work-related physical activities.²⁶⁸ In particular, sedentary office workers may over-report the time they spent walking or standing as they tend to report any walking instead of walking that lasted longer than 10 minutes. Although MVPA at work was not counted towards the overall MVPA in this analysis, the majority of women in the Pathways Study were older than 60 years old and spent most of their time sitting, who may also over-report MVPA due in part because of the tendency to recall any MVPA at home, which may explain the overestimation of overall MVPA.

In addition, this analysis may also suffer from selection bias. Because more than 50% of eligible women who were diagnosed with a breast cancer within the KPNC network refused to participate in the Pathways Study, women enrolled in this study might represent a subgroup of the source population that are more interested in lifestyle information after breast cancer diagnosis, or who are more motivated to seek healthier behavior change. Therefore, a selection bias may lead to a higher proportion of women who made a positive change in health-related behaviors after breast cancer diagnosis. However, in this analysis, the shape of behavior trajectory groups and the assignment of trajectory group membership were highly concordant under the analysis with and without adjustment for loss to follow-up, suggesting the impact of loss to follow-up was unlikely to have biased the identification of behavior trajectories.

Lack of generalizability is also a limitation of this analysis. The Pathways Study recruited participants within the KPNC healthcare system, which provides passive access to diagnoses and procedures for millions of patients. However, the participants may not be representative sample of a geographically defined population. For example, the Pathway Study may over-represent women who are

employed, and may exclude women who were diagnosed outside the health plan.²⁶⁹ In addition, members of the KPNC plan may change insurers over time. Furthermore, because members of the KPNC plan are employed, they may be systematically younger and healthier than the cancer survivors who are unemployed. Due to these reasons, the results regarding health behaviors of Pathways Study participants may not be generalized to breast cancer survivors living in northern California but outside of KPNC, or survivors living in other areas of the US. In addition, since the Pathways Study did not include women diagnosed with stage IV or higher stage breast cancer, these results may have limited applicability that extends only to populations with early stage (I-III) breast cancer. Finally, although a “teachable moment” may be common among survivors of various cancers, my analysis was only among BC survivors, and may not be generalizable to all cancer survivors.²¹⁹⁻²²¹

Furthermore, the statistical method used to identify behavior change trajectories is also limited by a few factors. The group-based modeling of trajectory groups is a data driven rather than a hypothesis-driven approach. As such, the model will define trajectory groups based on their shapes, rather than a set of *a priori* cutoff point to define the high and low level of healthy behaviors. However, given the limited literature on this topic, it could be used as a first step to building hypotheses for subsequent analyses. Another limitation of the group-based model is its assumption of a uniform shape of trajectory within the same group. Because the group-based model estimates a mean growth curve for each group, no individual variation around the mean group curves is allowed; the variation in the shape of trajectories within a group is assumed to be zero. A further complication of this limitation is that it may over simplify the trajectories of behavior change and regress behavior data to the mean. In this analysis, trajectories of absolute behavior were generally clustered by the mean baseline level and were not reflective of the change. The relatively small magnitude of change, the short period of data collection, and the limited number of repeated measures may explain the clustering by the baseline behavior. Future studies can explore the methodology to capture trajectory clusters by the slope of individual trajectories.

In summary, this analysis indicates that most women maintained their lifestyles after a BC diagnosis. There are a few notable patterns of behavior change. Half of women reported medium to high level of F/V intake at baseline, and slightly increased F/V intake over the 24 months following a BC

diagnosis. Approximately 42% of women reported medium to high level MVPA at baseline, but temporarily decreased engagement in MVPA at 6 months after diagnosis. A quarter of women increased and another quarter decreased time spent on sedentary behaviors over the 24 months after a BC diagnosis. Finally, 21% of women reported medium to high alcohol intake at baseline and temporarily decreased alcohol intake at 6 months after diagnosis. The predictors of health behavior trajectories included socioeconomic status, dispositional optimism, perceived social support, and the severity of CIPN during active treatment. Although higher socioeconomic status was generally associated with better health behaviors, women with higher education were more likely to stay inactive after a BC diagnosis. Given the potential benefit of healthy lifestyles on the overall survival of BC, it is important to prioritize health promotion in BC survivors who are at high risk of maintaining or adopting unhealthy behaviors post diagnosis. Moreover, these findings highlight important risk factors for maintaining unhealthy behaviors following a BC diagnosis, including lower education and income, lower dispositional optimism and social support, and the onset of CIPN during cancer treatment, suggesting a need for more efforts to promote healthy lifestyle behaviors in these BC survivors.

3.6 TABLES AND FIGURES

Table 6. Population characteristics at baseline, 6, and 24 months follow-up

Variable	Baseline (n=4505)		6 months (n=2874)			24 months (n=2666)		
	n	%	n	%	P ¹	n	%	P ¹
Age								
<50	996	22%	536	19%	<0.01	481	18%	<0.01
50-59	1316	29%	755	26%				
60-70	1297	29%	926	32%				
70+	896	20%	657	23%				
Race/ethnicity								
White	2894	64%	1996	69%	<0.01	1818	68%	<0.01
Black	358	8%	173	6%				
Asian	578	13%	337	12%				
Hispanic	557	12%	301	10%				
Other	118	3%	67	2%				
Education								
HS or less	707	16%	410	14%	<0.01	389	15%	<0.01
Some college	1568	35%	970	34%				
College or above	2222	49%	1491	52%				
Household income								
<\$50K	1949	43%	1259	44%	<0.01	1166	44%	0.05
\$50K-\$89K	2020	45%	1315	46%				
\$90K+	536	12%	300	10%				
Menopausal status								
Premenopausal	1352	30%	755	26%	<0.01	670	25%	<0.01
Postmenopausal	3153	70%	2119	74%				
Tumor stage								
I	2432	54%	1597	56%	<0.01	1504	56%	<0.01
II	1561	35%	972	34%				
III	439	10%	273	9%				
IV	73	2%	32	1%				
Number of positive nodes								
0	202	4%	125	4%	0.57	105	4%	0.09
1	978	22%	613	21%				
2+	3325	74%	2136	74%				
HER2 positivity								
Negative	3726	86%	2382	86%	0.71	2225	87%	0.09
Positive	590	14%	372	14%				
ER/PR positivity								
Negative	751	17%	455	16%	0.05	404	15%	<0.01
Positive	3749	83%	2414	84%				
Surgery type								
Lumpectomy	2017	45%	1320	46%	<0.01	1258	47%	<0.01
Mastectomy	2437	54%	1532	53%				
None	51	1%	22	1%				
Received chemotherapy								
Yes	2145	48%	1323	46%	<0.01	1199	45%	<0.01
No	2347	52%	1544	54%				
Received hormonal therapy								
Yes	3337	75%	2151	75%	0.14	2013	76%	0.01
No	1135	25%	703	25%				
Received radiation								
Yes	1972	44%	1294	45%	0.03	1220	46%	<0.01

No	2531	56%	1579	55%		1444	54%	
Depressive symptom								
Low	3149	74%	2154	77%	<0.01	1999	77%	<0.01
High	1127	26%	661	23%		590	23%	
Dispositional optimism								
Low	2945	69%	1908	68%	0.04	1766	68%	0.29
High	1340	31%	912	32%		827	32%	
Perceived social support								
Low	1394	33%	914	32%	0.83	821	32%	0.14
High	2890	67%	1906	68%		1771	68%	
Worse PWB at 6 months								
No	-	-	2101	77%	-	1638	79%	<0.01
Yes	-	-	613	23%		438	21%	
Worse CIPN at 6 months								
No	-	-	1350	66%	-	1084	67%	0.06
Yes	-	-	691	34%		529	33%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor

1. Chi-squared test compared the distribution of demographic, clinical and psychosocial characteristics between participants at baseline and follow-up

2. Missing data are not shown in the table

Table 7. Results for group-based trajectory modelling

Number of groups	BIC	AIC	Estimated probability for trajectory group (%)						
			1.0	2.0	3.0	4.0	5.0	6.0	
Change in fruit/vegetable intake									
1	-17759.5	-17744.6	100.0						
2	-16594.9	-16565.1	71.6	28.4					
3 (selected)	-16211.8	-16167.1	46.6	41.2	12.2				
4	-16040.5	-15980.9	42.1	35.3	19.8	2.8			
5	-16013.8	-15939.3	17.6	34.7	41.4	3.8	2.5		
6	-15991.7	-15902.3	19.5	33.8	3.9	41.0	1.6	0.2	
Change in dietary fat intake									
1	-25501.4	-25489.5	100.0						
2	-24864.6	-24840.7	51.2	48.8					
3	-24631.4	-24595.6	27.3	60.2	12.5				
4 (selected)	-24562.3	-24514.6	10.3	44.7	39.8	5.2			
5	-24554.3	-24494.7	2.2	23.2	45.9	25.1	3.5		
6	-24549.7	-24478.2	1.8	21.1	44.4	28.2	4.3	0.2	
Change in moderate to vigorous physical activity									
1	-23572.4	-23560.4	100.0						
2	-22551.3	-22527.3	85.8	14.2					
3 (selected)	-22161.1	-22125.0	70.2	26.1	3.7				
4	-21968.5	-21920.5	66.3	28.2	5.1	0.4			
5	-21870.2	-21810.1	64.1	29.0	4.6	1.9	0.4		
6	-21827.9	-21755.9	27.4	60.4	5.1	5.4	1.4	0.3	
Change in sedentary behavior									
1	-26622.1	-26610.1	100.0						
2	-25892.3	-25868.3	62.6	37.4					
3	-25658.5	-25622.5	38.9	51.0	10.2				
4 (selected)	-25612.6	-25564.6	27.8	46.9	22.0	3.2			
5	-25622.2	-25562.2	17.7	30.5	34.5	14.7	2.5		
6	-25615.9	-25543.9	17.3	30.6	0.2	34.7	14.8	2.5	
Change in alcohol intake									
1	-23153.0	-23141.0	100.0						
2	-21558.4	-21534.5	88.9	11.1					
3 (selected)	-21026.9	-20991.2	78.8	16.4	4.8				
4	-20918.8	-20871.2	16.0	66.5	13.8	3.7			
5	-20668.7	-20609.1	15.0	63.4	14.7	6.0	0.9		
6	-20494.6	-20423.0	15.3	5.0	62.1	14.9	1.8	0.9	

Note

Abbreviations: BIC, Bayesian information criterion; AIC, Akaike information criterion

Table 8. Comparison of trajectory groups derived from group-based trajectory modelling (GBTM) and K-means for longitudinal data analysis (KML)

Model 1: Unweighted GBTM			Model 2: Weighted GBTM			Model 3: KML			Cohen's kappa ¹			
Group	n	%	Group	n	%	Group	n	%	Model 1 1 vs. 2	Model 1 1 vs. 3	Model 2 vs. 3	Model choice
Change in fruit/vegetable intake												
High increase-stable	320	11.2%	High increase-stable	312	10.9%	High-stable	403	14.1%	0.99	-	-	Unweighted GBTM
Medium increase-stable	1180	41.2%	Medium increase-stable	1171	41.0%	Medium-stable	1175	41.0%				
Low increase-stable	1365	47.6%	Low increase-stable	1372	48.1%	Low-stable	1287	44.9%				
Change in dietary fat												
High-stable	131	4.6%	High-stable	130	4.6%	High-stable	392	13.7%	0.99	0.69	0.69	KML
Medium high-stable	1142	39.9%	Medium high-stable	1153	40.4%	Medium high-stable	1002	35.0%				
Medium low-stable	1336	46.6%	Medium low-stable	1326	46.4%	Medium low-stable	992	34.6%				
Low-stable	256	8.9%	Low-stable	246	8.6%	Low-stable	479	16.7%				
Change in moderate to vigorous physical activity												
High decrease-temporary	111	3.7%	High decrease-temporary	111	3.7%	High decrease-temporary	219	7.3%	0.99	0.66	0.65	KML
Medium decrease-temporary	753	25.1%	Medium decrease-temporary	739	24.7%	Medium decrease-temporary	1045	34.8%				
Low-stable	2131	71.2%	Low-stable	2136	71.5%	Low-stable	1736	57.9%				
Change in sedentary time												
High-stable	77	2.6%	High-stable	84	2.8%	High-stable	536	17.9%	0.98	-	-	KML
Medium high-stable	635	21.2%	Medium high-stable	645	21.6%	Medium increase-stable	728	24.3%				
Medium low-stable	1495	50.0%	Medium low-stable	1481	49.7%	Medium decrease-stable	816	27.2%				
Low-stable	783	26.2%	Low-stable	771	25.9%	Low-stable	917	30.6%				
Change in alcohol intake												
High decrease-temporary	137	4.8%	High decrease-temporary	139	4.9%	High decrease-temporary	189	6.6%	0.99	0.84	0.85	Unweighted GBTM
Medium decrease-temporary	459	16.0%	Medium decrease-temporary	461	16.1%	Medium decrease-temporary	527	18.4%				
Low-stable	2269	79.2%	Low-stable	2255	79.0%	Low-stable	2149	75.0%				

Note

Abbreviations: GBTM, Group based trajectory modelling; KML, K-means for longitudinal data analysis

1. Cohen's kappa measured agreement between group memberships identified from different analyses. A Cohen's kappa greater than 0.8 indicates concordance between two analyses. The Cohen's kappa was not computed when groups were not identical.

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Table 9. Mean changes in health behaviors by trajectory groups

Group	n	%	Baseline	6 months			24 months		
			Mean (SD)	Mean (SD)	Mean change (SD)	P ²	Mean (SD)	Mean change (SD)	P ²
Fruit/vegetable (servings/day)									
High increase-stable	320	11%	9.17 (3.13)	9.32 (3.17)	0.54 (0.17)	<0.01	9.07 (3.19)	0.39 (0.18)	0.03
Medium increase-stable	1180	41%	6.16 (2.23)	6.04 (2.13)	0.32 (0.07)	<0.001	6.14 (2.37)	0.17 (0.06)	0.01
Low increase-stable	1365	48%	3.31 (1.66)	3.23 (1.66)	0.33 (0.05)	<0.001	3.48 (1.83)	0.15 (0.05)	<0.01
Dietary fat (grams/day)¹									
High-stable	392	14%	46.52 (5.47)	46.6 (5.14)	0.03 (7.57)	1.00	46.56 (5.61)	-0.09 (7.43)	1.00
Medium high-stable	1002	35%	40.19 (3.94)	39.38 (4.03)	-0.83 (6.46)	<0.001	40.1 (4.09)	0.04 (6.5)	1.00
Medium low-stable	992	35%	34.07 (3.65)	34.72 (3.77)	0.67 (5.98)	<0.01	34.77 (4.14)	0.72 (6.08)	0.01
Low-stable	479	17%	28.36 (4.34)	27.85 (4.17)	-0.58 (5.74)	0.13	28.71 (4.66)	0.21 (6.32)	1.00
Moderate to vigorous physical activity (hours/week)									
High decrease-temporary	219	7%	18.09 (7.18)	15 (6.4)	-3.03 (8.99)	<0.001	16.57 (6.41)	-1.45 (8.56)	0.10
Medium decrease-temporary	1045	35%	9.05 (3.58)	6.69 (3.54)	-2.37 (5.4)	<0.001	8.21 (3.55)	-0.74 (5.49)	<0.001
Low-stable	1736	58%	2.73 (2.12)	2.26 (2.11)	-0.49 (2.73)	<0.001	2.85 (2.3)	0.04 (2.89)	1.00
Sedentary behavior (hours/week)¹									
High-stable	536	18%	27.94 (5.27)	26.58 (5.13)	-1.36 (7.03)	<0.001	26.46 (5.6)	-1.55 (7.24)	<0.001
Medium increase-stable	728	24%	15.41 (3.47)	20.1 (4.05)	4.66 (4.55)	<0.001	20.02 (4.46)	4.64 (5.34)	<0.001
Medium decrease-stable	816	27%	22.55 (3.64)	15.7 (4.14)	-6.85 (5.23)	<0.001	17.18 (4.31)	-5.31 (5.6)	<0.001
Low-stable	917	31%	11.29 (4.2)	10.63 (3.94)	-0.67 (5.46)	<0.001	10.56 (4.03)	-0.85 (5.85)	<0.001
Alcohol (grams/day)¹									
High decrease-temporary	137	5%	41.43 (16.44)	34.36 (15.86)	-6.95 (21.48)	<0.001	39.18 (12.74)	-1.23 (17.18)	1.00
Medium decrease-temporary	459	16%	18.81 (8.86)	14.02 (8.72)	-4.88 (12.86)	<0.001	15.82 (8.43)	-2.74 (12.85)	<0.001
Low-stable	2269	79%	1.95 (3.39)	1.38 (2.79)	-0.57 (3.43)	<0.001	1.68 (2.94)	-0.36 (3.43)	<0.001

Note

1. Changes in dietary fat, time spent on sedentary activities, and ethanol intake are reverse-coded so that higher value indicates positive change
2. T-test examined whether the mean changes were statistically significantly different from 0 at 6 and 24 months. For F/V, a linear regression tested the marginal change in F/V after adjusting for total energy intake. P-values were adjusted using Bonferroni correction to account for comparisons among multiple group within each behavior trajectory variable.
3. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Table 10. Multinomial logistic regression of socioeconomic status and health behavior change trajectory

Predictors	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
<i>Fruit/vegetable intake trajectory groups (referent group=low increase-stable)</i>						
	High increase-stable		Medium increase-stable			
Unadjusted						
Education (ref=high school or less)						
Some college	1.39 (0.88, 2.20)	0.16	1.73 (1.34, 2.24)	<0.001		
College and above	3.49 (2.29, 5.31)	<0.001	2.86 (2.23, 3.67)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	1.57 (1.21, 2.04)	<0.001	1.49 (1.26, 1.75)	<0.001		
\$90K+	1.30 (0.86, 1.96)	0.22	0.94 (0.71, 1.24)	0.65		
Fully adjusted¹						
Education (ref=high school or less)						
Some college	0.95 (0.55, 1.65)	0.87	1.24 (0.88, 1.75)	0.22		
College and above	2.74 (1.64, 4.57)	<0.001	2.33 (1.67, 3.26)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	1.07 (0.75, 1.53)	0.71	1.36 (1.07, 1.72)	0.01		
\$90K+	1.29 (0.76, 2.18)	0.34	0.80 (0.54, 1.18)	0.26		
<i>Dietary fat intake trajectory groups (referent group=low-stable)</i>						
	High-stable		Medium high-stable		Medium low-stable	
Unadjusted						
Education (ref=high school or less)						
Some college	0.88 (0.58, 1.34)	0.55	0.84 (0.59, 1.19)	0.33	0.95 (0.66, 1.36)	0.78
College and above	0.72 (0.48, 1.08)	0.11	0.80 (0.58, 1.12)	0.20	0.94 (0.67, 1.32)	0.73
Income (ref=<\$50K)						
\$50K-\$89K	1.28 (0.97, 1.69)	0.09	1.12 (0.89, 1.41)	0.33	1.16 (0.92, 1.46)	0.21
\$90K+	0.91 (0.55, 1.48)	0.69	0.89 (0.61, 1.31)	0.56	1.36 (0.94, 1.96)	0.11
Fully adjusted¹						
Education (ref=high school or less)						
Some college	1.13 (0.65, 1.98)	0.66	1.01 (0.64, 1.61)	0.95	1.29 (0.80, 2.08)	0.30
College and above	0.68 (0.39, 1.17)	0.17	0.75 (0.48, 1.17)	0.21	1.12 (0.71, 1.78)	0.62
Income (ref=<\$50K)						
\$50K-\$89K	1.31 (0.88, 1.94)	0.18	1.05 (0.76, 1.45)	0.77	1.10 (0.80, 1.52)	0.56
\$90K+	0.91 (0.47, 1.77)	0.79	0.81 (0.48, 1.38)	0.45	1.36 (0.82, 2.25)	0.23
<i>Moderate to vigorous physical activity trajectory groups (referent group=low-stable)</i>						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Education (ref=high school or less)						
Some college	1.64 (0.99, 2.72)	0.06	1.59 (1.22, 2.07)	<0.001		
College and above	2.28 (1.41, 3.69)	<0.001	2.29 (1.78, 2.93)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	1.92 (1.43, 2.59)	<0.001	1.65 (1.40, 1.95)	<0.001		
\$90K+	0.56 (0.29, 1.08)	0.08	0.94 (0.72, 1.24)	0.66		
Fully adjusted¹						
Education (ref=high school or less)						
Some college	3.48 (1.45, 8.38)	0.01	1.63 (1.16, 2.3)	<0.001		
College and above	4.36 (1.83, 10.35)	<0.001	2.04 (1.46, 2.84)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	1.48 (0.97, 2.25)	0.07	1.37 (1.09, 1.71)	0.01		

\$90K+	0.97 (0.45, 2.09)	0.94	1.03 (0.71, 1.5)	0.87		
Sedentary time trajectory groups (referent group=low-stable)						
	High-stable		Medium increase-stable		Medium decrease-stable	
Unadjusted						
Education (ref=high school or less)						
Some college	1.53 (1.07, 2.20)	0.02	1.08 (0.80, 1.47)	0.61	1.21 (0.90, 1.61)	0.20
College and above	1.69 (1.20, 2.38)	<0.001	1.20 (0.90, 1.60)	0.21	0.98 (0.75, 1.30)	0.91
Income (ref=<\$50K)						
\$50K-\$89K	0.70 (0.56, 0.88)	<0.001	0.83 (0.68, 1.02)	0.07	0.84 (0.69, 1.03)	0.10
\$90K+	0.75 (0.52, 1.10)	0.14	0.80 (0.57, 1.14)	0.22	1.09 (0.79, 1.50)	0.58
Fully adjusted¹						
Education (ref=high school or less)						
Some college	1.41 (0.87, 2.29)	0.17	1.13 (0.75, 1.71)	0.55	1.22 (0.82, 1.81)	0.33
College and above	1.83 (1.15, 2.93)	0.01	1.04 (0.70, 1.56)	0.85	1.02 (0.70, 1.51)	0.90
Income (ref=<\$50K)						
\$50K-\$89K	0.66 (0.48, 0.91)	0.01	0.85 (0.64, 1.14)	0.28	1.02 (0.76, 1.35)	0.92
\$90K+	0.64 (0.38, 1.09)	0.10	0.93 (0.58, 1.48)	0.76	1.14 (0.73, 1.78)	0.56
Alcohol intake trajectory groups (referent group=low-stable)						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Education (ref=high school or less)						
Some college	1.76 (0.92, 3.36)	0.09	1.60 (1.09, 2.34)	0.02		
College and above	2.02 (1.09, 3.75)	0.03	2.33 (1.63, 3.34)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	2.23 (1.53, 3.26)	<0.001	1.66 (1.34, 2.05)	<0.001		
\$90K+	0.81 (0.38, 1.76)	0.60	0.90 (0.61, 1.33)	0.59		
Fully adjusted¹						
Education (ref=high school or less)						
Some college	0.63 (0.30, 1.32)	0.22	1.51 (0.91, 2.5)	0.11		
College and above	0.79 (0.40, 1.6)	0.52	2.21 (1.35, 3.6)	<0.001		
Income (ref=<\$50K)						
\$50K-\$89K	2.54 (1.49, 4.34)	<0.001	1.64 (1.21, 2.21)	<0.001		
\$90K+	0.18 (0.02, 1.33)	0.09	0.84 (0.50, 1.43)	0.53		

Note

Abbreviations: OR, odds ratio; CI, confidence interval

1. Fully adjusted model controlled for age, race, menopausal status, tumor stage, number of positive nodes, receipt of surgery, chemotherapy, hormonal therapy, and radiation therapy
2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Table 11. Multinomial logistic regression of stress coping and health behavior change trajectory

Predictors	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Fruit/vegetable intake trajectory groups (referent group=low increase-stable)						
	High increase-stable		Medium increase-stable			
Unadjusted						
Depressive symptoms (high vs. low)	0.55 (0.40, 0.75)	<0.001	0.68 (0.56, 0.81)	<0.001		
Optimism (high vs. low)	2.01 (1.56, 2.58)	<0.001	1.30 (1.10, 1.54)	<0.01		
Social support (high vs. low)	2.13 (1.59, 2.86)	<0.001	1.24 (1.05, 1.46)	0.01		
Fully adjusted¹						
Depressive symptoms (high vs. low)	0.78 (0.51, 1.18)	0.24	0.84 (0.65, 1.09)	0.18		
Optimism (high vs. low)	1.83 (1.31, 2.54)	<0.001	1.50 (1.19, 1.89)	<0.001		
Social support (high vs. low)	1.82 (1.25, 2.65)	<0.01	1.08 (0.86, 1.36)	0.51		
Dietary fat intake trajectory groups (referent group=low-stable)						
	High-stable		Medium high-stable		Medium low-stable	
Unadjusted						
Depressive symptoms (high vs. low)	0.99 (0.71, 1.38)	0.96	1.23 (0.94, 1.60)	0.13	1.28 (0.98, 1.67)	0.07
Optimism (high vs. low)	1.18 (0.89, 1.56)	0.26	0.92 (0.73, 1.17)	0.50	1.08 (0.86, 1.37)	0.51
Social support (high vs. low)	0.84 (0.63, 1.12)	0.23	0.91 (0.72, 1.15)	0.43	0.90 (0.71, 1.14)	0.39
Fully adjusted¹						
Depressive symptoms (high vs. low)	1.09 (0.69, 1.70)	0.72	1.08 (0.75, 1.56)	0.67	1.20 (0.83, 1.73)	0.33
Optimism (high vs. low)	1.36 (0.93, 1.98)	0.11	0.79 (0.58, 1.08)	0.14	1.22 (0.89, 1.66)	0.22
Social support (high vs. low)	0.80 (0.54, 1.18)	0.26	1.01 (0.74, 1.39)	0.94	0.95 (0.69, 1.31)	0.75
Moderate to vigorous physical activity trajectory groups (referent group=low-stable)						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Depressive symptoms (high vs. low)	0.99 (0.71, 1.38)	0.95	0.82 (0.68, 0.98)	0.03		
Optimism (high vs. low)	1.96 (1.47, 2.62)	<0.001	1.59 (1.35, 1.88)	<0.001		
Social support (high vs. low)	1.56 (1.13, 2.15)	0.01	1.46 (1.23, 1.72)	<0.001		
Fully adjusted¹						
Depressive symptoms (high vs. low)	1.24 (0.79, 1.95)	0.34	0.95 (0.74, 1.23)	0.71		
Optimism (high vs. low)	1.85 (1.25, 2.75)	<0.001	1.61 (1.29, 2.00)	<0.001		
Social support (high vs. low)	1.23 (0.80, 1.89)	0.34	1.33 (1.06, 1.67)	0.02		
Sedentary time trajectory groups (referent group=low-stable)						
	High-stable		Medium increase-stable		Medium decrease-stable	
Unadjusted						
Depressive symptoms (high vs. low)	0.73 (0.56, 0.96)	0.02	1.07 (0.85, 1.34)	0.56	0.97 (0.77, 1.21)	0.78
Optimism (high vs. low)	1.57 (1.25, 1.97)	<0.001	1.20 (0.97, 1.48)	0.09	1.16 (0.94, 1.42)	0.17
Social support (high vs. low)	1.68 (1.32, 2.13)	<0.001	1.16 (0.94, 1.42)	0.16	1.29 (1.05, 1.58)	0.01
Fully adjusted¹						
Depressive symptoms (high vs. low)	1.00 (0.69, 1.45)	0.99	1.19 (0.86, 1.63)	0.29	1.23 (0.91, 1.68)	0.18
Optimism (high vs. low)	1.31 (0.96, 1.78)	0.09	1.09 (0.81, 1.45)	0.57	1.16 (0.88, 1.52)	0.30
Social support (high vs. low)	1.86 (1.34, 2.57)	<0.001	1.25 (0.94, 1.66)	0.12	1.42 (1.08, 1.87)	0.01
Alcohol intake trajectory groups (referent group=low-stable)						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Depressive symptoms (high vs. low)	0.81 (0.53, 1.25)	0.35	0.81 (0.63, 1.04)	0.10		
Optimism (high vs. low)	1.58 (1.12, 2.25)	0.01	1.17 (0.95, 1.45)	0.14		
Social support (high vs. low)	1.44 (0.97, 2.13)	0.07	1.26 (1.00, 1.57)	0.05		
Fully adjusted¹						
Depressive symptoms (high vs. low)	1.26 (0.72, 2.21)	0.41	0.90 (0.64, 1.28)	0.57		
Optimism (high vs. low)	1.17 (0.71, 1.91)	0.54	1.04 (0.78, 1.38)	0.79		
Social support (high vs. low)	1.07 (0.64, 1.79)	0.80	1.26 (0.93, 1.71)	0.14		

Note

Abbreviations: F/V, fruit/vegetable; CIPN, chemotherapy-induced peripheral neuropathy; OR, odds ratio; CI, confidence interval

1. Fully adjusted model controlled for age, race, menopausal status, tumor stage, number of positive nodes, receipt of surgery, chemotherapy, hormonal therapy, and radiation therapy
2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable)

Table 12. Multinomial logistic regression of cancer treatment side effect and health behavior change trajectory

Predictors	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
<i>Fruit/vegetable intake trajectory groups (referent group=low increase-stable)</i>						
	High increase-stable		Medium increase-stable			
Unadjusted						
Worse PWB at 6 months (yes vs. no)	0.84 (0.61, 1.14)	0.26	0.82 (0.67, 1.00)	0.04		
Worse CIPN at 6 months (yes vs. no)	0.73 (0.53, 1.01)	0.06	1.06 (0.87, 1.30)	0.55		
Fully adjusted¹						
Worse PWB at 6 months (yes vs. no)	1.00 (0.68, 1.49)	0.99	0.82 (0.63, 1.06)	0.13		
Worse CIPN at 6 months (yes vs. no)	0.82 (0.56, 1.19)	0.30	1.27 (1.00, 1.61)	0.05		
<i>Dietary fat intake trajectory groups (referent group=low-stable)</i>						
	High-stable		Medium high-stable		Medium low-stable	
Unadjusted						
Worse PWB at 6 months (yes vs. no)	1.18 (0.84, 1.66)	0.34	1.22 (0.92, 1.62)	0.16	1.10 (0.83, 1.47)	0.50
Worse CIPN at 6 months (yes vs. no)	1.46 (1.03, 2.08)	0.04	1.57 (1.17, 2.10)	<0.01	1.36 (1.01, 1.82)	0.04
Fully adjusted¹						
Worse PWB at 6 months (yes vs. no)	0.88 (0.57, 1.37)	0.58	1.01 (0.71, 1.44)	0.96	0.86 (0.60, 1.24)	0.42
Worse CIPN at 6 months (yes vs. no)	1.46 (0.97, 2.18)	0.07	1.48 (1.06, 2.06)	0.02	1.39 (1.00, 1.95)	0.05
<i>Moderate to vigorous physical activity trajectory groups (referent group=low-stable)</i>						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Worse PWB at 6 months (yes vs. no)	0.86 (0.59, 1.24)	0.42	0.95 (0.78, 1.15)	0.60		
Worse CIPN at 6 months (yes vs. no)	0.78 (0.54, 1.12)	0.18	0.80 (0.66, 0.98)	0.03		
Fully adjusted¹						
Worse PWB at 6 months (yes vs. no)	0.97 (0.61, 1.56)	0.91	1.03 (0.80, 1.32)	0.83		
Worse CIPN at 6 months (yes vs. no)	0.92 (0.60, 1.4)	0.69	0.84 (0.67, 1.06)	0.14		
<i>Sedentary time trajectory groups (referent group=low-stable)</i>						
	High-stable		Medium increase-stable		Medium decrease-stable	
Unadjusted						
Worse PWB at 6 months (yes vs. no)	0.99 (0.75, 1.30)	0.93	1.09 (0.86, 1.40)	0.48	0.98 (0.77, 1.24)	0.84
Worse CIPN at 6 months (yes vs. no)	1.14 (0.86, 1.50)	0.36	1.42 (1.10, 1.83)	0.01	1.24 (0.97, 1.59)	0.09
Fully adjusted¹						
Worse PWB at 6 months (yes vs. no)	1.13 (0.79, 1.61)	0.52	1.13 (0.82, 1.56)	0.45	1.08 (0.79, 1.47)	0.63
Worse CIPN at 6 months (yes vs. no)	1.21 (0.87, 1.67)	0.26	1.30 (0.97, 1.74)	0.08	1.15 (0.87, 1.53)	0.32
<i>Alcohol intake trajectory groups (referent group=low-stable)</i>						
	High decrease-temporary		Medium decrease-temporary			
Unadjusted						
Worse PWB at 6 months (yes vs. no)	0.73 (0.46, 1.15)	0.18	0.74 (0.56, 0.96)	0.02		
Worse CIPN at 6 months (yes vs. no)	0.94 (0.60, 1.46)	0.77	0.72 (0.55, 0.94)	0.01		
Fully adjusted¹						
Worse PWB at 6 months (yes vs. no)	1.03 (0.58, 1.86)	0.91	0.85 (0.60, 1.20)	0.36		
Worse CIPN at 6 months (yes vs. no)	1.13 (0.67, 1.88)	0.65	0.91 (0.68, 1.24)	0.56		

Note

Abbreviations: PWB, physical wellbeing; CIPN, chemotherapy-induced peripheral neuropathy; OR, odds ratio; CI, confidence interval
 1. Fully adjusted model controlled for age, race, menopausal status, tumor stage, number of positive nodes, receipt of surgery, chemotherapy, hormonal therapy, and radiation therapy
 2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable)

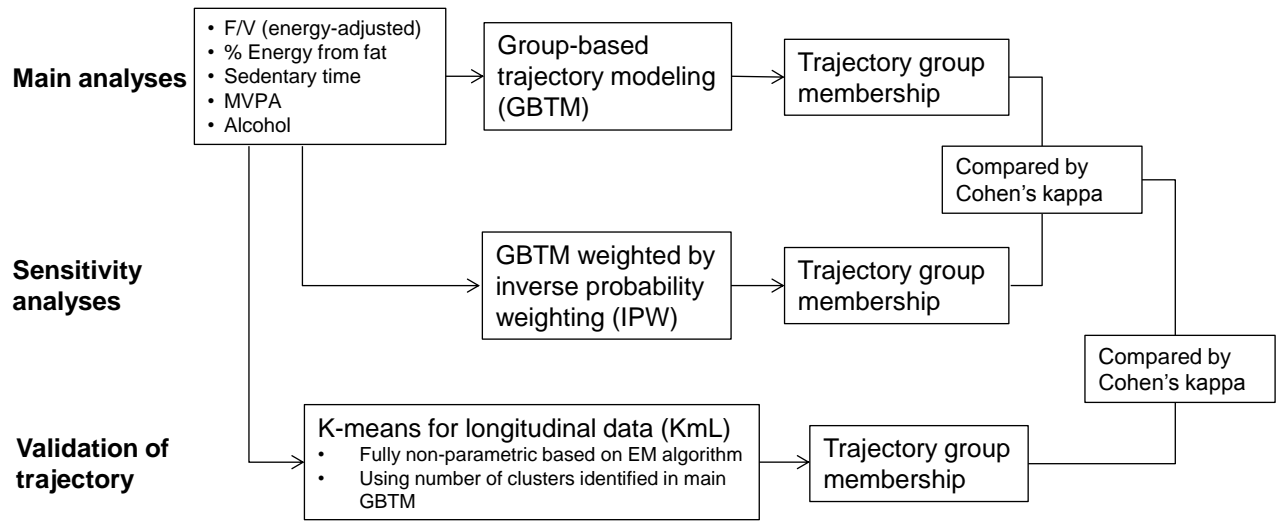


Figure 17. Analytical workflow of the trajectory analysis

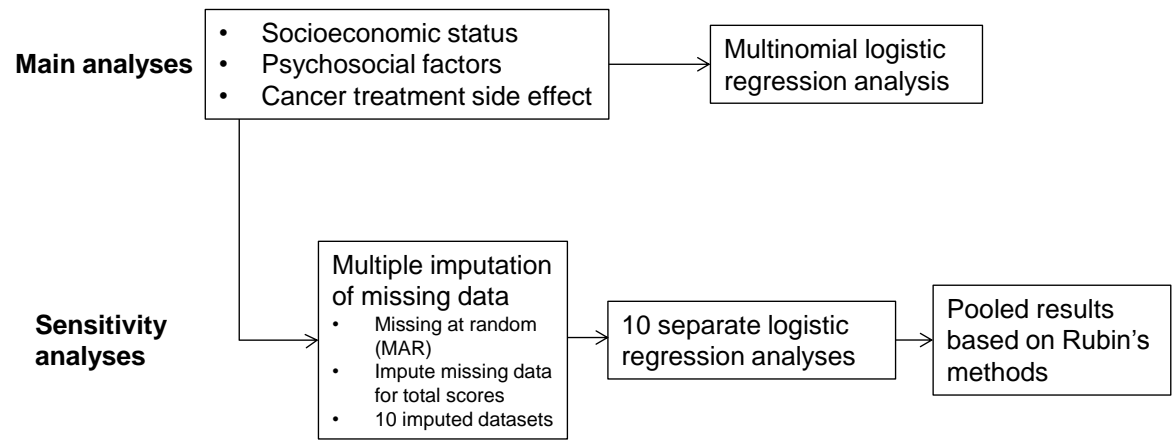


Figure 33. Analytical workflow to identify the predictors of behavior change trajectory

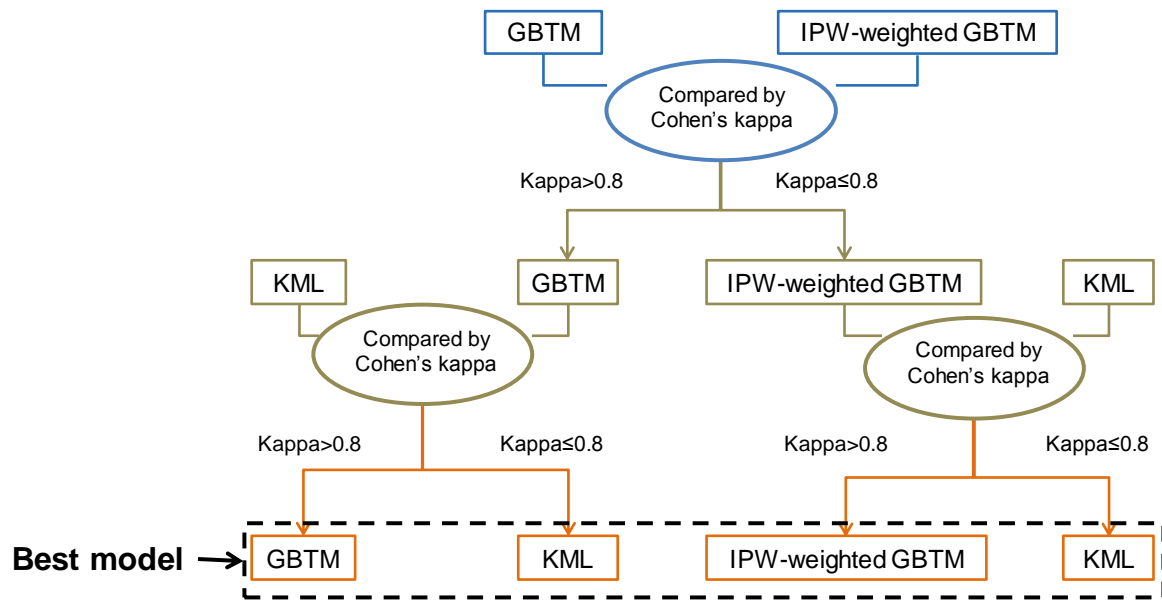


Figure 49. Analytical workflow to select the best trajectory group analysis results

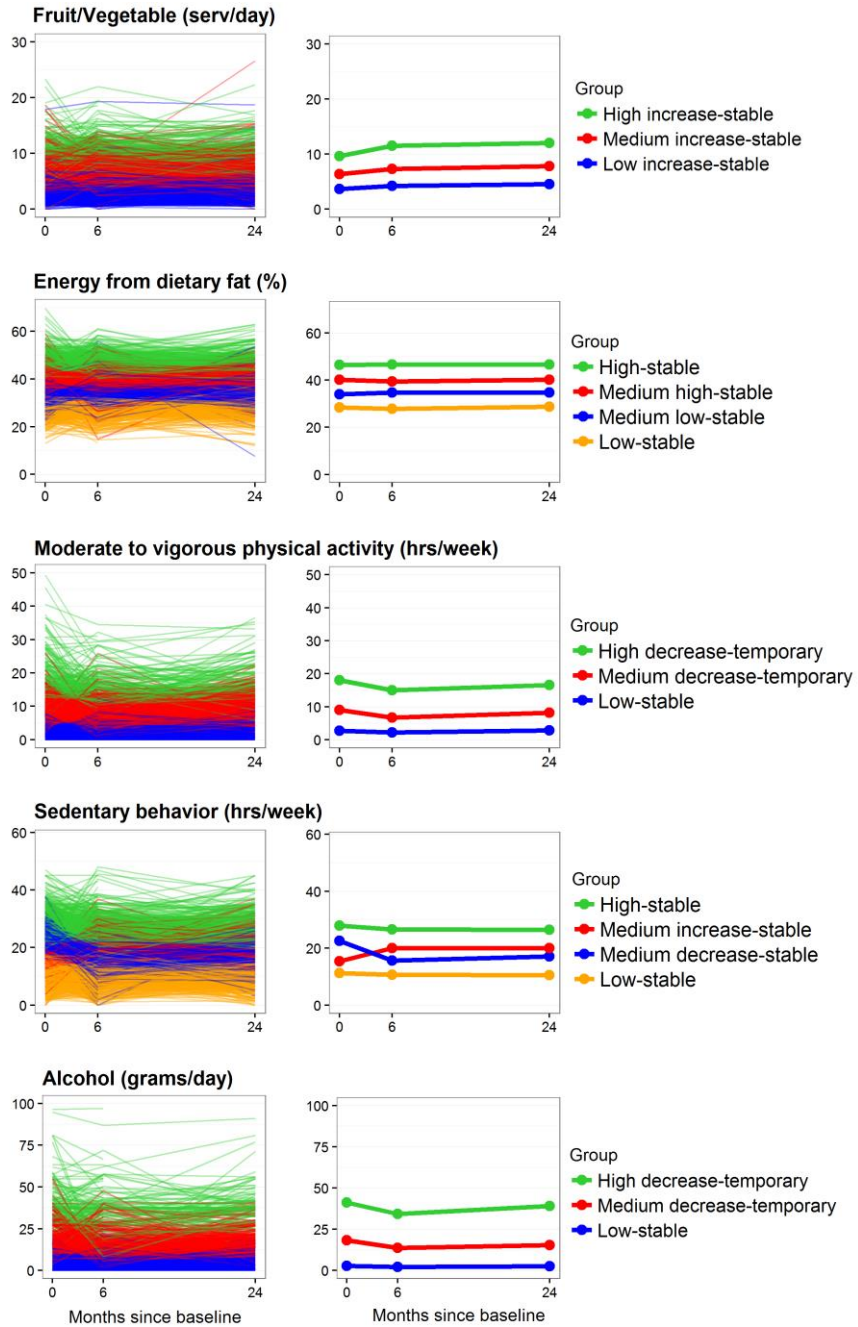


Figure 65. Trajectories of health behavior after a breast cancer diagnosis among the Pathways Study participants. This figure shows the individual trajectories (left panel) and group mean trajectories (right panel) of behavioral change during the first 24 months following a BC diagnosis.

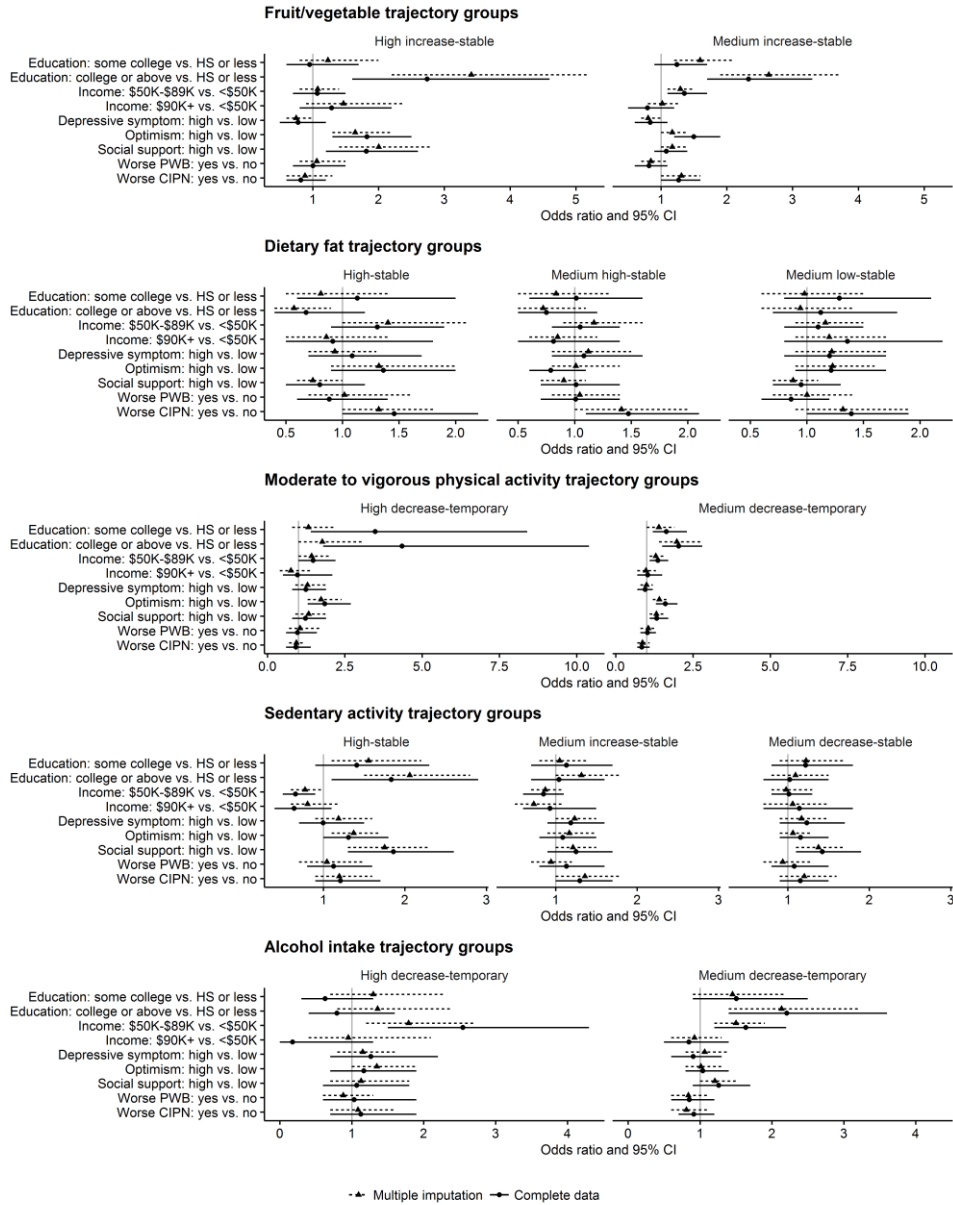


Figure 81. Trajectories of health behavior after a breast cancer diagnosis among the Pathways Study participants. This figure displays the fully adjusted odds ratios of following each trajectory of post-diagnosis behavioral change under the complete case analysis (solid line) and that under the multiple imputations (dash lines). The two analyses yielded similar associations of behavioral change trajectories with socioeconomic status, stress and coping, and cancer treatment related side effects.

CHAPTER 4: IDENTIFYING DISTINCT TRAJECTORIES AND PREDICTORS OF BMI AFTER A BREAST CANCER DIAGNOSIS

4.1 ABSTRACT

Background: Body mass index (BMI) has been associated with breast cancer outcomes, yet the distribution of BMI change patterns and predictors of BMI trajectories have not been assessed in breast cancer (BC) survivors. This analysis aimed to 1) identify distinct trajectories of BMI in a population-based cohort study of female BC survivors over the first 24 months after diagnosis, and 2) identify specific health behavior trajectories that were associated with BMI trajectories.

Methods: Data on self-reported body weight and height were collected from the 4,505 women enrolled in the Pathways Study at baseline (n with BMI data=4,479), 6 months (n=2,773) and 24 months (n=2,058) follow-up. BMI at baseline and each follow-up were analyzed using two methods, including semi-parametric, group-based trajectory modeling and non-parametric K-means for longitudinal data analysis. Multinomial logistic regression was used to examine predictors of BMI trajectories.

Results: Trajectory analyses identified three distinct BMI trajectories over the 24 month period: the majority (56%) of women maintained a healthy weight [baseline mean \pm SD=23.5 \pm 2.5 kg/m², median=23.5 kg/m², inter-quartile range (IQR)=3.7 kg/m²], 36% of women remained overweight/obese (baseline mean \pm SD=31.3 \pm 3.0 kg/m², median=30.8 kg/m², IQR=4.3 kg/m²), and 8% women were severely obese (baseline mean \pm SD=42.4 \pm 5.0 kg/m², median=40.8 kg/m², IQR=5.9 kg/m²). There was very little change in BMI over the two-year period. Women who maintain a high level of F/V (high increase-stable: OR=0.41, 95% CI: 0.19-0.89; medium increase-stable group: OR=0.61, 95% CI: 0.40-0.94), high level of MVPA (high decrease-temporary group: OR=0.26, 95% CI: 0.10-0.63; medium decrease-temporary group: OR=0.24, 95% CI: 0.15-0.39), and high level of alcohol intake (high decrease-temporary group: OR=0.16, 95% CI: 0.04-0.70; medium decrease-temporary group: OR=0.36, 95% CI: 0.19-0.68) were less likely to remained overweight/obese as compared to maintaining a healthy weight. Conversely, maintaining a high dietary fat intake (high-stable group: OR=2.24, 95% CI: 1.09-4.58) and high level of sedentary behavior (high-stable group: OR=2.43, 95% CI: 1.39-4.26) were associated with membership in the severely obese

trajectory group. Similarly, higher level of F/V, MVPA, and alcohol intake, but lower dietary fat intake and sedentary behavior were associated with the membership in the overweight/obese trajectory group.

Conclusion: Three distinct BMI trajectories were identified over the 24 months following a breast cancer diagnosis. BMI trajectories were stable over time and were based upon BMI at baseline. Trajectories of diet, physical activity and alcohol intake were strongly associated with memberships in the overweight/obese and severely obese trajectory group, independent of clinical factors and cancer treatment. These data suggest that women who kept an unhealthy lifestyle after a BC diagnosis are important targets for weight management programs.

4.2 INTRODUCTION

Overweight and obesity at the time of breast cancer diagnosis have been associated with worse survival.^{2,111,270,271} A growing number of studies have also observed an association of weight gain following a breast cancer diagnosis with a higher risk of recurrence and mortality,^{2,113,272} while other studies have reported that weight loss after breast cancer diagnosis is associated with the greatest mortality risk.^{111,273} Weight gain is a common and persistent problem for many BC survivors, both during treatment and in the months and years after diagnosis.²⁷ Weight gain is also known to impact negatively on the quality of life and to increase the risk of developing comorbid conditions.²⁸⁻³⁰ Furthermore, unfavorable changes in body composition including fat gain and loss of lean tissue, which is known as sarcopenic obesity,^{31,32} may further exacerbate the problem of weight gain and combined with gains in adipose tissue, may lead to metabolic disturbance, treatment complications, and poor survival outcomes.³¹⁻³⁴ Despite these findings, the typical trajectories and predictors of post-diagnosis BMI have not been described.

Although data are accumulating on the adverse prognostic effects of weight gain and sarcopenic obesity, the underlying behavior determinants of these changes in the post-diagnosis period are not well understood. Previous studies have evaluated diet and exercise patterns after diagnosis and possible treatment-related reductions in resting energy expenditure.^{31,32,35} However, the extent to which these individual components of energy balance contribute to weight change is not yet clear. Poorer diet has been implicated in weight gain among breast cancer survivors, but there are significant gaps in knowledge, and the limited reports on this issue have important methodological limitations.

The majority of previous studies have considered weight gain as a result of breast cancer treatment regimens, most notably chemotherapy and hormonal therapy.^{26,27,164,165} Behavior changes that cause energy imbalance may also contribute to the weight change after a breast cancer diagnosis. However, whether post-diagnosis weight change is caused by changes in behavior change after diagnosis has not been tested. To date, most studies of weight change in BC survivors defined weight gain and weight loss based on the percent change in body weight between two time points, thus ignoring the fluctuation in body weight over multiple assessments. Therefore, fluctuation of body weight and its associations with changes in energy balance-related behaviors after diagnosis remain largely

unexamined. For instance, weight cycling, also known as “yo-yo” dieting, refers to the repeated periods of weight loss followed by regaining.^{274,275} Weight cycling occurs as a result of initial success in weight loss through modified diet and physical activity, and subsequent weight regain after reversion into prior behavior patterns. Approximately 20-55% women experience weight cycling,²⁷⁶⁻²⁷⁸ and some observational studies have linked weight cycling with increased all-cause mortality and mortality from cardiovascular disease.^{275,279-281} As a result, weight cycling may explain the increased risk of mortality in breast cancer survivors.²⁷¹ However, the prevalence of weight cycling and its relationship with changes in health behaviors have not been studied in breast cancer survivors.

In this chapter, my goals are to identify the distinctive trajectories of BMI after a breast cancer diagnosis and identify the specific changes in health behaviors that are associated with each type of BMI trajectory. Based on previous studies, I hypothesize that women will follow five different trajectories of BMI after a breast cancer diagnosis, which include: 1) maintaining a high weight, 2) losing weight persistently, 3) losing weight temporarily, also known as weight cycling, 4) gaining weight persistently, 5) gaining weight temporarily (weight cycling), and 6) maintaining a low weight. The analysis also tests the hypotheses that stable improvement in health behaviors is associated with persistent weight loss, and that stable decline in health behaviors is associated with weight gain, and temporary improvement in health behavior is associated with weight cycling.

4.3 METHODS

4.3.1 Study participants

The study used data from the Pathways Study,³⁶ a population-based prospective cohort of women newly diagnosed with invasive breast cancer within the Kaiser Permanente Northern California (KPNC) network from January 2006 to April 2013. Women who were at least 21 years of age at diagnosis and a current KP member, had a recent diagnosis of invasive breast cancer, had no previous history of malignant cancer, spoke English, Spanish, Cantonese, or Mandarin, and lived within a 65-mile radius of a field interviewer were eligible for recruitment. The Pathways Study recruited women from the KPNC patient population immediately after a breast cancer diagnosis through rapid case ascertainment. Most

participants were recruited within two months (mean time = 1.8 months, range = 0.3-7.2 months) post-diagnosis. Baseline demographic and lifestyle data were collected during an in-person interview. During the follow-up period, lifestyle data were collected at 6, 24, and 72 months via mailed questionnaires, and breast cancer outcomes were identified via telephone interviews every 12 months after baseline and confirmed using KPNC electronic databases. The study protocol was approved by the institutional review board of all collaborating institutions. Written informed consent was obtained from all participating subjects. A total of 11,233 potentially eligible women were invited to participate in the study, and 4,505 enrolled.

4.3.2 Baseline and follow-up data collection

Interviewers administered detailed questionnaires on diet, exercise, and psychosocial and quality-of-life measures during the baseline interview. The interviewers also collected anthropometric measures, including arm, waist, and hip measurements, and a saliva sample. Blood samples were collected during the baseline interview by the interviewer, at KPNC, or at home by an outside vendor (Examination Management Services, Inc. Irving, TX). Clinical and tumor characteristics were obtained from the KPNC Cancer Registry approximately four months post-diagnosis. At 6 and 24 months, follow-up questionnaires, phone interview, and web survey were used to update the lifestyle information, with interviewer assistance offered if needed.

4.3.3 Measurement of health behaviors

Physical activity

Baseline physical activity data were collected using the Arizona Activity Frequency Questionnaire,¹⁸⁶ which assesses frequency and duration of daily household, recreational, transportation, and sedentary activities. This set of analyses use data specific to time spent on moderate-to-vigorous physical activities (MVPA) and sedentary activities. Moderate physical activity refers to activities equivalent in intensity to brisk walking or bicycling (3-6 METs). Vigorous physical activity produces large increases in breathing or heart rate, such as jogging, aerobic dance or bicycling uphill (>6 METs). For the purposes of this analysis, MVPA was defined as time spent on activities of ≥ 3 METs. Sedentary activity

included sitting during commuting, in the workplace, in the domestic environment, and during leisure time. Typical sedentary behaviors include TV viewing, computer use, or sitting in an automobile (1-1.5 METs).

Diet

Dietary history was collected using a 139-item modified version of the Block 2005 FFQ (NutritionQuest, Berkeley, CA). The FFQ included food items selected by identifying the top population contributors of each nutrient among whites, African Americans and Hispanics in the National Health and Nutrition Examination Survey (1999–2002). The 139 food items and additional questions were selected to be representative of a wide range of dietary factors, as well as to capture foods that are popular in Hispanic and Asian populations. The primary dietary variables include intakes of fruit/vegetable (F/V), dietary fat, dietary fibers, meat, total calories, and alcohol intakes. The FFQ assessed a number of vegetable groups, including daily intake of dark-green vegetables, deep-yellow vegetables, tomatoes, white potatoes, fried potatoes, legumes, other starchy vegetables, avocado and similar, and other vegetables (in cups). Fruit groups included citrus fruit and fruit excluding citrus fruit (in cups). Dietary fat intakes included daily intake of total fat, saturated fat, monounsaturated fatty acids, polyunsaturated fatty acids, and trans-fats (in grams). The percent energy from fat was used as the analytical variable for trajectory analysis. Alcohol intake was measured by the FFQ and converted into daily ethanol intake (in grams).

4.3.4 Key variables

Body weight

Body weight (kg) and height (m) were assessed at baseline and each follow-up via self-reported weight and height data from the Pathways Study participants. Weight and height were used to calculate body mass index (BMI) using the formula:

$$\text{BMI} = \text{Weight (kg)} / \text{Height (m)}^2$$

Other variables

The sociodemographic, clinical, psychosocial characteristics and cancer treatment side effect variables were described in Chapter 3. Briefly, the Pathways Study collected data on sociodemographic

factors included age at diagnosis, race/ethnicity, education, and household income at interview. *Data on clinical and breast cancer characteristics* were collected from the KPNC cancer registry and EHR. The analysis also included measures of stress and coping and measures of cancer treatment side effects, such as physical well-being (PWB) and chemotherapy-induced peripheral neuropathy (CIPN).¹⁹⁷

4.3.5 Statistical analysis

The primary goal of this study was to identify latent groups of BMI trajectories after a breast cancer diagnosis and to examine the associations between specific behaviors (F/V, dietary fat, MVPA, sedentary behavior, and alcohol intake) and weight change trajectories. BMI trajectory groups were identified using the same methodology as described in Chapter 3. Briefly, the study started with the main analysis using group-based trajectory modeling (GBTM) procedure,³⁹ and then performed a sensitivity analysis by applying the inverse probability weight (IPW)²⁰⁶ of remaining at 24 months to the main GBTM. The selected model was then validated using the K-means for longitudinal data (KML)⁴⁰ method. These analytical steps are described below and shown in Figure 7.

Analytical variables: The outcome variable was BMI at baseline, 6 and 24 month follow-up.

Main analyses: The study first used the GBTM procedure proposed by Nagin³⁹ to identify the optimal number of BMI trajectories that best fit the observed data. The analysis was restricted to participants with at least two out of three non-missing BMI data from baseline to the 24 months follow-up. Under the assumption that the outcome variable followed a normal distribution, a single-group model saturated with quadratic parameters was tested initially, and then one additional group was included in successive models. The study hypothesized that five distinct trajectories would be identified, and therefore tested models composed of one to six trajectory groups to find the optimal number of trajectories. Model fit was assessed based on the Bayesian Information Criterion (BIC), whereby the model with the lower BIC was favored. Once the number of groups was determined, participants were assigned to the trajectory group that best corresponded to their observed weight change according to the maximum posterior probability of group membership. The final model was selected based on parsimony, interpretability and prior knowledge of common behavior patterns in BC survivors.^{208,209}

Sensitivity analysis: To evaluate the influence of loss to follow-up on the identification of trajectory groups, a sensitivity analysis was performed by applying the IPW at 24 months to the main GBTM. To calculate the IPW, the probability of loss to follow-up at the 24-month wave was estimated in a logistic regression with baseline demographic and clinical characteristics as independent variables. Women who had interim missing data at 6 months but not 24 months (n=467) were not considered lost to follow-up and therefore were included in the analysis. Baseline demographic characteristics (age, race, education, and household income), tumor characteristics (tumor stage, size, grade, hormonal receptor status, and number of positive nodes), and treatment received (surgery, chemotherapy, hormonal therapy, and radiation) that were empirically associated with loss to follow-up at 24 months were included to impute IPW. The IPW was calculated as the reciprocal of the probability of remaining in follow-up at 24 months.

Validation analysis: To verify the efficiency and success of the GBTM, the study performed a validation analysis to identify the BMI trajectory groups using the KmL, which is a fully non-parametric method.⁴⁰ The KmL is a robust classification algorithm based on the Expectation-Maximization (EM) method.²¹¹ The KmL starts by assigning each observation to a random cluster, then uses the EM algorithm to alternate between 1) computing the center of each cluster (the *Expectation* phase), and 2) assigning each observation to its nearest cluster based on its distance to the cluster center (the *Maximization* phase). The EM algorithm repeats these two phases until cluster assignments become stable. Because there are no absolute criteria for an optimal number of clusters in KmL, the optimal number of cluster identified through GBTM will be used to verify if KmL produces similar trajectory groups.

Final model selection: The best trajectory group membership was identified through a series of pairwise comparisons among the above trajectory analyses. First, when the main GBTM and the IPW-weighted sensitivity analysis generated identical categories of trajectory groups, agreement between the two sets of group membership was measured using the Cohen's kappa,²¹² which is a common measure of agreement between two classifications of category a finite number of subjects belong to while accounting for agreement due to chance. A Cohen's kappa >0.8 indicates good agreement between the two sets of group membership. If the two trajectory groups were of good agreement, the unweighted GBTM result was retained since the loss to follow-up had little impact on the identification of trajectory of BMI. Otherwise, if the two trajectory groups identified different trajectory groups or were of poor

agreement (Cohen's kappa ≤ 0.8), results from the IPW-weighted GBTM were favored. In the second step, the optimal group memberships derived from GBTM were then compared with that identified via K_mL using Cohen's kappa. If the two trajectory analyses produced concordant group memberships (Cohen's kappa > 0.8), results from the GBTM were retained; otherwise, results from the K_mL were considered a better fit.

To investigate the associations of behavior trajectory and BMI trajectory, we first tested the difference in percent weight change between different behavior trajectory groups using the Z-test and linear regression and then tested if group membership of BMI was associated with behavior trajectory group membership using the chi-squared test and logistic regression. Baseline demographic (age, race/ethnicity, education, household income), clinical (menopausal status, tumor stage, number of positive nodes, HER2 status, EP/PR status, CIPN), cancer treatment received (surgery, chemotherapy, hormonal therapy, and radiation, physical wellbeing), and psychosocial factors (depressive symptom, dispositional optimism, and perceived social support) associated with 1) any health behavior change trajectories, 2) BMI trajectory and 3) modified any beta coefficients for the association of behavior and BMI trajectory by $\geq 10\%$ were considered as potential confounders. Confounders were entered simultaneously into a multivariable multinomial logistic regression model with all behavior trajectory variables to assess their associations with the BMI trajectory group membership.

Cancer treatments, such as chemotherapy and hormonal therapy, that are known to influence body weight changes among BC survivors^{26,27,164,165} but did not meet the criteria as a potential confounder based on the above criteria were additionally adjusted in a sensitivity analysis. In analyzing the association of F/V and BMI trajectories, sensitivity analyses were conducted to evaluate the influence of total energy intake and change in total energy intake by additionally adjusting for total energy intake at baseline and 24 months, and change in total energy intake from baseline to 24 months, respectively. Additionally, a sensitivity analysis was conducted to compare the association of F/V intake and BMI trajectories with and without adjustment of dietary fat intake trajectory, as changes in percent energy from dietary fat may be determined by changes in F/V intake. Similarly, a sensitivity analysis tested the association of dietary fat trajectory and BMI trajectory without adjustment of F/V trajectory to evaluate the potential mediation effect of F/V. Because the "low-stable" or "low increase-stable" groups of

behavior/BMI trajectories was commonly observed for all health behaviors, it was used as the referent group in multinomial logistic regression analyses for consistency in reporting results.

Missing data in health behavior and covariates were addressed in multiple steps throughout the analyses. In the trajectory identification stage, participants who had at least two assessments of body weight. GBTM used Full Information Maximum Likelihood (FIML) method to fill in missing behavior data under the assumption that data were missing at random. The KmL analysis used an innovative imputation method known as “copy mean”, which estimated the intermittent missing value of longitudinal data by treating the last observed value before each missing data as a starting value, and refined the imputation by finding the value that gives the imputed trajectory the same shape as the population mean trajectory.²¹³ The “copy mean” method has been shown to be robust under various missing data mechanisms and is considered superior over traditional imputation methods.²¹³ In analyses of the association of hypothesized predictors with behavior trajectory, only participants with complete covariate data and known group membership were included in the main analysis. However, the study performed a sensitivity analysis to examine how missing data influenced the observed association by filling missing covariate and outcome data using multiple imputations.²⁰⁷ Logistic regression based on 10 imputed datasets were then pooled to estimate the beta coefficients and 95% confidence interval using Rubin’s methods.²⁰⁷ Briefly, beta coefficients estimated in each of the ten data sets were averaged to calculate the pooled beta coefficient; the pooled confidence interval was estimated as a function of variance within each imputed dataset and between-imputation variance. The analytical workflow is shown in Figure 8.

The GBTM was performed using the PROC TRAJ command in SAS.²¹⁴ The KmL was implemented in R using the “kml” package.²¹⁵ Multiple imputations of missing data in baseline characteristics and trajectory group membership was conducted using the R “mi” package.²¹⁶

4.4 RESULTS

4.4.1 Participant characteristics

The demographic, clinical and psychosocial characteristics of the 4,505 Pathways Study participants were reported in Chapter 3 (Table 6). Briefly, participants were diagnosed with BC at the age

of 59 years (standard deviation (SD) =12) and were enrolled within 2 months post-diagnosis (SD=0.8 months). The majority of women were white, received at least some college education, earned more than \$50,000 a year, and were postmenopausal. Most women were diagnosed with stage I-III breast cancer with tumors that were negative for human epidermal growth factor receptor 2 (HER2) and positive for estrogen receptor (ER) and/or progesterone receptor (PR). Almost all women underwent surgery, and 48% women were treated with chemotherapy, 75% with hormonal therapy, and 44% with radiation. A total of 2,874 (63.8%) participants responded to 6-month follow-up questionnaires, and 2666 (59.2%) responded to the 24-month follow-up. Factors associated with loss to follow-up included age, race, education, income, tumor stage, receipt of breast surgery and chemotherapy at baseline as significant indicators of loss to follow-up, which were used to estimate the inverse probability weight for providing follow up data.

4.4.2 Identification of BMI trajectory groups

The analysis used GBTM to test models with one to six trajectories of BMI using data from baseline (n with BMI data=4479), 6 months (n=2773) and 24 months (n=2058). A total of 2,955 (65.6%) women who had at least two non-missing BMI data points over the first three waves of follow-up were included to identify weight trajectory groups. The distributions of BMI at each assessment were close to following a normal distribution. Table 13 shows the model fit statistics and estimated group distribution for models with one to six trajectories. Although the model with six trajectories yielded the lowest BIC value, the trajectory group solutions did not identify unique trajectory groups with unique change patterns or adequate group sizes. A three-group model that clearly distinguished women who maintained high, medium, and low BMI over the observation period was selected over the model with four or more trajectories. The rationale for this selection is that the four-trajectory model only separated the medium-stable group into two smaller groups with stable trends and therefore did not provide more insights into the BMI change trajectories. The trajectory groups and their distributions are summarized in Table 14. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² (“healthy weight”), who maintained a BMI between 25-35 kg/m² (“overweight/obese”), and who remained Class II-III obesity (BMI >35 kg/m², “severely obese”).

Next, the group memberships derived from the main GBTM analysis were compared against group membership identified through GBTM analysis with IPW and the validation analysis using K_mL to determine the final group assignment. The unweighted, IPW-weighted GBTM, and K_mL analyses identified the same trajectory groups. The three sets of group membership assignments were highly concordant (all Cohen's kappa > 0.8), suggesting the influence of loss to follow-up is minimal. Therefore, trajectory groups derived from unweighted GBTM was selected as the final group membership: 8% of women maintained a healthy weight [baseline mean±SD=23.5±2.5 kg/m², median=23.5 kg/m², inter-quartile range (IQR)=3.7 kg/m²], 36% of women remained overweight/obese (baseline mean±SD=31.3±3.0 kg/m², median=30.8 kg/m², IQR=4.3 kg/m²), and 8% women were severely obese (baseline mean±SD=42.4±5.0 kg/m², median=40.8 kg/m², IQR=5.9 kg/m²).

Trajectory groups from the three sets of analyses, as well as the final model choices, are shown in Table 14. Figure 9 illustrates the individual weight change trajectories color-coded by the trajectory groups (Figure 9 column A) and the mean weight change trajectories for each group (Figure 9 column B). Visual assessment of the final group assignments suggested that the final models successfully isolated three groups with distinct BMI trajectories.

4.4.3 Characteristics of trajectory groups

Table 15 summarizes the demographic, clinical, and psychosocial characteristics of the BMI trajectory groups. Compared to the healthy weight group, women who were in the severely obese group were more likely to be older at diagnosis, black or Hispanic, received lower education, had lower annual household income, and were more likely to be postmenopausal. The severely obese group was also more likely to receive a lumpectomy compared to a mastectomy and more likely to initiate radiation therapy. There were no differences in chemotherapy and hormonal therapy initiation across BMI trajectory groups. Women who reported high baseline depressive symptoms, worsening of physical well-being and CIPN at 6 months were also more likely to be in the severely obese group of BMI.

4.4.4 Mean baseline weight and mean weight change by trajectory groups

Table 16 describes the mean baseline weight and mean weight changes for each BMI trajectory group. Baseline weight differed significantly by trajectory group (P for ANOVA <0.001, not shown in

Table 16). The mean weight was 113.2 kg for the severely obese group, 82.8 kg for the overweight/obese group, and 62.4 kg for the healthy weight group. Although the mean change and percent change in body weight at 6 and 24 months were generally not statistically significantly different from zero, women in the severely obese group experienced a mean weight loss of 2.9 kg (2.2%) at 24 months ($P<0.01$), and the overweight/obese group lost a mean of 0.5 kg (0.3%) body weight at 6 months ($P=0.01$).

4.4.5 Associations of health behaviors with mean weight change

Figure 10 shows the mean weight change by behavior trajectory groups that were identified in Chapter 2. Based on the t-test of mean percent changes, women who were in the low-stable dietary fat group and the low-stable MVPA group had statistically significantly decreased body weight at 6 months and 24 months after a BC diagnosis.

In multivariable analysis of all behavior trajectories and controlled for age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline depressive symptom, worsening of physical well-being, and worsening of CIPN at 6 months, women who were in the high decrease-temporary MVPA group gained more weight than women in the healthy weight MVPA group (difference in percent weight change =1.16%, 95% CI: 0.12-2.19%) at 6 months (Table 5). Analysis of the mean weight change further showed that women who were in the high-stable dietary fat trajectory group gained more weight than women in the low-stable dietary fat group (difference in mean weight change =1.12 kg, 95% CI: 0.06-2.17 kg), and women in the high-stable sedentary behavior group also gained more weight than women in the low-stable sedentary behavior group (difference in mean weight change =0.89 kg, 95% CI: 0.03-1.75 kg) (Appendix 15).

4.4.6 Associations of health behaviors with BMI trajectory

Figure 11 provides a visual representation of the distribution of BMI trajectory groups by behavior trajectory groups. Across behavior trajectory groups, the majority of women were in the healthy weight group of BMI. There is a trend towards lower proportion of women who maintained a low BMI in the low-stable F/V group, high-stable dietary fat group, low-stable MVPA group, high-stable sedentary behavior group and low-stable alcohol intake group (chi-squared test of independence P value <0.001 for all pairs of association).

Multinomial logistic regression analysis examined the associations of behavior trajectories with group membership of BMI trajectories. An omnibus test was performed first to examine the overall association between BMI and behavior trajectory groups. To examine the adjusted odds ratio of being in each BMI group relative to the “healthy weight” group, unadjusted and fully adjusted models that included all confounders and all behavior trajectories were fit. The results of the regression analyses are summarized in Tables 18-22. The analysis screened and tested for confounding from demographic and clinical characteristics, and identified age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN as potential confounders. The results of the fully adjusted model are summarized below. Because the omnibus test and tests specific to each BMI trajectory group showed the same associations with behavior trajectories, the omnibus test results are not reported here.

F/V and BMI trajectories: Compared to women who were in the low increase-stable F/V trajectory group, women who were in the high-stable F/V group were less likely to be in the severely obese group (OR=0.41, 95% CI: 0.19-0.89; Table 18), and women in the medium increase-stable FV group were less likely to be in the severely obese (OR=0.61, 95% CI: 0.40-0.94; Table 18) and overweight/obese group (OR=0.73, 95% CI: 0.57-0.93; Table 18). Associations were similar when dietary fat intake trajectory was not adjusted for in the model, or when we included total energy intake and change in total energy as a covariate in the model (Table 18).

Dietary fat and BMI trajectories: Compared to women in the low-stable dietary fat group, women in the high-stable dietary fat group were more likely to follow the severely obese (OR=2.24, 95% CI: 1.09-4.58; Table 19) and overweight/obese trajectory (OR=2.34, 95% CI: 1.55-3.54; Table 19). Additionally, women in the medium high-stable dietary fat group (OR=1.62, 95% CI: 1.16-2.27; Table 19) and medium low-stable group (OR=1.47, 95% CI: 1.05-2.06; Table 19) were also more likely to follow the overweight/obese trajectory. In a sensitivity analysis without adjusting for F/V trajectory, the above associations were not changed.

MVPA and BMI trajectories: Compared to women in the low-stable MVPA group, women in the high decrease-temporary MVPA group were less likely to follow the severely obese (OR=0.26, 95% CI: 0.10-0.63; Table 20) and overweight/obese trajectory (OR=0.46, 95% CI: 0.29-0.72; Table 20). Women in the medium decrease-temporary MVPA group were also less likely to follow the severely obese (OR=0.24, 95% CI: 0.15-0.39; Table 20) and overweight/obese trajectory (OR=0.58, 95% CI: 0.45-0.74; Table 20).

Sedentary behavior and BMI trajectories: Compared to women in the low-stable sedentary behavior group, women in the high-stable sedentary behavior group were more likely to follow the severely obese (OR=2.43, 95% CI: 1.39-4.26; Table 21) and overweight/obese trajectory (OR=2.27, 95% CI: 1.62-3.18; Table 21).

Alcohol and BMI trajectories: Compared to women in the low-stable alcohol intake group, women in the high decrease-temporary alcohol intake group were less likely to follow the severely obese trajectory (OR=0.16, 95% CI: 0.04-0.70; Table 22). Similarly, women in the medium-stable alcohol intake group were also less likely to follow the severely obese (OR=0.36, 95% CI: 0.19-0.68; Table 22) and overweight/obese trajectory of BMI (OR=0.64, 95% CI: 0.47-0.87; Table 22).

4.4.7 Sensitivity analysis with multiple imputations

Using the multiple imputations (MI) method under the assumption that data were missing at random, the study imputed ten separate datasets to fill in missing data in the key analytical variables and BMI trajectories. Pooled results of fully adjusted multinomial logistic regression analyses from the ten imputed datasets were compared with results based on the complete case analysis (Figure 12). In general, the missing data have a minor influence on the observed associations of behavior change trajectories with weight change trajectories. However, after imputing the missing data, women in the medium increase-stable (OR=1.38, 95% CI: 1.08-1.76; data not shown) and medium decrease-stable groups (OR=1.29, 95% CI: 1.02-1.63; data not shown) of sedentary behavior were more likely to follow the overweight/obese trajectory, and women in the high-stable alcohol intake group were less likely to follow the overweight/obese trajectory (OR=0.63, 95% CI: 0.43-0.93; data not shown).

4.4.8 Sensitivity analysis by excluding extreme dietary data

To test whether the association between high alcohol intake and low BMI was due to lower total energy intake in women who had higher alcohol intake, I first examined the distribution of energy intake by alcohol intake groups (Appendix 19). The mean total energy intakes were higher in women who maintained high alcohol intake vs. non-drinkers. However, extremely high energy intake was more frequent in women in the low-stable alcohol intake group, as evidenced by the number of data points greater than the mean plus three standard deviations of total energy intake. Subsequent sensitivity analyses after the exclusion of extreme dietary data and adjusted for baseline energy intake showed similar association between alcohol intake trajectory and BMI trajectory (Appendix 16). These results suggested that the trajectory analyses of diet were minimally impacted by the extreme diet data, and that the conclusion about alcohol intake trajectory and BMI trajectory was not changed after exclusion of extreme dietary data.

4.4.9 Sensitivity analysis by restricting to women with complete BMI data

To examine the influence of missing BMI data, I performed a sensitivity analyses by restricting the trajectory analyses to women who had complete BMI data. A total of 1,862 women with three BMI measures were included in the sensitivity analysis. The trajectory analyses based on complete BMI data identified similar BMI trajectory groups as those identified with at least two data points. The results suggested that the trajectory analyses were robust against one missing data point and were not likely to be biased by missing BMI data.

4.4.10 Correlation between clinical BMI classifications and BMI trajectory groups

Appendix 17 showed the cross-tabulation of clinical classification of BMI and BMI trajectory groups. These two types of BMI classifications were highly correlated, indicating the healthy weight trajectory group mostly included women with a BMI <25 kg/m², the overweight/obese group included women who had a BMI between 25-30 kg/m², and the severely obese group mostly included women whose BMI were greater than 35 kg/m². Therefore, the trajectory analyses showed that women in the overweight and obese categories followed similar trajectories, and identified a unique cluster of women who were in the Class II obesity (BMI of 35 kg/m²) group.

4.5 DISCUSSION

This analysis identified three distinct trajectories of BMI during the first 24 months after a BC diagnosis: the majority (56%) of women maintained a low BMI during this period, 36% of women maintained a medium BMI, and 8% women maintained a high BMI. These trajectories of BMI were statistically significantly associated with the trajectory of diet, physical activity and alcohol intake over the same period of time, independent of demographic background, tumor characteristics and cancer treatment received. In particular, the severely obese group was negatively associated with the high/medium increase-stable F/V groups, the high/medium decrease-temporary MVPA groups and the high decrease-temporary alcohol intake group. The severely obese group was also positively associated with the high-stable dietary fat intake group and the high-stable sedentary behavior group. Similarly, the overweight/obese group was negatively associated with the medium increase-stable F/V groups, the high/medium decrease-temporary MVPA group, and the high/medium decrease-temporary alcohol intake group. The overweight/obese group was also positively associated with the high/medium dietary fat intake group and the high-stable sedentary behavior group.

This analysis provides a novel application of trajectory analysis to measure and define weight change patterns after a BC diagnosis, which could be used in analyzing the effect of longitudinal pattern of health behaviors on BC survival. Currently, the association between post-diagnosis weight change and BC survival are considered as a U-shaped relationship, in which both weight gain and weight loss are associated with poorer overall survival.^{80,271,282} A recent meta-analysis of observational studies concluded that a gain of $\geq 5\%$ body weight post-diagnosis is associated with increased all-cause mortality compared with maintaining weight.²⁸² The hazard associated with weight gain was particularly pronounced in women who gained more than 10% weight, and among those who were not obese at the time of diagnosis.²⁸² Two recent observational studies in the US further suggested that post-diagnosis weight gain may only increase all-cause mortality at 3-5 years after diagnosis.^{80,283} However, other observational studies have reported a strong association between weight loss and increased BC recurrence and all-cause mortality during the early period (18–54 months post diagnosis) after BC diagnosis, irrespective of initial body weight.^{80,271,284} These studies, however, are limited by the way weight change was defined.

Weight change has been commonly defined as weight maintenance ($< \pm 5.0\%$ body weight), weight gain ($\geq 5\%$ weight gain), or weight loss ($\geq 5\%$ weight loss).^{80,122,271,284,285} Some studies defined a large weight gain or loss as a change of $\geq 10\%$ body weight.^{80,122,271,284} However, this measurement of weight change is based on weight data at two time points, which may span over a few years after diagnosis, and thus may ignore the weight fluctuations between measurement time points. The choices of 5% and 10% as the cutoff points to define low and high weight change in previous studies are largely arbitrary, which may introduce bias due to non-differential misclassification of weight change.

This analysis showed that the majority of women maintained their body weight during the first 24 months after diagnosis. In contrast, previous studies reported that approximately 19%-84% of women diagnosed with BC experience significant weight gain during the 1-2 years after diagnosis,^{77,80,91,92,112,122} and the weight gain maintained in 30% of BC survivors long-term.^{93,95} Four population-based cohort studies in the US and China measured self-reported weight and height among BC survivors.^{80,91,113,116} The After Breast Cancer Pooling Project (n=12,915 stage I-IV BC survivors) compared weight at 1 year prior to BC diagnosis and weight at 18-48 months post-diagnosis, and reported an average of 1.6 kg increase in body weight.⁹¹ Approximately 34.7% of women gained weight while 14.7% lost weight during this period. A recent study using data from the LACE and the Pathways Study (n=3,109 stage I-III BC survivors) reported similar findings, with 25% of women reporting weight gain and 14% reporting weight loss at 24 months after diagnosis.⁹² However, results from the Long Island Breast Cancer Study Project (n=1,436) suggested that weight gain (23%) and weight loss (22%) were equally common in BC survivors at 1 year after diagnosis.¹¹³ One study followed 345 early stage BC survivors who received chemotherapy after diagnosis and 305 healthy women over 6 years and reported that 42% of BC survivors and 32% of healthy women experienced a weight gain of $\geq 5\%$ baseline weight.¹¹⁶ In contrast, the current analysis did not identify a subgroup of women who experienced significant weight gain after a BC diagnosis. The reported differences in the prevalence of weight gain may be due to the underlying differences in population characteristics, the timing of weight measurement, and type of treatment received. Additionally, previous studies may have misclassified women with a small amount of weight gain as true weight gain, who would have been classified as weight maintenance under the trajectory analysis.

However, it is unclear whether the trajectory analysis is capable of detecting weight change patterns than traditional methods.

This analysis contributes to the literature that identified modifiable targets for weight management among BC survivors. While there is an established link between adjuvant chemotherapy and weight gain, especially for women on longer duration treatments^{26,27,164,165}, potential changes in diet and physical activity in response to the stress of cancer and its treatment is an area of active research. Behavior changes affecting energy balance may play an important etiologic role underlying weight change after a BC diagnosis, because weight gain is evidenced among breast cancer patients who did not receive adjuvant treatment, and many breast cancer survivors reported progressive weight gain after initial treatment.²⁶ Despite recent efforts to capture possible changes in dietary intake during and after treatment, empirical analyses supporting an association between increased energy intake after diagnosis and post-diagnosis weight gain is lacking.¹¹⁴ A study by Irwin et al.,⁹⁶ however, reported a significant reduction in physical activity during and after treatment, which may play a role in post-diagnosis weight gain. This study by Irwin et al.⁹⁶ reported results from the Health, Eating, Activity, and Lifestyle (HEAL) study of 514 women with stage 0-III breast cancer, almost half of whom used tamoxifen, but only 27% received chemotherapy. At two years post treatment, women increased their weight by a mean of 1.7 kg. Women who reported a decrease in their physical activity from diagnosis to up to 3 years after diagnosis reported greater weight gain than women who did not. The current analysis further demonstrated that, even for women who had high level of MVPA at time of diagnosis, a temporary decrease in engagement in MVPA was associated with a temporary weight gain after a BC diagnosis. Furthermore, maintaining a high MVPA was associated with a stable and low BMI during the first 24 months of BC survivorship. This analysis also suggested that physical inactivity may also play a role in weight management for BC survivors. In this population, women who reported high level of sedentary behavior throughout the 4 months after a BC diagnosis gained 0.89 kg more weight than those who reported a persistently low level of sedentary behavior. Although these results offer limited inference regarding the effect of changing MVPA and sedentary behavior on post-diagnosis weight change, it confirms and highlights the strong association of physical activity with weight maintenance in BC survivors.

These results also demonstrated the importance of diet in weight management for BC survivors. Previous studies suggested that dietary change may be related to weight change in breast cancer patients and survivors, but the evidence is not consistent.^{27,114} Goodwin et al. reported that caloric intake and physical activity did not explain weight gain during the first year after BC diagnosis among 535 Canadian BC survivors.²⁷ The WHEL study observed that higher energy intake after BC diagnosis was independently associated with increased risk for weight gain up to 4 years after cancer diagnosis.²⁸⁶ In this current analysis, instead of establishing a link between dietary change and weight change, the results indicated that maintaining a diet high in F/V and low in dietary fat was associated with a stable and low BMI after a BC diagnosis. Furthermore, women who consumed a high-fat diet gained 1.12 kg more weight than women with a low-fat diet during the first 24 months after diagnosis. However, it remains unclear whether increasing F/V intake and reducing dietary fat intake will protect against weight gain after a BC diagnosis.

This analysis further showed that reduced alcohol intake post-diagnosis was associated with low and stable BMI after a BC diagnosis. This result is consistent with previous studies that reported the association between increase in alcohol intake and increased body weight.^{287,288} Alcohol is an energy-dense yet nutritionally poor food source with an energy content of 7.1 kilocalories per gram.²⁸⁹ Epidemiological studies showed that alcohol-derived calories added to food intake do not appreciably alter the average daily intake of other macronutrients.²⁹⁰ Therefore, alcohol seems to make an independent contribution to metabolic energy. Therefore, effects of alcohol consumption on body weight may be explained by the extra energy intake from alcohol. The results further suggested that, even for women reported higher alcohol intake at baseline, reducing alcohol intake may protect against maintaining a high BMI after diagnosis. However, the interpretation of the results of my analysis is complicated by the fact that BC survivors who reduced alcohol intake were the same women who maintained a higher alcohol intake at time of diagnosis. It is possible that higher alcohol intake at baseline may be associated with lower BMI. Although there is little evidence to justify this possible explanation, my analysis showed that extreme energy intake was more common among non-drinkers. Analysis after exclusion of the extreme energy intake did not change my results, suggesting other mechanisms may link high alcohol intake with low BMI among the Pathways Study participants. Therefore, the role of alcohol

intake in weight management among BC survivors is complicated and warrants further investigation, and alcohol reduction may be a potential target for weight loss interventions among BC survivors.

This analysis has a number of limitations. Although the analysis failed to identify groups of weight gain and weight loss, it does not mean that BC survivors did gain weight or lose weight. In fact, the failure to detect a change in BMI trajectory may be due to the small magnitude of weight change relative to baseline weight. Instead of identifying changing trends in BMI, the trajectory analysis revealed that the BMI of Pathways Study participants were clustered into three levels. These levels correspond with the normal weight, overweight/obese and class II obesity defined by clinical classification of BMI, suggesting that the trajectory analysis offered similar classification of body fatness as that based on traditional BMI cutoffs. Therefore, the BMI category at time of BC diagnosis is a stable indicator of subsequent BMI within the 24 months after diagnosis. Additionally, only three waves of BMI data were available for analysis, which further limited the ability to observe a steady change in BMI. Although the Pathways Study partially completed the 72 months data collection, this analysis did not include the 72 months primarily because it is difficult to determine the nature of incomplete follow-up while the 72 months follow-up is ongoing. Furthermore, because the exposure variable, behavior change trajectories, depends on the success of identifying behavior change trajectories in Chapter 3, the exposure status may be misclassified if the behavior change group membership is incorrect. If the misclassification of exposure is dependent on the outcome, that is, if women are misclassified as having a negative trend towards unhealthy behaviors, and if the misclassification is more likely to occur in women who gain weight, the association between behavior change and weight change will be overestimated. Another limitation is that weight may not reflect body composition. Unlike typical weight gain that characterized by increases in both lean body mass and adipose tissue, cancer treatment-induced weight gain may occur either in the absence of lean tissue gain or in the presence of lean tissue loss.^{31,32} However, the Pathways study does not currently have data on body composition to assess whether changes in health-related behaviors are associated with changes in body fat or lean mass specifically. A previous study suggests that the waist circumference might be a good indicator of visceral fat,²⁹¹ which could be used as a separate outcome to examine the association between behavior changes and changes in body fat. In addition, there is strong emerging evidence that WHO cutoff values for BMI may not be appropriate in older populations.^{292,293} A

recent meta-analysis of 32 cohort studies (n=197,940) of community-dwelling elderly people aged ≥ 65 years found a U-shaped association between all-cause mortality, with mortality risk lowest at BMI 24-31 kg/m². This relationship remained when adjusting for smoking status, early death, pre-existing disease and geographical location.²⁹³ Therefore, it may be inappropriate to consider BMI between 25-30 kg/m² as overweight or obese for women aged ≥ 65 years. Additionally, the relationship between BMI, body fat and health risks differed by race and ethnicity. The BMI cutoff values are lower for the Asian population (23.0, 27.5, 32.5, and 37.5 kg/m² for overweight, obese I, obese II and obese III, respectively).²⁹⁴ Finally, although the analyses used longitudinal data for analyses, this analysis only examined the cross-sectional association between variables that measures change over the same time period. Analyses that evaluate the effect of behavior trajectory on future weight change will provide stronger evidence to elucidate the causal relationship. Other limitations include the lack of pre-diagnosis data, self-reported behavior data, and the data-driven nature of group-based modeling, which may all introduce bias or errors as discussed in Chapter 3.

In summary, this analysis did not observe a latent trajectory of weight gain or weight loss in the first 24 months after a BC diagnosis in the Pathways Study. Instead, my analysis suggests that most women maintained their body weight following a BC diagnosis. The BMI trajectories were strongly associated with trajectory of F/V, dietary fat intake, MVPA, sedentary behavior, and alcohol intake over the same period, independent of demographic characteristics, tumor characteristics and receipt of cancer therapies. These results highlight the importance of health behaviors in maintaining a healthy body weight after a BC diagnosis. Future studies should also examine the associations of these BMI trajectories and BC prognosis to better understand the effect of post-diagnosis weight change on BC-specific and all-cause mortality.

4.6 TABLES AND FIGURES

Table 13. Results for group-based trajectory modelling of body mass index

Number of groups	BIC	AIC	Estimated probability for trajectory group (%)						
			1.0	2.0	3.0	4.0	5.0	6.0	
1	-25327.5	-25315.5	100.0						
2	-23307.0	-23283.0	76.6	23.4					
3 (selected)	-22045.8	-22009.8	55.8	35.8	8.3				
4	-21329.8	-21281.8	46.8	35.9	14.4	2.9			
5	-20843.3	-20783.4	37.4	34.1	20.0	7.3	1.2		
6	-20468.0	-20396.1	25.8	31.4	24.1	12.0	5.6	1.1	

Note

Abbreviations: BIC, Bayesian information criterion; AIC, Akaike information criterion

Table 14. Comparison of body mass index trajectory groups derived from group-based trajectory modelling (GBTM) and K-means for longitudinal data analysis (KML)

Model 1. Unweighted GBTM			Model 2. Weighted GBTM			Model 3. KML			Cohen's kappa ¹			
Group	n	%	Group	n	%	Group	n	%	Model 1 vs. 2	Model 1 vs. 3	Model 2 vs. 3	Model choice
Healthy weight	243	8%	Healthy weight	239	8%	Healthy weight	337	11%	0.99	0.87	0.86	Unweighted GBTM
Overweight/obese	1058	36%	Overweight/obese	1047	36%	Overweight/obese	1102	37%				
Severely obese	1654	56%	Severely obese	1661	56%	Severely obese	1520	51%				

Note

Abbreviations: GBTM, Group based trajectory modelling; KML, K-means for longitudinal data analysis

1. Cohen's kappa measured agreement between group memberships identified from different analyses. A Cohen's kappa greater than 0.8 indicates concordance between two analyses. The Cohen's kappa was not computed when groups were not identical.
2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² ("healthy weight"), who maintained a BMI between 25-35 kg/m² ("overweight/obese"), and who remained Class II-III obesity (BMI >35 kg/m², "severely obese").

Table 15. Comparison of trajectory group characteristics: fruit/vegetable intake

Variable	Severely obese (n=243)		Overweight/obese (n=1058)		Healthy weight (n=1654)		P ¹
	n	%	n	%	n	%	
Age							
<50	40	16%	152	14%	360	22%	<0.001
50-59	71	29%	297	28%	427	26%	
60-70	98	40%	358	34%	490	30%	
70+	34	14%	251	24%	377	23%	
Race/ethnicity							
White	152	63%	730	69%	1148	69%	<0.001
Black	46	19%	80	8%	51	3%	
Asian	6	2%	79	7%	279	17%	
Hispanic	31	13%	140	13%	143	9%	
Other	8	3%	29	3%	33	2%	
Education							
HS or less	47	19%	202	19%	173	10%	<0.001
Some college	111	46%	419	40%	468	28%	
College or above	85	35%	437	41%	1013	61%	
Household income							
<\$50K	135	56%	526	50%	643	39%	<0.001
\$50K-\$89K	89	37%	417	39%	846	51%	
\$90K+	19	8%	115	11%	165	10%	
Menopausal status							
Premenopausal	57	23%	228	22%	502	30%	<0.001
Postmenopausal	186	77%	830	78%	1152	70%	
Tumor stage							
I	131	54%	586	55%	918	56%	0.21
II	80	33%	359	34%	570	34%	
III	28	12%	108	10%	144	9%	
IV	4	2%	5	0%	22	1%	
Number of positive nodes							
0	11	5%	51	5%	65	4%	0.65
1	45	19%	228	22%	356	22%	
2+	187	77%	779	74%	1233	75%	
HER2 positivity							
Negative	203	87%	887	87%	1367	86%	0.83
Positive	31	13%	131	13%	217	14%	
ER/PR positivity							
Negative	47	20%	152	14%	263	16%	0.12
Positive	192	80%	905	86%	1391	84%	
Surgery type							
Lumpectomy	122	50%	518	49%	720	44%	0.01
Mastectomy	117	48%	536	51%	919	56%	
None	4	2%	4	0%	15	1%	
Received chemotherapy							
Yes	120	50%	470	45%	778	47%	0.24
No	121	50%	584	55%	874	53%	
Received hormonal therapy							
Yes	186	77%	811	77%	1224	74%	0.23
No	56	23%	238	23%	419	26%	
Received radiation							

Yes	117	48%	504	48%	710	43%	0.03
No	126	52%	554	52%	943	57%	
Depressive symptom							
Low	166	72%	801	77%	1244	77%	0.22
High	65	28%	238	23%	376	23%	
Dispositional optimism							
Low	162	70%	730	70%	1065	66%	0.05
High	70	30%	312	30%	557	34%	
Perceived social support							
Low	74	32%	345	33%	518	32%	0.78
High	158	68%	695	67%	1106	68%	
Worse physical well-being at 6 months							
No	147	71%	711	75%	1193	80%	<0.001
Yes	60	29%	242	25%	292	20%	
Worse CIPN at 6 months							
No	100	61%	428	62%	783	69%	<0.01
Yes	64	39%	257	38%	349	31%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.

2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² ("healthy weight"), who maintained a BMI between 25-35 kg/m² ("overweight/obese"), and who remained Class II-III obesity (BMI >35 kg/m², "severely obese").

Table 16. Mean changes in body mass index by trajectory groups

Group	Baseline		6 months						24 months				
			Absolute change (kg)			Percent change (%)			Absolute change (kg)			Percent change (%)	
	n	%	Mean (SD)	Mean (SD)	Mean (SD)	P-value ¹	Mean (SD)	P-value ¹	Mean (SD)	Mean (SD)	P-value ¹	Mean (SD)	P-value ¹
Severely obese	243	8%	113.2 (16.8)	111.8 (17.3)	-0.9 (8.1)	0.09	-0.6 (6.8)	0.16	110.8 (18.6)	-2.9 (11)	<0.01	-2.2 (9.2)	<0.01
Overweight/obese	1058	36%	82.8 (11)	82.1 (10.6)	-0.5 (5.9)	0.01	-0.3 (6.4)	0.12	81.9 (10.8)	-0.7 (7.1)	0.01	-0.5 (8.1)	0.07
Healthy weight	1654	56%	62.4 (8.4)	62.4 (8.4)	-0.1 (3.2)	0.30	0.0 (4.8)	0.85	62.4 (8.4)	-0.1 (4.2)	0.25	-0.1 (6.3)	0.76

Note

1. T-test examined whether the mean changes were statistically significantly different from 0. Bonferroni correction was used to account for multiple comparisons.

2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² ("healthy weight"), who maintained a BMI between 25-35 kg/m² ("overweight/obese"), and who remained Class II-III obesity (BMI >35 kg/m², "severely obese").

Table 17. Linear regression analysis of difference in percent weight change at 6 and 24 months following a breast cancer diagnosis by behavior trajectories

Behavior trajectory groups	6 months				24 months			
	Unadjusted		Fully adjusted ¹		Unadjusted		Fully adjusted ¹	
	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
Fruit/vegetable (ref=Low increase-stable)								
High increase-stable	0.52 (-0.16, 1.20)	0.14	0.84 (-0.03, 1.71)	0.06	0.07 (-0.93, 1.07)	0.89	-0.02 (-1.22, 1.19)	0.98
Medium increase-stable	0.03 (-0.41, 0.47)	0.91	0.23 (-0.36, 0.82)	0.45	-0.17 (-0.83, 0.49)	0.62	-0.36 (-1.20, 0.48)	0.40
Dietary fat (ref=Low-stable)								
High-stable	0.50 (-0.25, 1.26)	0.19	0.59 (-0.38, 1.56)	0.23	0.94 (-0.18, 2.07)	0.10	1.05 (-0.30, 2.41)	0.13
Medium high-stable	0.40 (-0.22, 1.01)	0.21	0.16 (-0.62, 0.95)	0.69	0.55 (-0.37, 1.47)	0.24	-0.15 (-1.27, 0.97)	0.79
Medium low-stable	0.51 (-0.11, 1.12)	0.10	0.23 (-0.55, 1.00)	0.57	0.36 (-0.56, 1.27)	0.44	0.34 (-0.77, 1.44)	0.55
Moderate to vigorous physical activity (ref=Low-stable)								
High decrease-temporary	1.03 (0.21, 1.84)	0.01	1.16 (0.12, 2.19)	0.03	0.71 (-0.47, 1.90)	0.24	0.45 (-0.98, 1.89)	0.53
Medium decrease-temporary	0.51 (0.06, 0.95)	0.02	0.41 (-0.17, 0.99)	0.17	0.93 (0.26, 1.60)	0.01	0.43 (-0.38, 1.24)	0.30
Sedentary activity (ref=Low-stable)								
High-stable	-0.22 (-0.84, 0.39)	0.48	0.07 (-0.73, 0.87)	0.86	0.16 (-0.77, 1.09)	0.73	0.70 (-0.41, 1.81)	0.21
Medium high-stable	0.10 (-0.46, 0.66)	0.72	0.21 (-0.52, 0.93)	0.58	-0.11 (-0.97, 0.75)	0.80	0.11 (-0.94, 1.15)	0.84
Medium low-stable	-0.28 (-0.82, 0.26)	0.31	-0.14 (-0.83, 0.56)	0.69	0.38 (-0.44, 1.20)	0.36	0.29 (-0.69, 1.27)	0.56
Alcohol (ref=Low-stable)								
High decrease-temporary	0.18 (-0.78, 1.14)	0.71	-0.10 (-1.37, 1.17)	0.87	0.06 (-1.39, 1.50)	0.94	0.42 (-1.40, 2.23)	0.65
Medium decrease-temporary	0.01 (-0.55, 0.57)	0.97	-0.03 (-0.75, 0.68)	0.93	0.20 (-0.63, 1.03)	0.64	0.16 (-0.83, 1.16)	0.75

Note

Abbreviations: CI, confidence interval

1. The fully adjusted analysis controlled for age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline depressive symptom, worsening of physical well-being, and worsening of CIPN at 6 months

2. The difference was calculated as the difference between two percentages. For instance, an unadjusted difference of 0.52 comparing the high increase-stable vs. the low increase-stable F/V groups means that women in the high increase-stable F/V group had 0.52 more percent weight change than women in the low increase-stable F/V group at 6 months.

3. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² ("healthy weight"), who maintained a BMI between 25-35 kg/m² ("overweight/obese"), and who remained Class II-III obesity (BMI >35 kg/m², "severely obese").

Table 18. Multinomial logistic regression fruit/vegetable trajectory and BMI trajectory

Behavior change trajectory groups (Referent=Low increase-stable)	BMI trajectory groups (Referent= Healthy weight)			
	Severely obese OR (95% CI)	P	Overweight/obese OR (95% CI)	P
Unadjusted				
High increase-stable	0.30 (0.17, 0.55)	<0.001	0.62 (0.48, 0.81)	<0.001
Medium increase-stable	0.49 (0.36, 0.66)	<0.001	0.59 (0.50, 0.70)	<0.001
Fully adjusted¹				
High increase-stable	0.41 (0.19, 0.89)	0.02	0.79 (0.55, 1.13)	0.20
Medium increase-stable	0.61 (0.40, 0.94)	0.02	0.73 (0.57, 0.93)	0.01
Fully adjusted, without adjusting for dietary fat trajectory²				
High increase-stable	0.37 (0.17, 0.81)	0.01	0.73 (0.51, 1.05)	0.09
Medium increase-stable	0.58 (0.38, 0.88)	0.01	0.69 (0.54, 0.88)	<0.001
Fully adjusted, additionally adjusted for total energy³				
High increase-stable	0.32 (0.31, 0.33)	<0.001	0.74 (0.53, 1.05)	0.09
Medium increase-stable	0.52 (0.44, 0.63)	<0.001	0.72 (0.56, 0.92)	0.01
Fully adjusted, additionally adjusted for change in total energy⁴				
High increase-stable	0.32 (0.13, 0.83)	0.02	0.77 (0.50, 1.17)	0.22
Medium increase-stable	0.52 (0.30, 0.88)	0.02	0.73 (0.54, 0.98)	0.04

Note

Abbreviations: OR, odds ratio; CI, confidence interval

1. Fully adjusted model simultaneously controlled for group membership of all other health behaviors (dietary fat intake, moderate to vigorous physical activity, sedentary time, and alcohol intake), age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN
2. This model included all covariates in the fully adjusted model except for the group membership of dietary fat intake
3. This model included all covariates in the fully adjusted model, and additionally adjusted for total energy intake at baseline and 6- and 24-month follow-up
4. This model included all covariates in the fully adjusted model, and additionally adjusted for change in total energy intake from baseline to 6- and 24-month follow-up
5. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² ("healthy weight"), who maintained a BMI between 25-35 kg/m² ("overweight/obese"), and who remained Class II-III obesity (BMI >35 kg/m², "severely obese").

Table 19. Multinomial logistic regression of dietary fat trajectory and BMI trajectory

Behavior change trajectory groups (Referent=Low-stable)	BMI trajectory groups (Referent= Healthy weight)			
	Severely obese		Overweight/obese	
	OR (95% CI)	P	OR (95% CI)	P
Unadjusted				
High-stable	3.73 (2.20, 6.32)	<0.001	2.57 (1.91, 3.46)	<0.001
Medium high-stable	2.09 (1.30, 3.36)	<0.001	1.68 (1.32, 2.15)	<0.001
Medium low-stable	1.63 (1.01, 2.64)	0.05	1.38 (1.08, 1.76)	0.01
Fully adjusted¹				
High-stable	2.24 (1.09, 4.58)	0.03	2.34 (1.55, 3.54)	<0.001
Medium high-stable	1.64 (0.87, 3.08)	0.13	1.62 (1.16, 2.27)	0.01
Medium low-stable	1.39 (0.73, 2.64)	0.32	1.47 (1.05, 2.06)	0.02
Fully adjusted, without adjusting for fruit/vegetable trajectory²				
High-stable	2.54 (1.25, 5.16)	0.01	2.48 (1.64, 3.73)	<0.001
Medium high-stable	1.79 (0.96, 3.35)	0.07	1.68 (1.20, 2.35)	<0.001
Medium low-stable	1.42 (0.75, 2.70)	0.28	1.49 (1.06, 2.08)	0.02

Note

Abbreviations: OR, odds ratio; CI, confidence interval

1. Fully adjusted model simultaneously controlled for group membership of all other health behaviors (dietary fat intake, moderate to vigorous physical activity, sedentary time, and alcohol intake), age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN

2. This model included all covariates in the fully adjusted model except for the group membership of fruit/vegetable intake

3. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² (“healthy weight”), who maintained a BMI between 25-35 kg/m² (“overweight/obese”), and who remained Class II-III obesity (BMI >35 kg/m², “severely obese”).

Table 20. Multinomial logistic regression of change in moderate to vigorous physical activity and BMI trajectory

Behavior change trajectory groups (Referent=Low-stable)	BMI trajectory groups (Referent= Healthy weight)			
	Severely obese		Overweight/obese	
	OR (95% CI)	P	OR (95% CI)	P
Unadjusted				
High decrease-temporary	0.24 (0.12, 0.48)	<0.001	0.38 (0.27, 0.52)	<0.001
Medium decrease-temporary	0.24 (0.17, 0.34)	<0.001	0.52 (0.44, 0.61)	<0.001
Fully adjusted¹				
High decrease-temporary	0.26 (0.10, 0.63)	<0.001	0.46 (0.29, 0.72)	<0.001
Medium decrease-temporary	0.24 (0.15, 0.39)	<0.001	0.58 (0.45, 0.74)	<0.001

Note

Abbreviations: OR, odds ratio; CI, confidence interval

1. Fully adjusted model simultaneously controlled for group membership of all other health behaviors (dietary fat intake, moderate to vigorous physical activity, sedentary time, and alcohol intake), age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN
2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² (“healthy weight”), who maintained a BMI between 25-35 kg/m² (“overweight/obese”), and who remained Class II-III obesity (BMI >35 kg/m², “severely obese”).

Table 21. Multinomial logistic regression of change in sedentary time trajectory and BMI trajectory

Behavior change trajectory groups (Referent=Low-stable)	BMI trajectory groups (Referent=Healthy weight)			
	Severely obese		Overweight/obese	
	OR (95% CI)	P	OR (95% CI)	P
Unadjusted				
High-stable	1.70 (1.16, 2.50)	0.01	1.94 (1.54, 2.45)	<0.001
Medium increase-stable	0.96 (0.66, 1.40)	0.84	1.23 (1.00, 1.53)	0.06
Medium decrease-stable	1.02 (0.71, 1.46)	0.94	1.27 (1.03, 1.56)	0.02
Fully adjusted¹				
High-stable	2.43 (1.39, 4.26)	<0.001	2.27 (1.62, 3.18)	<0.001
Medium increase-stable	0.90 (0.52, 1.56)	0.70	1.21 (0.89, 1.65)	0.22
Medium decrease-stable	1.21 (0.73, 2.01)	0.46	1.26 (0.93, 1.69)	0.13

Note

Abbreviations: OR, odds ratio; CI, confidence interval

1. Fully adjusted model simultaneously controlled for group membership of all other health behaviors (dietary fat intake, moderate to vigorous physical activity, sedentary time, and alcohol intake), age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN

2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² (“healthy weight”), who maintained a BMI between 25-35 kg/m² (“overweight/obese”), and who remained Class II-III obesity (BMI >35 kg/m², “severely obese”).

Table 22. Multinomial logistic regression of change in alcohol intake trajectory and BMI trajectory

Behavior change trajectory groups (Referent=Low-stable)	BMI trajectory groups (Referent= Healthy weight)			
	Severely obese		Overweight/obese	
	OR (95% CI)	P	OR (95% CI)	P
Unadjusted				
High decrease-temporary	0.12 (0.03, 0.51)	<0.001	0.65 (0.45, 0.95)	0.02
Medium decrease-temporary	0.29 (0.17, 0.48)	<0.001	0.54 (0.43, 0.68)	<0.001
Fully adjusted¹				
High decrease-temporary	0.16 (0.04, 0.70)	0.01	0.62 (0.36, 1.05)	0.07
Medium decrease-temporary	0.36 (0.19, 0.68)	<0.001	0.64 (0.47, 0.87)	<0.001

Note

Abbreviations: OR, odds ratio; CI, confidence interval; NE, not estimable

1. Fully adjusted model simultaneously controlled for group membership of all other health behaviors (dietary fat intake, moderate to vigorous physical activity, sedentary time, and alcohol intake), age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, and worsening of CIPN
2. Trajectory groups were labeled according to the clinical classification of BMI, including women who maintained a mean BMI less than 25 kg/m² (“healthy weight”), who maintained a BMI between 25-35 kg/m² (“overweight/obese”), and who remained Class II-III obesity (BMI >35 kg/m², “severely obese”).

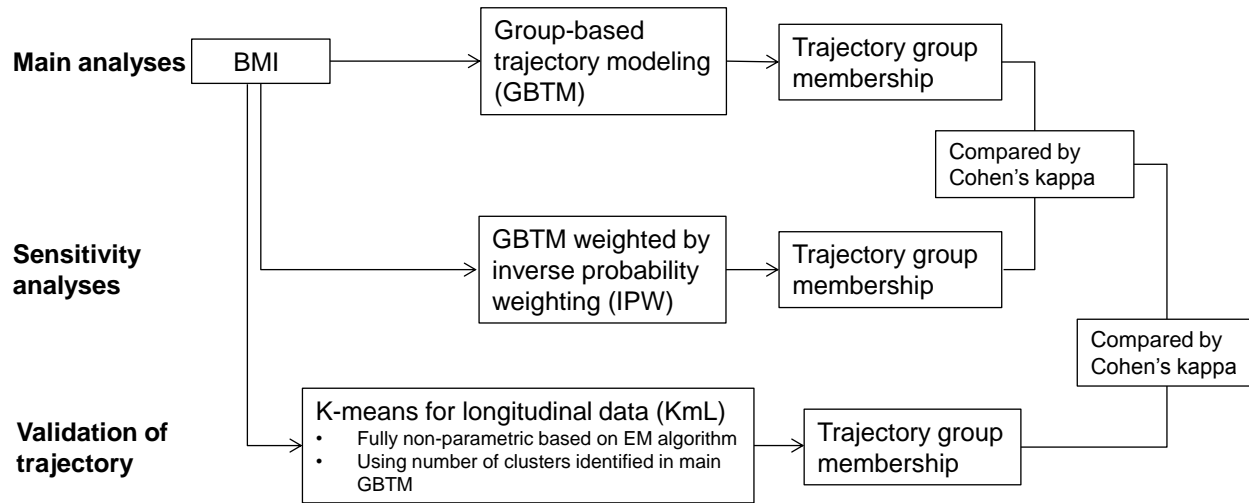


Figure 97. Analytical workflow of the trajectory analysis

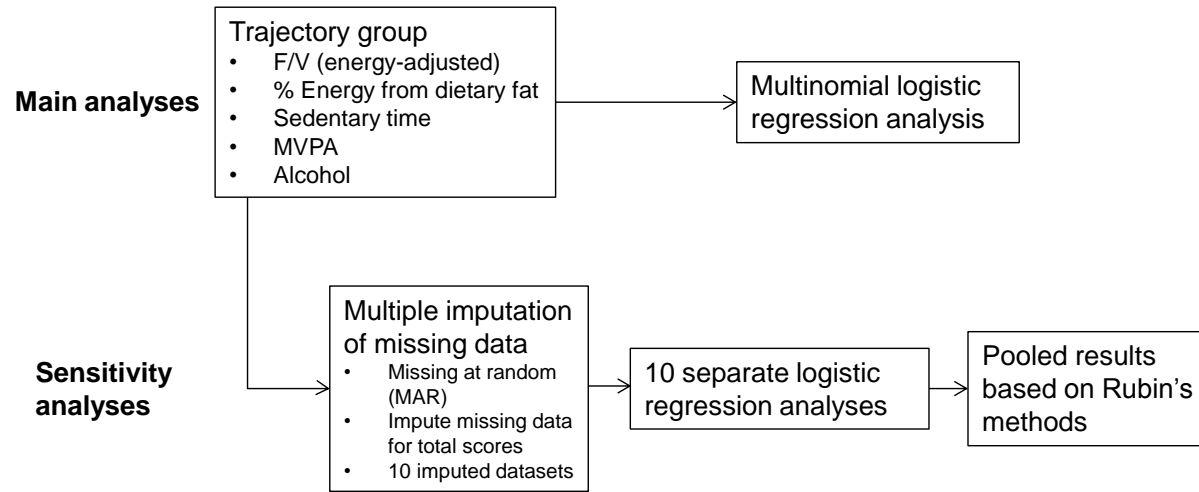


Figure 113. Analytical workflow to identify the predictors of BMI trajectory

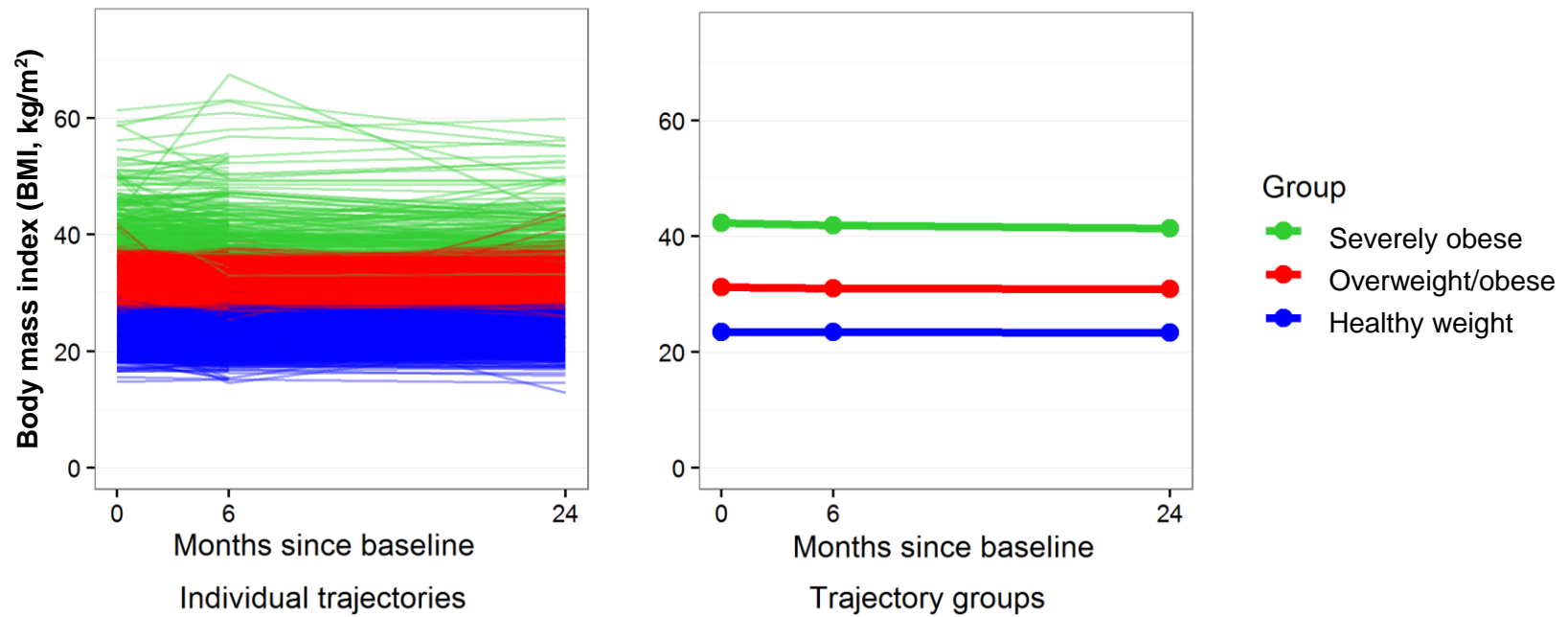


Figure 129. Trajectories of body mass index (BMI) after a breast cancer diagnosis among the Pathways Study participants. This figure shows the individual trajectories (left panel) and group mean trajectories (right panel) of BMI during the first 24 months following a BC diagnosis.

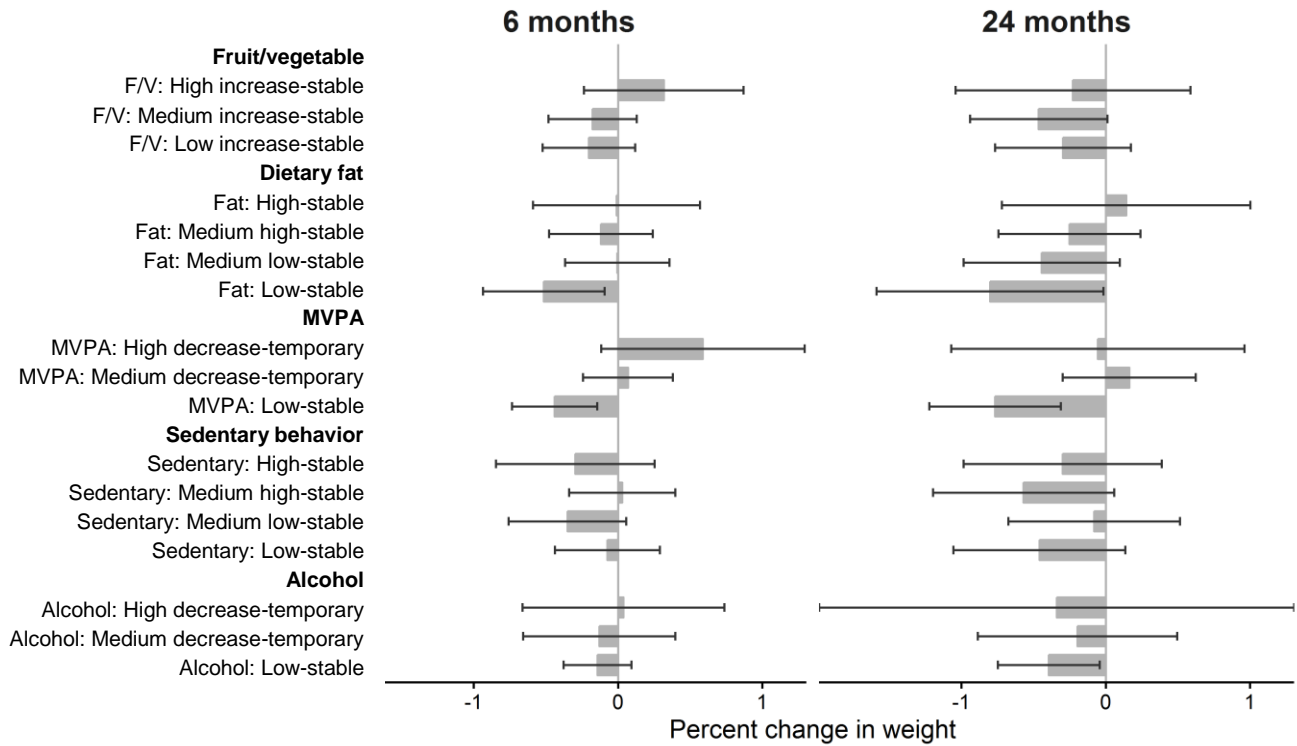


Figure 145. Mean percent weight change by behavior trajectory groups. The bars represent the mean percent of weight change in each behavior trajectory group. The lines represent the 95% confidence interval of means.

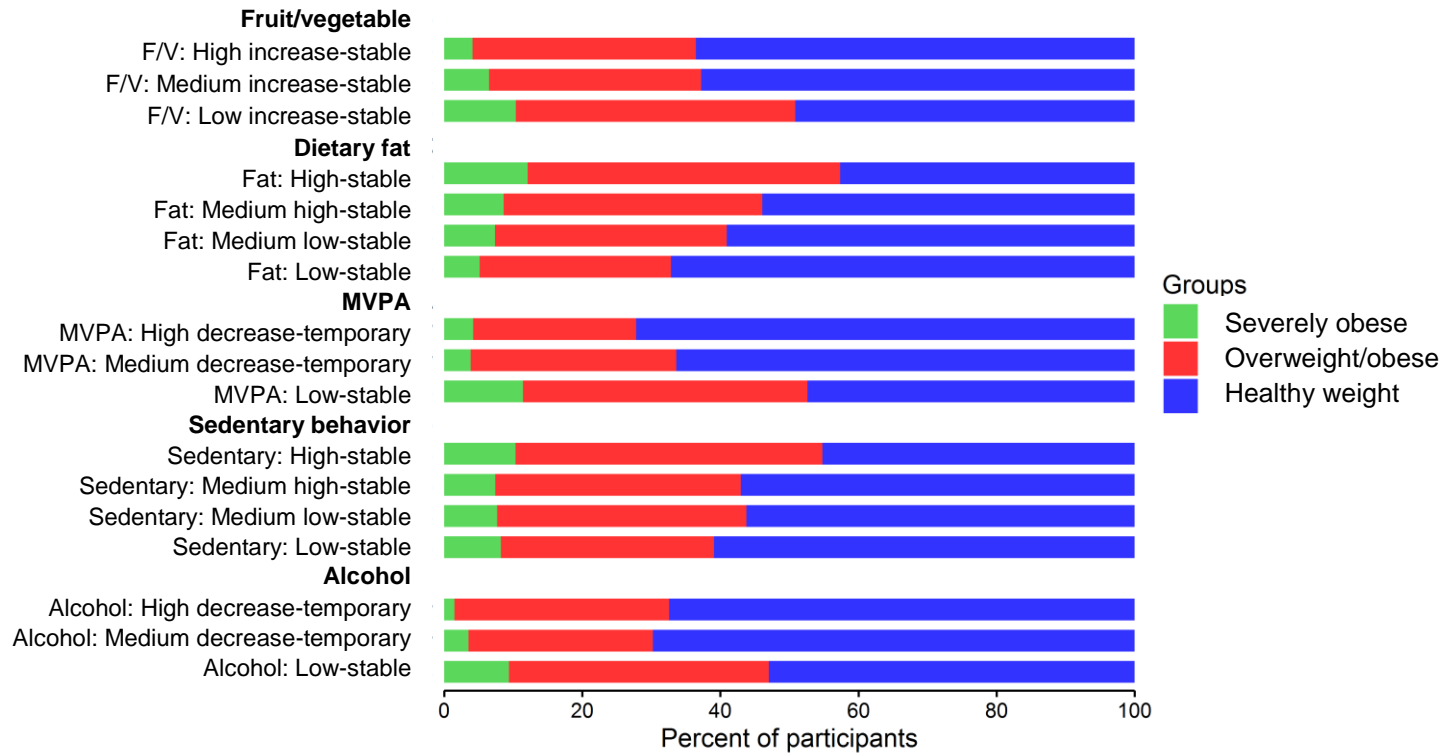


Figure 161. Distribution of BMI trajectory groups by behavior trajectory groups. The bars in the figure indicate the percent of women following each BMI trajectory, and color-coded according to the BMI group membership.

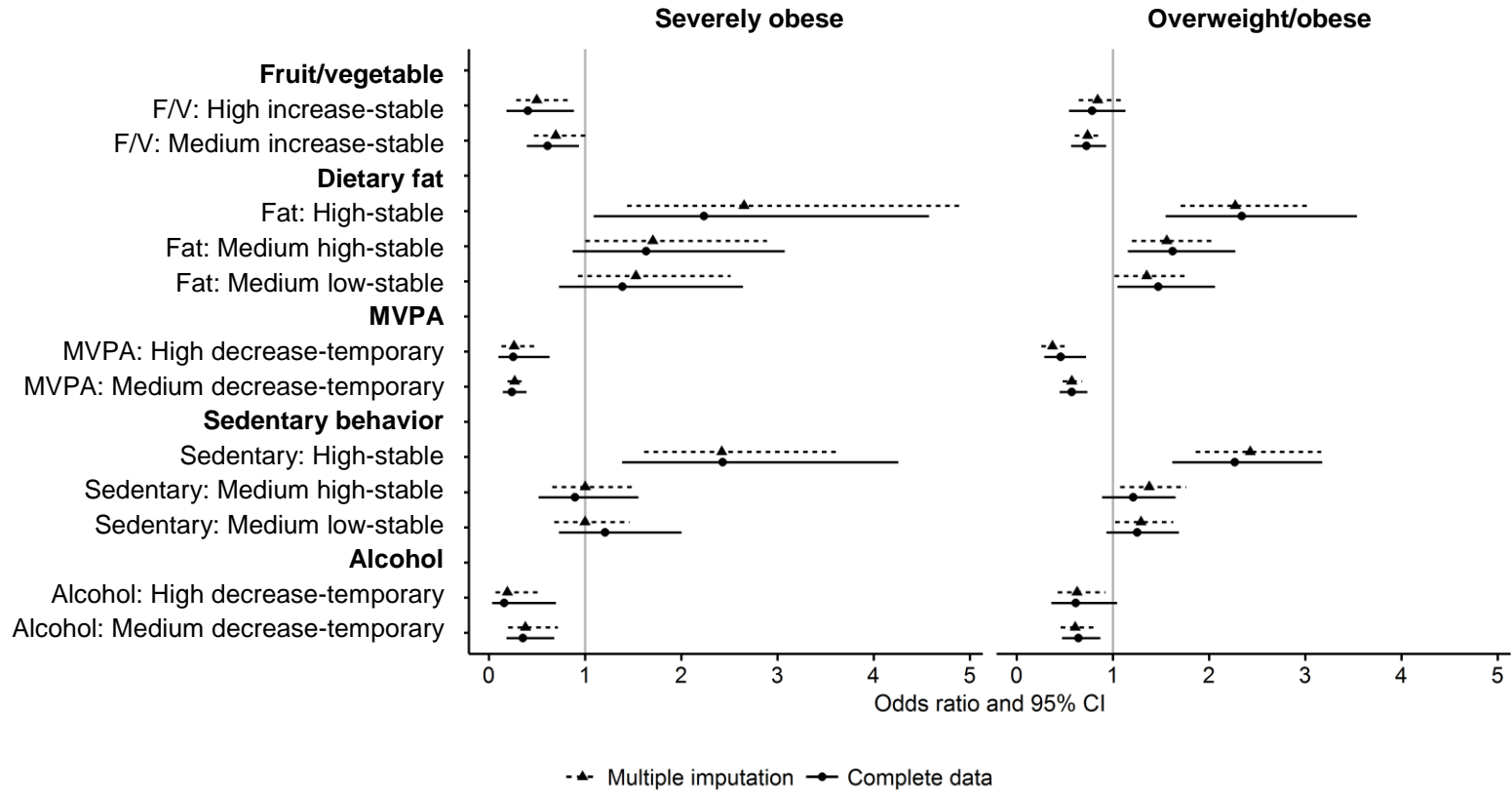


Figure 162. Multinomial logistic regression analyses under complete case analysis and multiple imputations. This figure displays the fully adjusted odds ratios of following each trajectory of BMI under the complete case analysis (solid line) and that under the multiple imputations (dash lines). The two analyses yielded similar associations of behavioral change trajectory and BMI trajectory.

CHAPTER 5: CONCLUSIONS

The overall goals of my dissertation were to test the hypotheses that breast cancer (BC) survivors follow distinct trajectories of health behaviors during the first 24 months after diagnosis, and that their behavior trajectories will be associated with trajectories of body mass index (BMI). Using data from the Pathways Study, a large population-based cohort study of women newly diagnosed a BC within the Kaiser Permanente Northern California network, my dissertation identified latent trajectories of health behaviors and BMI during the first 24 months after a BC diagnosis using two novel methods, the group based trajectory modeling and the K-means for longitudinal data analysis. This chapter summarizes the results and implications of my dissertation.

In Chapter Two, I conducted a systematic review of literature related to changes in diet (F/V, dietary fat), physical activity (time spent on MVPA and sedentary behaviors), drinking, and body weight after a BC diagnosis. A total of 2,552 publications that reported a longitudinal change in health behaviors among BC survivors were screened and 66 observational studies were included in a systematic review. These studies reported change in health behaviors/body weight from BC diagnosis to 6 months or up to 15 years after diagnosis, with the majority focusing on the first 1-2 years after diagnosis. There was strong evidence that women generally reduce alcohol intake and gain weight following a BC diagnosis. Furthermore, moderate evidence was found for a decrease in time spent on moderate to vigorous physical activities (MVPA) after a BC diagnosis. However, there was insufficient evidence to determine the change in fruit/vegetable (F/V) intake, dietary fat intake, and time spent on sedentary behaviors after a BC diagnosis. Moreover, most prior studies reported the mean changes in health behaviors; few studies have considered the heterogeneity of behavior changes among BC survivors. The understanding of the determinants of behavior change among BC survivors was also limited. This systematic review is one of the first to summarize and evaluate previous reports of changes in health behaviors after a BC diagnosis. The review suggested that there was relatively weak evidence to support the hypothesis that a cancer diagnosis would encourage women to engage in more health behaviors. Instead, most previous reports indicated that women made little to no change in diet and decreased engagement in exercise after a

diagnosis. The absence of spontaneous improvement in health behaviors suggests the importance of promoting health behaviors among BC survivors.

In Chapter Three, I analyzed the trajectory of diet (F/V and dietary fat intake), physical activity (MVPA and sedentary behavior), and alcohol intake from baseline to the 24-month follow-up in the Pathways Study. To identify the latent trajectory of health behaviors, I used a combination of semi-parametric, group-based trajectory modeling and non-parametric K-means for longitudinal data analysis. These methods classified women into subgroups based on the similarity of their behavior and BMI trajectories. This analysis identified three distinct trajectories of F/V intake (11% high increase-stable, 41% medium increase-stable, 48% low increase-stable), MVPA (7% high decrease-temporary, 35% medium decrease-temporary, 58% low stable) and alcohol intake (5% high decrease-stable, 16% medium decrease-temporary, and 79% low-stable), and four trajectories of dietary fat intake (14% high-stable, 35% medium high-stable, 35% medium low-stable, 17% low-stable) and sedentary behaviors (18% high-stable, 24% medium increase-stable, 27% medium decrease-stable, 31% low stable). However, this analysis did not identify the hypothesized weight gain or weight cycling groups. Compared to the low increase-stable F/V group, women who were in the high or medium increase-stable F/V group had higher education and income, higher dispositional optimism and perceived social support. Women who were in the medium high-stable dietary fat group were more likely to experience chemotherapy-induced peripheral neuropathy at 6 months after a BC diagnosis. For MVPA, women who were in the high or medium decrease-temporary trajectory groups had higher education and income, higher dispositional optimism and perceived social support. Women who were in the high-stable and medium decrease-stable sedentary behavior groups had higher education, lower income, and reported higher perceived social support. Finally, women who follow the high or medium decrease-temporary alcohol intake groups had higher education and income. These results identified subgroups of women who maintained unhealthy behaviors following a breast cancer diagnosis. The findings suggest that there are subgroups of women who may benefit from targeted efforts in effective health behavior education and promotion programs.

Chapter Four further analyzed BMI trajectory groups during the first 24 months after a BC diagnosis. The trajectory analysis showed very little change in BMI over the two-year period: the majority

(56%) of women maintained a healthy weight, 36% of women remained overweight/obese, and 8% women were severely obese. Compared to the healthy weight group, women who remained severely obese were less likely to maintain a high-F/V diet, less likely to engage in high level of MVPA, and less likely to maintain a high intake of alcohol over the two-year period. Moreover, women who remained severely obese were more likely to have maintained a high-fat diet and sedentary behavior. Similar to women who were in the high-stable group of BMI, membership in the overweight/obese trajectory group was also negatively associated with the maintenance of a high-F/V diet, high MVPA, and high alcohol intake, but positively associated with the maintenance of high-fat diet and high sedentary behavior. These associations were independent of demographic and clinical characteristics, psychosocial factors related to stress coping, cancer treatment received, and change in total energy intake. The results were robust to multiple imputations of missing data.

The results of my dissertation delineate the typical trajectories of health behaviors after a BC diagnosis, which may help identify women who could be classified as a high-risk group for maintaining an unfavorable lifestyle and thus would be particularly important targets for lifestyle counseling and interventions. Identifying the target population for health behavior promotion is an important first step to designing a successful behavior intervention among cancer survivors. A well-selected and implemented targeting method will maximize the health benefits from a diet and physical activity intervention by excluding patients who engage in sufficient health behaviors, while minimizing the cost by only including those who have the potential to benefit the most. In situations where educational and material resources to support a healthy lifestyle are not universally available to BC survivors in immediate need, targeted interventions can ensure optimal impact by directing limited resources to patients at the greatest risk of maintaining unhealthy lifestyles or losing healthy diet or exercise habit during and after cancer treatment. Currently, behavior interventions and programs of health behaviors cover a broad range of BC survivors and therefore are less specific to certain subgroups of women who engage in unhealthy behaviors. Improved targeting can lead to substantial reductions in cost associated with these interventions, without necessarily reducing their impact on those who could benefit the most. A previous behavior intervention tailored to Hispanic/Latina BC survivors, who have poor knowledge of and access to materials that sustain healthy lifestyle, proved highly effective in increasing intake of F/V.²⁹⁵⁻²⁹⁷

This analysis proposed new ways to identify the target population for behavior interventions. By depicting latent trajectories of health behaviors, future studies can potentially identify and directly target patients who are at high likelihood of following unfavorable trajectories of health behaviors. This analysis revealed that the level of health behavior at time of diagnosis is highly predictive of subsequent health behaviors during treatment and early survivorship after a BC diagnosis. For instance, a woman who engages in unhealthy behaviors at the time of cancer diagnosis is most likely to maintain an unfavorable lifestyle in the first 24 months after a BC diagnosis. Therefore, screening for health behavior at the time of cancer diagnosis could effectively identify targets to deliver behavior interventions. When direct measures of health behaviors are unavailable, the high-risk group could be identified based on a patient's demographic characteristics, such as education and household income, or based on the psychosocial response to stress due to cancer, such as depressive symptom and dispositional optimism.

This dissertation also provides strong evidence to support the association of persistently unhealthy behavior with the maintenance of high BMI after a BC diagnosis. Furthermore, the analysis suggested that there was a small but increasing trend in F/V intake over the first 24 months after a BC diagnosis, for all women irrespective of pre-diagnosis F/V intake. On the other hand, women generally reduced engagement in MVPA and reduced alcohol intake after a BC diagnosis, especially for women who reported high MVPA and alcohol intake pre-diagnosis. Identifying the population of BC survivors who do not engage in health lifestyle behaviors after a BC diagnosis could help future lifestyle interventions focus on a more specific target population, which may improve the efficiency of lifestyle interventions.

The results demonstrate that a high percentage of BC survivors did not adhere to the recommended level of health behaviors and patient-initiated behavior change was not evident during the first 24 months after diagnosis. Women who were of lower SES, had greater stress and fewer social support and experience cancer treatment side effect are most likely to maintain unhealthy behaviors. These findings provide strong evidence to support health behavior interventions among BC survivors. Interventions aimed at improvement of diet, physical activity levels and weight management have been implemented successfully among BC survivors.^{298,299} Dietary intervention studies utilizing face-to-face contact, print materials or telephone counseling reported an average increases of 0.6 servings per day of fruit and vegetable intake and an average of 7.3% decreases reduction in the percentage of calories from

fat.^{299,300} Supervised exercise as well as home-based exercise and telephone coaching have been successful in increasing physical activity levels, with increases seen up to 271 min/week.³⁰¹⁻³⁰³ Weight loss interventions, utilizing in person or telephone coaching have also been successful in this population with weight loss of up to 12.5 kg achieved.³⁰⁴⁻³⁰⁶ These studies demonstrate the potential for health behavior intervention following a BC diagnosis. However, access to these successful interventions remains limited. The majority of these interventions require training and resources that are not readily available to patients and clinical care providers. Currently, most health intervention studies targeting cancer survivors were conducted in developed countries, partly due to the limited resources for cancer screening and treatment in developing countries. For cancer survivors in developing countries, they also face limited resources to allow health education delivery and exercise coaching. Future studies are needed to evaluate effectiveness of intervention strategies that require limited resources and training to make such interventions readily accessible to patients and providers, and interventions that help cancer survivors overcome physical and psychosocial burdens.

My long-term research goal is to understand the effect of health behaviors on survival and cancer recurrence in Chinese cancer survivors. In China, the incidence of breast cancer has been increasing, with approximately 268,600 women diagnosed with breast cancer in 2015 alone.³⁰⁷ The five-year survival rate for breast cancer is approximately 73% in China, which is substantially lower than that in the US (90%).³⁰⁷ The increased BC risk among Chinese women may be partly due to the adoption of western dietary pattern, increased physical inactivity and higher obesity rate as a consequence of economic development. Therefore, promoting health behaviors among Chinese women diagnosed with breast cancer may reduce the risk of recurrence and other conditions related to unhealthy behaviors, and eventually improve overall survival.

Health behavior interventions targeting Chinese populations could take advantage of the advancement in information technology in China. The increasing availability of smartphones and popularity of social media have opened up new channels and tools for health education delivery. Previous studies suggest that it is feasible to deliver eHealth interventions to improve health literacy in various populations³⁰⁸, and social media may be an effective platform with promising applications in eHealth interventions³⁰⁹. Researchers have tested delivering culturally tailored learning modules about healthy

eating and physical activity to adolescents on Facebook, which has led to favorable changes in health behaviors.³¹⁰ In China, WeChat (Tencent Inc., Shenzhen, China) is the most popular social media platform, with more than 900 million active users worldwide. Like other social media platforms, WeChat offers a free instant multimedia messaging application for smartphone users. Researchers with a WeChat official account can deliver multimedia newsletters to WeChat users who subscribe to their accounts. Subscribers can read these newsletters, receive messages and interact with other subscribers via these official accounts. WeChat also has access to step count data if the users have pedometer-enabled smartphones, which allows researchers to collect physical activity data such as number of steps per day. However, it is unknown whether WeChat offers greater feasibility and effectiveness in promoting health behaviors in cancer survivors compared to traditional communication methods, such as print materials and telephone counseling.

Since the majority of BC survivors reported decreasing MVPA after diagnosis, it is important to develop effective and acceptable ways to motivate BC survivors to engage in adequate MVPA. Traditional intervention strategies to increase MVPA, such as supervised exercise sessions and gym membership incentives, are costly and often inflexible. In addition, these forms of exercise do not integrate fitness and recreation, and do not concurrently promote participant's physical and mental well-being. Square dance is a form of aerobic physical activity that gained increasing popularity among middle-aged and elderly populations in China. It integrates the advantages of social participation, exercise and psychological recreation. Compared to traditional exercise such as running and swimming, square dance is characterized by simple movements, little to no training and minimum risk. Additionally, it is not restricted by space, time, theme, or rhythm. As previous interventional studies showed, square dance could effectively reduce the depression and anxiety symptoms of middle-aged and old women in China, suggesting women may find mental relief through participation in square dance.³¹¹ Therefore, square dance is a promising and suitable way to increase MVPA among BC survivors and is worthy of further investigation.

Overall, based on the results of a trajectory analysis, my dissertation suggested that there is little change in lifestyle behaviors or BMI during the first 24 months following a BC diagnosis among early stage BC survivors enrolled in the Kaiser Permanente Northern California network – these behaviors

seem to be set based on pre-diagnosis behaviors. Women who had lower SES, lower dispositional optimism, and experience greater cancer treatment side effect were more likely to maintain an unhealthy lifestyle. Nevertheless, the trajectory analysis did not effectively identify subgroups of women with meaningful change in any health behavior, likely due to the small magnitude of change relative to the baseline and the relatively short period of observation. This analysis was also limited by the high loss to follow-up rate, self-reported behavior and anthropometric data, and limited generalizability to the population other than women within the KPNC network.

To validate the findings of this analysis and to gain better understanding of the variability of behavior change in BC survivors, future studies should examine the trajectory of health behaviors in other BC populations. The clinical implications of different trajectories of health behavior need to be investigated. As a new way to measure long-term health behavior pattern, behavior trajectories could be used to evaluate whether maintaining a healthy diet and engaging in exercise could reduce risk factors of mortality, including obesity, inflammation and metabolic disorders. Future studies should also evaluate the differences in BC prognosis and BC-specific and all-cause mortality among different behavior/BMI trajectories to better understand how health behaviors impact BC progression and survival.

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APPENDICES

Appendix 1. Search terms and results

Pubmed = 1,682 records

("diet"[Title/Abstract] OR "fruit"[Title/Abstract] OR "vegetable"[Title/Abstract] OR "dietary fat"[Title/Abstract] OR "total calories"[Title/Abstract] OR "caloric intake"[Title/Abstract] OR "alcohol"[Title/Abstract] OR "drinking"[Title/Abstract] OR "physical activity"[Title/Abstract] OR "moderate to vigorous activity"[Title/Abstract] OR "sedentary activity"[Title/Abstract] OR "exercise"[Title/Abstract] OR "smoking"[Title/Abstract] OR "cigarette"[Title/Abstract] OR "weight"[Title/Abstract] OR "body mass index"[Title/Abstract]) AND ("change"[Title/Abstract] OR "longitudinal change"[Title/Abstract] OR "difference"[Title/Abstract]) AND ("breast cancer"[Title/Abstract] OR "breast neoplasms"[Title/Abstract]) AND English[Language]

Web of Science = 37 records

(TI=(diet OR fruit OR vegetable OR dietary fat OR total calories OR caloric intake OR alcohol OR drinking OR physical activity OR moderate to vigorous activity OR sedentary activity OR exercise OR smoking OR cigarette OR weight OR body mass index) AND (change OR longitudinal change OR difference) AND (breast cancer survivors OR breast cancer diagnosis))) AND LANGUAGE: (English) AND DOCUMENT TYPES: (Article)

Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC.

PsychInfo = 6 records

Any Field : (Any Field : (breast cancer) OR Any Field : (breast neoplasms))) AND (Any Field : (change) OR Any Field : (longitudinal change) OR Any Field : (difference))) AND (Any Field : (diet) OR Any Field : (fruit) OR Any Field : (vegetable) OR Any Field : (dietary fat) OR Any Field : (total calories) OR Any

Field : (caloric intake) OR Any Field : (alcohol) OR Any Field : (drinking) OR Any Field : (physical activity) OR Any Field : (moderate to vigorous activity) OR Any Field : (sedentary activity) OR Any Field : (exercise) OR Any Field : (smoking) OR Any Field : (cigarette) OR Any Field : (weight) OR Any Field : (body mass index)))

Embase = 576 records

('diet' OR 'fruit' OR 'vegetable' OR 'dietary fat' OR 'total calories' OR 'caloric intake' OR 'alcohol' OR 'drinking' OR 'physical activity' OR 'moderate to vigorous activity' OR 'sedentary activity' OR 'exercise' OR 'smoking' OR 'cigarette' OR 'weight' OR 'body mass index') AND ("change" OR "longitudinal change" OR "difference") AND ('breast cancer survivors' OR 'breast cancer diagnosis')

Medline = 250 records

('diet' or 'fruit' or 'vegetable' or 'dietary fat' or 'total calories' or 'caloric intake' or 'alcohol' or 'drinking' or 'physical activity' or 'moderate to vigorous activity' or 'sedentary activity' or 'exercise' or 'smoking' or 'cigarette' or 'weight' or 'body mass index') and ("change" or "longitudinal change" or "difference") and ('breast cancer survivors' or 'breast cancer diagnosis')).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]; limit to English language

Appendix 2. Critical Appraisal Skills Program for cohort study⁵⁶

Appraisal questions

1. Was the cohort recruited in an acceptable way?

Look for selection bias which might compromise the generalizability of the findings:

Was the cohort representative of a defined population?

Was there something special about the cohort?

Was everybody included who should have been included?

2. Was the exposure accurately measured to minimize bias?

Look for measurement or classification bias:

Did they use subjective or objective measurements?

Do the measurements truly reflect what you want them to (have they been validated)?

Were all the subjects classified into exposure groups using the same procedure

3. Was the outcome accurately measured to minimize bias?

Look for measurement or classification bias:

Did they use subjective or objective measurements?

Do the measures truly reflect what you want them to (have they been validated)?

4. (a) Have the authors identified all important confounding factors?

List the ones you think might be important, that the author missed.

- (b) Have they taken account of the confounding factors in the design and/or analysis?

Look for restriction in design, and techniques e.g. modelling, stratified-, regression-, or sensitivity analysis to correct, control or adjust for confounding factors

5. Was the follow up of subjects long enough?

The good or bad effects should have had long enough to reveal themselves

6. (a) Was the follow up of subjects complete enough?
(b) Did the study assessed influence of missing data?

The persons that are lost to follow-up may have different outcomes than those available for assessment

In an open or dynamic cohort, was there anything special about the outcome of the people leaving, or the exposure of the people entering the cohort?

Appendix 3. Comparison of trajectory group characteristics: fruit/vegetable intake

Variable	High increase-stable (n=320)		Medium increase-stable (n=1180)		Low increase-stable (n=1365)		P ¹
	n	%	n	%	n	%	
Age							
<50	39	12%	202	17%	285	21%	<0.001
50-59	94	29%	293	25%	381	28%	
60-70	127	40%	402	34%	393	29%	
70+	60	19%	283	24%	306	22%	
Race/ethnicity							
White	240	75%	881	75%	862	63%	<0.001
Black	15	5%	64	5%	84	6%	
Asian	33	10%	129	11%	185	14%	
Hispanic	25	8%	81	7%	196	14%	
Other	7	2%	25	2%	38	3%	
Education							
HS or less	28	9%	110	9%	264	19%	<0.001
Some college	76	24%	372	32%	516	38%	
College or above	216	68%	696	59%	584	43%	
Household income							
<\$50K	122	38%	478	41%	659	48%	<0.001
\$50K-\$89K	162	51%	600	51%	556	41%	
\$90K+	36	11%	102	9%	150	11%	
Menopausal status							
Premenopausal	71	22%	304	26%	383	28%	0.08
Postmenopausal	249	78%	876	74%	982	72%	
Tumor stage							
I	189	59%	670	57%	741	54%	0.16
II	99	31%	396	34%	471	35%	
III	28	9%	98	8%	144	11%	
IV	4	1%	16	1%	9	1%	
Number of positive nodes							
0	8	3%	54	5%	64	5%	0.23
1	77	24%	261	22%	275	20%	
2+	235	73%	865	73%	1026	75%	
HER2 positivity							
Negative	271	89%	996	88%	1113	85%	0.06
Positive	34	11%	140	12%	198	15%	
ER/PR positivity							
Negative	53	17%	171	15%	222	16%	0.40
Positive	267	83%	1008	85%	1139	84%	
Surgery type							
Lumpectomy	162	51%	554	47%	605	44%	0.01
Mastectomy	156	49%	611	52%	756	55%	
None	2	1%	15	1%	4	0%	
Received chemotherapy							
Yes	135	42%	516	44%	669	49%	0.01
No	185	58%	661	56%	692	51%	
Received hormonal therapy							
Yes	225	71%	908	77%	1024	76%	0.04
No	94	29%	264	23%	332	24%	
Received radiation							

Yes	159	50%	558	47%	566	41%	<0.01
No	161	50%	622	53%	798	59%	
Depressive symptom							
Low	262	83%	924	80%	979	73%	<0.001
High	54	17%	234	20%	367	27%	
Dispositional optimism							
Low	175	55%	762	66%	961	71%	<0.001
High	141	45%	398	34%	386	29%	
Perceived social support							
Low	65	21%	358	31%	479	36%	<0.001
High	251	79%	803	69%	868	64%	
Worse physical well-being at 6 months							
No	230	79%	858	79%	928	76%	0.11
Yes	61	21%	222	21%	294	24%	
Worse CIPN at 6 months							
No	171	72%	532	64%	573	66%	0.07
Yes	65	28%	293	36%	297	34%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.
2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 4. Comparison of trajectory group characteristics: dietary fat intake

Variable	High-stable (n=392)		Medium high-stable (n=1002)		Medium low-stable (n=992)		Low-stable (n=479)		P-value ¹
	n	%	n	%	n	%	n	%	
Age									
<50	67	17%	191	19%	194	20%	74	15%	0.12
50-59	105	27%	265	26%	267	27%	131	27%	
60-70	144	37%	320	32%	315	32%	143	30%	
70+	76	19%	226	23%	216	22%	131	27%	
Race/ethnicity									
White	257	66%	688	69%	678	68%	360	75%	0.06
Black	26	7%	62	6%	56	6%	19	4%	
Asian	57	15%	132	13%	116	12%	42	9%	
Hispanic	41	10%	92	9%	118	12%	51	11%	
Other	11	3%	28	3%	24	2%	7	1%	
Education									
HS or less	61	16%	150	15%	131	13%	60	13%	0.52
Some college	142	36%	333	33%	330	33%	159	33%	
College or above	189	48%	519	52%	530	53%	258	54%	
Household income									
<\$50K	165	42%	450	45%	420	42%	224	47%	0.05
\$50K-\$89K	195	50%	466	47%	450	45%	207	43%	
\$90K+	32	8%	86	9%	122	12%	48	10%	
Menopausal status									
Premenopausal	99	25%	265	26%	280	28%	114	24%	0.30
Postmenopausal	293	75%	737	74%	712	72%	365	76%	
Tumor stage									
I	224	57%	516	51%	573	58%	287	60%	0.07
II	125	32%	368	37%	327	33%	146	30%	
III	40	10%	108	11%	83	8%	39	8%	
IV	3	1%	10	1%	9	1%	7	1%	
Number of positive nodes									
0	22	6%	37	4%	42	4%	25	5%	0.13
1	69	18%	206	21%	235	24%	103	22%	
2+	301	77%	759	76%	715	72%	351	73%	
HER2 positivity									
Negative	333	88%	827	86%	827	87%	393	86%	0.78
Positive	46	12%	136	14%	126	13%	64	14%	
ER/PR positivity									
Negative	54	14%	152	15%	169	17%	71	15%	0.40
Positive	338	86%	847	85%	821	83%	408	85%	
Surgery type									
Lumpectomy	181	46%	442	44%	476	48%	222	46%	0.58
Mastectomy	210	54%	551	55%	508	51%	254	53%	
None	1	0%	9	1%	8	1%	3	1%	
Received chemotherapy									
Yes	181	46%	480	48%	457	46%	202	42%	0.22
No	209	54%	521	52%	531	54%	277	58%	
Received hormonal therapy									
Yes	298	77%	766	77%	743	75%	350	73%	0.35
No	91	23%	225	23%	246	25%	128	27%	
Received radiation									

Yes	171	44%	439	44%	447	45%	226	47%	0.61
No	221	56%	563	56%	545	55%	252	53%	
Depressive symptom									
Low	309	80%	745	76%	739	75%	372	79%	0.14
High	79	20%	236	24%	244	25%	96	21%	
Dispositional optimism									
Low	248	64%	685	69%	648	66%	317	68%	0.19
High	139	36%	301	31%	334	34%	151	32%	
Perceived social support									
Low	131	34%	315	32%	316	32%	140	30%	0.68
High	257	66%	671	68%	666	68%	328	70%	
Worse physical well-being at 6 months									
No	273	77%	698	76%	703	78%	342	80%	0.52
Yes	81	23%	215	24%	195	22%	86	20%	
Worse CIPN at 6 months									
No	169	65%	435	63%	441	66%	231	73%	0.02
Yes	92	35%	254	37%	223	34%	86	27%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 5. Comparison of trajectory group characteristics: moderate to vigorous physical activity

Variable	High decrease-temporary (n=219)		High decrease-temporary (n=1045)		Low-stable (n=1736)		P ¹
	n	%	n	%	n	%	
Age							
<50	52	24%	203	19%	308	18%	<0.001
50-59	70	32%	297	28%	430	25%	
60-70	70	32%	354	34%	537	31%	
70+	27	12%	191	18%	461	27%	
Race/ethnicity							
White	160	73%	766	73%	1153	66%	<0.01
Black	12	5%	54	5%	116	7%	
Asian	21	10%	107	10%	227	13%	
Hispanic	18	8%	92	9%	205	12%	
Other	8	4%	26	2%	35	2%	
Education							
HS or less	21	10%	101	10%	304	18%	<0.001
Some college	70	32%	327	31%	619	36%	
College or above	128	58%	616	59%	811	47%	
Household income							
<\$50K	80	37%	401	38%	836	48%	<0.001
\$50K-\$89K	128	58%	552	53%	696	40%	
\$90K+	11	5%	92	9%	204	12%	
Menopausal status							
Premenopausal	73	33%	301	29%	421	24%	<0.01
Postmenopausal	146	67%	744	71%	1315	76%	
Tumor stage							
I	135	62%	597	57%	928	53%	<0.01
II	71	32%	358	34%	595	34%	
III	11	5%	86	8%	187	11%	
IV	2	1%	4	0%	26	1%	
Number of positive nodes							
0	9	4%	29	3%	93	5%	0.01
1	47	21%	244	23%	354	20%	
2+	163	74%	772	74%	1289	74%	
HER2 positivity							
Negative	189	90%	874	87%	1429	86%	0.37
Positive	22	10%	134	13%	231	14%	
ER/PR positivity							
Negative	32	15%	162	16%	279	16%	0.81
Positive	187	85%	882	84%	1453	84%	
Surgery type							
Lumpectomy	93	42%	489	47%	799	46%	0.06
Mastectomy	125	57%	554	53%	918	53%	
None	1	0%	2	0%	19	1%	
Received chemotherapy							
Yes	91	42%	486	47%	808	47%	0.34
No	128	58%	557	53%	922	53%	
Received hormonal therapy							
Yes	164	76%	780	75%	1306	76%	0.97
No	53	24%	256	25%	419	24%	
Received radiation							

Yes	100	46%	479	46%	762	44%	0.60
No	119	54%	566	54%	972	56%	
Depressive symptom							
Low	163	75%	810	79%	1276	75%	0.09
High	53	25%	217	21%	419	25%	
Dispositional optimism							
Low	123	57%	637	62%	1224	72%	<0.001
High	93	43%	391	38%	472	28%	
Perceived social support							
Low	57	26%	286	28%	608	36%	<0.001
High	159	74%	744	72%	1087	64%	
Worse physical well-being at 6 months							
No	153	80%	751	78%	1184	77%	0.67
Yes	39	20%	212	22%	352	23%	
Worse CIPN at 6 months							
No	105	70%	506	69%	727	64%	0.06
Yes	46	30%	229	31%	409	36%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 6. Comparison of trajectory group characteristics: sedentary activity

Variable	High-stable (n=536)		Medium increase-stable (n=728)		Medium decrease-stable (n=816)		Low-stable (n=917)		P ¹
	n	%	n	%	n	%	n	%	
Age									
<50	52	10%	144	20%	139	17%	225	25%	<0.001
50-59	101	19%	184	25%	217	27%	296	32%	
60-70	218	41%	239	33%	243	30%	260	28%	
70+	165	31%	161	22%	217	27%	136	15%	
Race/ethnicity									
White	443	83%	514	71%	561	69%	558	61%	<0.001
Black	24	4%	60	8%	51	6%	46	5%	
Asian	28	5%	74	10%	91	11%	160	17%	
Hispanic	24	4%	66	9%	84	10%	142	15%	
Other	17	3%	14	2%	29	4%	11	1%	
Education									
HS or less	55	10%	101	14%	121	15%	144	16%	<0.01
Some college	177	33%	230	32%	307	38%	303	33%	
College or above	303	57%	396	54%	388	48%	469	51%	
Household income									
<\$50K	261	49%	328	45%	353	43%	370	40%	0.03
\$50K-\$89K	225	42%	333	46%	365	45%	453	49%	
\$90K+	50	9%	67	9%	98	12%	94	10%	
Menopausal status									
Premenopausal	76	14%	199	27%	201	25%	315	34%	<0.001
Postmenopausal	460	86%	529	73%	615	75%	602	66%	
Tumor stage									
I	322	60%	386	53%	446	55%	509	56%	0.13
II	167	31%	255	35%	297	36%	302	33%	
III	43	8%	75	10%	66	8%	97	11%	
IV	4	1%	12	2%	7	1%	9	1%	
Number of positive nodes									
0	23	4%	28	4%	28	3%	51	6%	0.22
1	110	21%	147	20%	177	22%	211	23%	
2+	403	75%	553	76%	611	75%	655	71%	
HER2 positivity									
Negative	455	88%	595	85%	680	87%	761	86%	0.59
Positive	62	12%	102	15%	102	13%	120	14%	
ER/PR positivity									
Negative	78	15%	126	17%	125	15%	143	16%	0.57
Positive	456	85%	601	83%	691	85%	772	84%	
Surgery type									
Lumpectomy	287	54%	323	44%	365	45%	406	44%	0.01
Mastectomy	248	46%	400	55%	445	55%	501	55%	
None	1	0%	5	1%	6	1%	10	1%	
Received chemotherapy									
Yes	206	38%	365	51%	370	45%	440	48%	<0.001
No	330	62%	357	49%	445	55%	476	52%	
Received hormonal therapy									

Yes	400	75%	535	74%	622	76%	694	77%	0.60
No	134	25%	187	26%	192	24%	211	23%	
Received radiation									
Yes	273	51%	311	43%	351	43%	408	45%	0.02
No	263	49%	417	57%	464	57%	508	55%	
Depressive symptom									
Low	424	81%	538	75%	614	76%	673	76%	0.05
High	99	19%	183	25%	189	24%	214	24%	
Dispositional optimism									
Low	318	61%	484	67%	546	68%	629	71%	<0.01
High	205	39%	238	33%	259	32%	258	29%	
Perceived social support									
Low	134	26%	241	33%	249	31%	326	37%	<0.001
High	389	74%	482	67%	554	69%	563	63%	
Worse physical well-being at 6 months									
No	374	78%	502	76%	580	78%	633	78%	0.82
Yes	105	22%	156	24%	161	22%	180	22%	
Worse CIPN at 6 months									
No	254	67%	304	62%	367	65%	413	70%	0.05
Yes	124	33%	185	38%	195	35%	177	30%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 7. Comparison of trajectory group characteristics: alcohol intake

Variable	High decrease-temporary (n=137)		High decrease-temporary (n=459)		Low-stable (n=2269)		P-value ¹
	n	%	n	%	n	%	
Age							
<50	15	11%	79	17%	432	19%	0.02
50-59	49	36%	115	25%	604	27%	
60-70	49	36%	144	31%	729	32%	
70+	24	18%	121	26%	504	22%	
Race/ethnicity							
White	130	95%	392	85%	1461	64%	<0.001
Black	1	1%	17	4%	145	6%	
Asian	2	1%	17	4%	328	14%	
Hispanic	2	1%	23	5%	277	12%	
Other	2	1%	10	2%	58	3%	
Education							
HS or less	12	9%	38	8%	352	16%	<0.001
Some college	47	34%	135	29%	782	34%	
College or above	78	57%	285	62%	1133	50%	
Household income							
<\$50K	42	31%	167	36%	1050	46%	<0.001
\$50K-\$89K	87	64%	257	56%	974	43%	
\$90K+	8	6%	35	8%	245	11%	
Menopausal status							
Premenopausal	22	16%	119	26%	617	27%	0.02
Postmenopausal	115	84%	340	74%	1652	73%	
Tumor stage							
I	89	65%	269	59%	1242	55%	0.20
II	39	28%	143	31%	784	35%	
III	9	7%	43	9%	218	10%	
IV	0	0%	4	1%	25	1%	
Number of positive nodes							
0	1	1%	22	5%	103	5%	0.15
1	37	27%	95	21%	481	21%	
2+	99	72%	342	75%	1685	74%	
HER2 positivity							
Negative	119	89%	390	88%	1871	86%	0.33
Positive	15	11%	52	12%	305	14%	
ER/PR positivity							
Negative	21	15%	49	11%	376	17%	0.01
Positive	116	85%	410	89%	1888	83%	
Surgery type							
Lumpectomy	79	58%	227	49%	1015	45%	0.01
Mastectomy	58	42%	231	50%	1234	54%	
None	0	0%	1	0%	20	1%	
Received chemotherapy							
Yes	57	42%	183	40%	1080	48%	0.01
No	79	58%	275	60%	1184	52%	
Received hormonal therapy							

Yes	107	79%	364	79%	1686	75%	0.08
No	29	21%	94	21%	567	25%	
Received radiation							
Yes	71	52%	237	52%	975	43%	<0.001
No	66	48%	221	48%	1294	57%	
Depressive symptom							
Low	109	80%	359	80%	1697	76%	0.19
High	28	20%	92	20%	535	24%	
Dispositional optimism							
Low	79	58%	294	65%	1525	68%	0.02
High	58	42%	160	35%	707	32%	
Perceived social support							
Low	35	26%	128	28%	739	33%	0.03
High	102	74%	325	72%	1495	67%	
Worse physical well-being at 6 months							
No	104	82%	348	82%	1564	77%	0.04
Yes	23	18%	78	18%	476	23%	
Worse CIPN at 6 months							
No	61	66%	233	72%	982	65%	0.05
Yes	31	34%	91	28%	533	35%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; CIPN, chemotherapy-induced peripheral neuropathy

1. Chi-squared test determined whether the distributions of demographic, clinical and psychosocial characteristics were independent of trajectory groups.

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 8. Multinomial logistic regression of tumor characteristics and treatment and health behavior change trajectory

Predictors	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Fruit/vegetable intake trajectory groups (referent group=low increase-stable)						
	High increase-stable		Medium increase-stable			
Stage						
Stage II vs. Stage I	0.99 (0.67, 1.49)	0.98	1.08 (0.84, 1.41)	0.54		
Stage III vs. Stage I	1.07 (0.56, 2.04)	0.83	0.84 (0.55, 1.28)	0.42		
Stage IV vs. Stage I	3.73 (0.68, 20.41)	0.13	1.83 (0.51, 6.64)	0.36		
Positive node removed						
1 vs. 0	2.58 (0.80, 8.36)	0.11	1.36 (0.73, 2.51)	0.33		
2+ vs. 0	2.73 (0.88, 8.5)	0.08	1.22 (0.68, 2.19)	0.50		
ER/PR						
Positive vs. negative	1.45 (0.78, 2.68)	0.24	0.85 (0.54, 1.33)	0.47		
Surgery						
Mastectomy vs. lumpectomy	0.81 (0.56, 1.17)	0.27	1.02 (0.80, 1.3)	0.87		
None vs. lumpectomy	1.20 (0.08, 18.69)	0.89	3.83 (0.66, 22.18)	0.13		
Chemotherapy (yes vs. no)	1.38 (0.89, 2.13)	0.15	1.16 (0.87, 1.55)	0.31		
Hormonal therapy (yes vs. no)	1.85 (1.14, 3)	0.01	0.90 (0.62, 1.31)	0.59		
Radiation (yes vs. no)	1.06 (0.73, 1.56)	0.75	0.83 (0.65, 1.07)	0.15		
Dietary fat intake trajectory groups (referent group=low-stable)						
	High-stable		Medium high-stable		Medium low-stable	
Stage						
Stage II vs. Stage I	1.30 (0.84, 2.02)	0.25	1.41 (0.98, 2.03)	0.06	1.05 (0.73, 1.52)	0.79
Stage III vs. Stage I	1.12 (0.56, 2.23)	0.75	1.05 (0.60, 1.85)	0.86	0.82 (0.46, 1.47)	0.50
Stage IV vs. Stage I	0.56 (0.09, 3.57)	0.54	0.53 (0.14, 2.08)	0.36	0.46 (0.10, 2.03)	0.30
Positive node removed						
1 vs. 0	0.79 (0.32, 1.97)	0.61	1.39 (0.64, 3.04)	0.41	2.37 (1.01, 5.56)	0.05
2+ vs. 0	0.91 (0.39, 2.14)	0.84	1.43 (0.69, 2.99)	0.34	2.22 (0.98, 4.99)	0.05
ER/PR						
Positive vs. negative	0.81 (0.39, 1.67)	0.57	0.65 (0.35, 1.2)	0.17	0.57 (0.31, 1.04)	0.07
Surgery						
Mastectomy vs. lumpectomy	1.04 (0.70, 1.56)	0.84	1.04 (0.75, 1.45)	0.81	0.79 (0.57, 1.1)	0.17
None vs. lumpectomy	0.76 (0.05, 11.37)	0.85	2.55 (0.38, 17.19)	0.34	0.96 (0.10, 9.12)	0.97
Chemotherapy (yes vs. no)	1.12 (0.69, 1.81)	0.64	1.06 (0.72, 1.57)	0.76	1.07 (0.72, 1.59)	0.73
Hormonal therapy (yes vs. no)	1.05 (0.59, 1.86)	0.88	0.74 (0.46, 1.19)	0.21	0.83 (0.52, 1.34)	0.45
Radiation (yes vs. no)	0.97 (0.64, 1.47)	0.88	1.11 (0.79, 1.55)	0.56	1.09 (0.78, 1.54)	0.61
Moderate to vigorous physical activity trajectory groups (referent group=low-stable)						
	High decrease-temporary		Medium decrease-temporary			
Stage						
Stage II vs. Stage I	0.82 (0.51, 1.3)	0.40	1.04 (0.81, 1.34)	0.76		
Stage III vs. Stage I	0.35 (0.14, 0.86)	0.02	0.72 (0.48, 1.09)	0.12		
Stage IV vs. Stage I	0.77 (0.14, 4.17)	0.76	0.31 (0.07, 1.48)	0.14		
Positive node removed						
1 vs. 0	0.78 (0.27, 2.2)	0.63	2.50 (1.24, 5.04)	0.01		
2+ vs. 0	0.87 (0.33, 2.3)	0.78	2.03 (1.03, 3.99)	0.04		
ER/PR						
Positive vs. negative	0.74 (0.32, 1.67)	0.47	1.13 (0.74, 1.74)	0.56		
Surgery						
Mastectomy vs. lumpectomy	1.50 (0.97, 2.32)	0.07	1.08 (0.86, 1.37)	0.51		
None vs. lumpectomy	0.73 (0.07, 7.77)	0.79	NE	NE		
Chemotherapy (yes vs. no)	1.75 (1.06, 2.89)	0.03	1.11 (0.84, 1.46)	0.47		
Hormonal therapy (yes vs. no)	0.71 (0.35, 1.43)	0.34	1.10 (0.77, 1.57)	0.59		
Radiation (yes vs. no)	1.17 (0.75, 1.84)	0.48	1.09 (0.86, 1.4)	0.47		
Sedentary time trajectory groups (referent group=low-stable)						
	High-stable		Medium increase-stable		Medium decrease-stable	
Stage						
Stage II vs. Stage I	0.85 (0.59, 1.21)	0.36	0.89 (0.64, 1.23)	0.48	0.94 (0.69, 1.28)	0.69
Stage III vs. Stage I	0.78 (0.44, 1.38)	0.39	0.77 (0.47, 1.27)	0.31	0.50 (0.30, 0.84)	0.01
Stage IV vs. Stage I	1.32 (0.24, 7.14)	0.75	1.95 (0.47, 8.15)	0.36	1.26 (0.30, 5.31)	0.75
Positive node removed						
1 vs. 0	1.29 (0.56, 2.96)	0.55	1.74 (0.80, 3.79)	0.17	1.43 (0.69, 2.95)	0.33
2+ vs. 0	1.81 (0.82, 3.97)	0.14	2.00 (0.95, 4.19)	0.07	1.62 (0.81, 3.21)	0.17
ER/PR						
Positive vs. negative	0.94 (0.52, 1.7)	0.83	1.08 (0.63, 1.85)	0.78	0.86 (0.51, 1.48)	0.59
Surgery						
Mastectomy vs. lumpectomy	0.87 (0.63, 1.21)	0.41	1.10 (0.82, 1.48)	0.53	1.06 (0.80, 1.42)	0.67
None vs. lumpectomy	NE	NE	0.48 (0.08, 2.9)	0.42	0.72 (0.14, 3.62)	0.69
Chemotherapy (yes vs. no)	0.85 (0.57, 1.26)	0.42	0.77 (0.54, 1.09)	0.14	0.81 (0.58, 1.14)	0.23
Hormonal therapy (yes vs. no)	1.03 (0.63, 1.68)	0.90	1.13 (0.72, 1.78)	0.60	0.78 (0.50, 1.23)	0.29
Radiation (yes vs. no)	1.02 (0.72, 1.43)	0.92	1.15 (0.84, 1.56)	0.39	1.16 (0.86, 1.57)	0.32
Alcohol intake trajectory groups (referent group=low-stable)						
	High decrease-temporary		Medium decrease-temporary			
Stage						
Stage II vs. Stage I	0.69 (0.38, 1.27)	0.23	0.89 (0.64, 1.25)	0.51		
Stage III vs. Stage I	0.95 (0.37, 2.41)	0.91	0.87 (0.50, 1.52)	0.63		

Stage IV vs. Stage I	NE	NE	1.34 (0.37, 4.8)	0.65
Positive node removed				
1 vs. 0	NE	NE	0.80 (0.38, 1.68)	0.56
2+ vs. 0	NE	NE	0.83 (0.41, 1.68)	0.60
ER/PR				
Positive vs. negative	0.75 (0.26, 2.19)	0.60	1.36 (0.77, 2.41)	0.29
Surgery				
Mastectomy vs. lumpectomy	0.55 (0.33, 0.94)	0.03	1.02 (0.75, 1.38)	0.90
None vs. lumpectomy	NE	NE	0.39 (0.04, 3.77)	0.42
Chemotherapy (yes vs. no)	1.44 (0.76, 2.73)	0.26	1.19 (0.83, 1.72)	0.34
Hormonal therapy (yes vs. no)	0.60 (0.24, 1.47)	0.26	0.97 (0.62, 1.5)	0.88
Radiation (yes vs. no)	1.38 (0.80, 2.39)	0.25	0.79 (0.58, 1.08)	0.14

Note

Abbreviations: OR, odds ratio; CI, confidence interval; NE, not estimable

1. Other variables included in the model were age, race, menopausal status, baseline depressive symptoms, dispositional optimism, social support, worsening of physical well-being chemotherapy induced peripheral neuropathy

2. Trajectory groups were labeled by the relative level of baseline behavior (high, medium, low), direction of change (increase or decrease), and the persistence of change (temporary or stable).

Appendix 9. Population characteristics comparing early vs. late enrollees

Variable	0-2 months after diagnosis (n=2447)		2-3 months after diagnosis (n=1512)		3+ months after diagnosis (n=546)		P ¹
	n	%	n	%	n	%	
Age							
<50	523	21%	345	23%	128	23%	0.78
50-59	715	29%	437	29%	164	30%	
60-70	712	29%	428	28%	157	29%	
70+	497	20%	302	20%	97	18%	
Race/ethnicity							
White	1622	66%	934	62%	338	62%	0.12
Black	171	7%	137	9%	50	9%	
Asian	303	12%	204	13%	71	13%	
Hispanic	293	12%	194	13%	70	13%	
Other	58	2%	43	3%	17	3%	
Education							
HS or less	397	16%	230	15%	80	15%	0.44
Some college	832	34%	528	35%	208	38%	
College or above	1211	50%	753	50%	258	47%	
Household income							
<\$50K	1066	44%	656	43%	227	42%	0.92
\$50K-\$89K	1096	45%	674	45%	250	46%	
\$90K+	285	12%	182	12%	69	13%	
Menopausal status							
Premenopausal	729	30%	457	30%	166	30%	0.94
Postmenopausal	1718	70%	1055	70%	380	70%	
Tumor stage							
I	1333	54%	793	52%	306	56%	0.80
II	837	34%	543	36%	181	33%	
III	240	10%	149	10%	50	9%	
IV	37	2%	27	2%	9	2%	
Number of positive nodes							
0	118	5%	66	4%	18	3%	0.35
1	538	22%	312	21%	128	23%	
2+	1791	73%	1134	75%	400	73%	
HER2 positivity							
Negative	2022	87%	1242	86%	462	88%	0.51
Positive	315	13%	209	14%	66	13%	
ER/PR positivity							
Negative	410	17%	252	17%	89	16%	0.97
Positive	2036	83%	1257	83%	456	84%	

Surgery type							
Lumpectomy	1151	47%	643	43%	223	41%	0.01
Mastectomy	1266	52%	852	56%	319	58%	
None	30	1%	17	1%	4	1%	
Received chemotherapy							
Yes	1181	48%	741	49%	223	41%	<0.01
No	1257	52%	770	51%	320	59%	
Received hormonal therapy							
Yes	1836	76%	1104	74%	397	73%	0.29
No	594	24%	397	26%	144	27%	
Received radiation							
Yes	1080	44%	654	43%	238	44%	0.87
No	1367	56%	857	57%	307	56%	
Depressive symptom							
Low	1730	74%	1047	73%	372	74%	0.85
High	610	26%	385	27%	132	26%	
Dispositional optimism							
Low	1607	69%	977	68%	361	71%	0.43
High	738	31%	456	32%	146	29%	
Perceived social support							
Low	777	33%	449	31%	168	33%	0.47
High	1569	67%	985	69%	336	67%	
Worse PWB at 6 months							
No	1169	76%	691	77%	241	84%	0.02
Yes	365	24%	201	23%	47	16%	
Worse CIPN at 6 months							
No	670	64%	490	67%	190	73%	0.02
Yes	380	36%	241	33%	70	27%	

Note

Abbreviations: HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor

1. Chi-squared test compared the distribution of demographic, clinical and psychosocial characteristics between participants at baseline and follow-up

Appendix 10. Exclusion of extreme diet data based on total energy intake

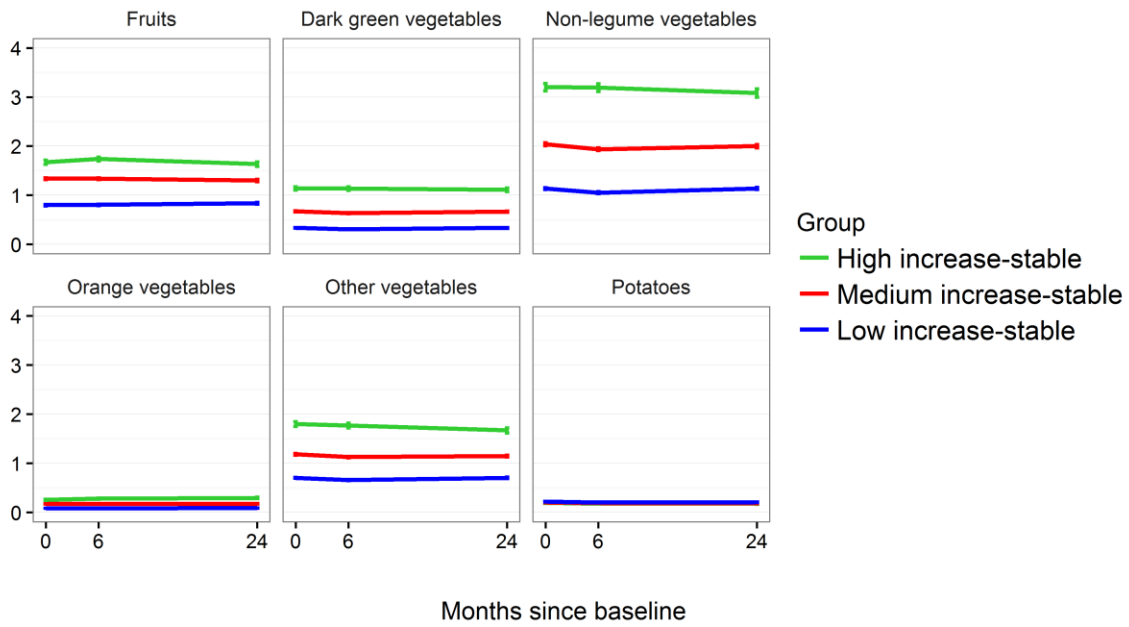
	Mean total energy intake (Kcal/day)	Standard deviation (Kcal/day)	Mean+3*SD	N excluded
Baseline	1483.8	638.2	3398.3	51
6 months	1362.6	574.0	3084.6	27
24 months	1377.8	599.2	3175.2	21

Appendix 11. Agreement between diet trajectory before and after exclusion of extreme diet data

Trajectory groups after excluding extreme energy intake						
Trajectory groups using all data	Fruit/vegetable	High increase-stable	Medium increase-stable	Low increase-stable	Kap pa	
	High increase-stable	317	3	0	0.99	
	Medium increase-stable	1	1150	2		
	Low increase-stable	0	12	1321		
	Dietary fat	High-stable	Medium high-stable	Medium low-stable	Low-stable	Kap pa
	High-stable	130	0	0	0	0.98
	Medium high-stable	0	1087	0	0	
	Medium low-stable	0	27	1298	0	
	Low-stable	0	0	8	256	
	Alcohol intake	High decrease-temporary	Medium decrease-temporary	Low-stable	Kap pa	
	High decrease-temporary	128	0	0	0.99	
	Medium decrease-temporary	4	454	0		
	Low-stable	0	1	2219		

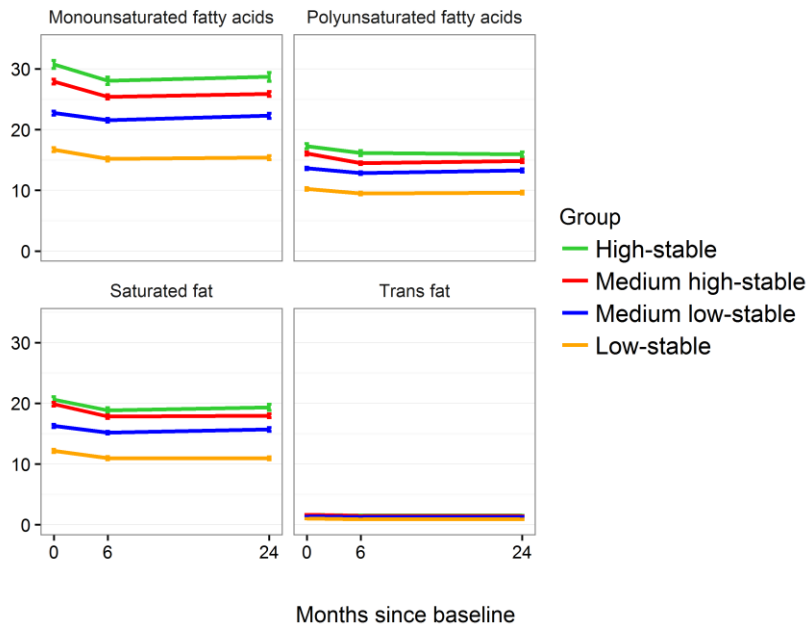
A

Change in each subcategory of fruit/vegetable intake (servings/day)



B

Change in each subcategory of dietary fat intake (grams/day)

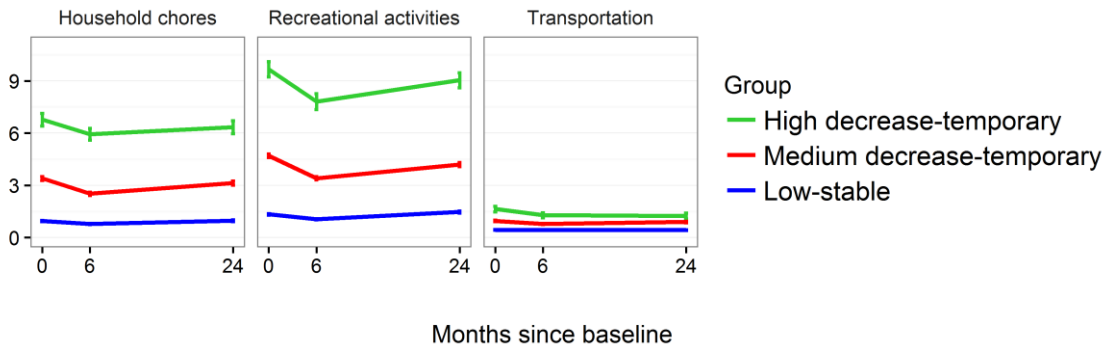


Appendix 12. Average change in subcategories of diet and physical activity by behavior change trajectories.

The figure shows the mean and 95% CI of changes in each subcategory of fruit/vegetable (A) and dietary fat (B) by behavioral change trajectories.

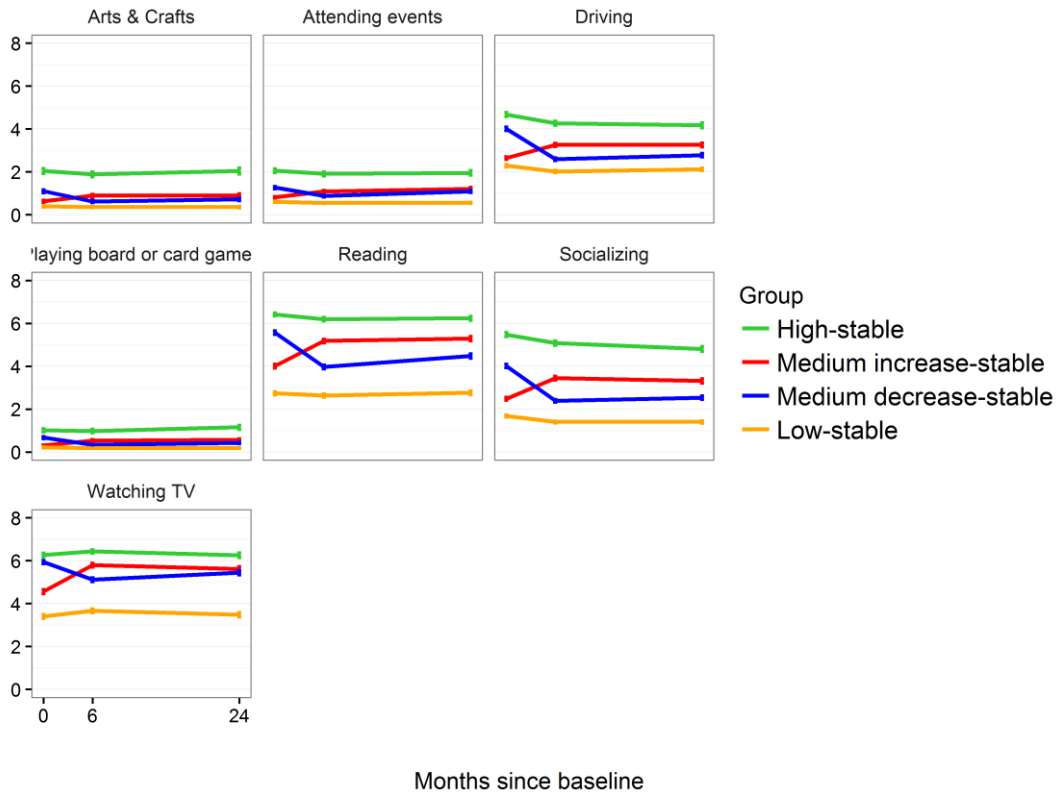
A

Change in time spent on each subcategory of moderate to vigorous activities (hours/week)



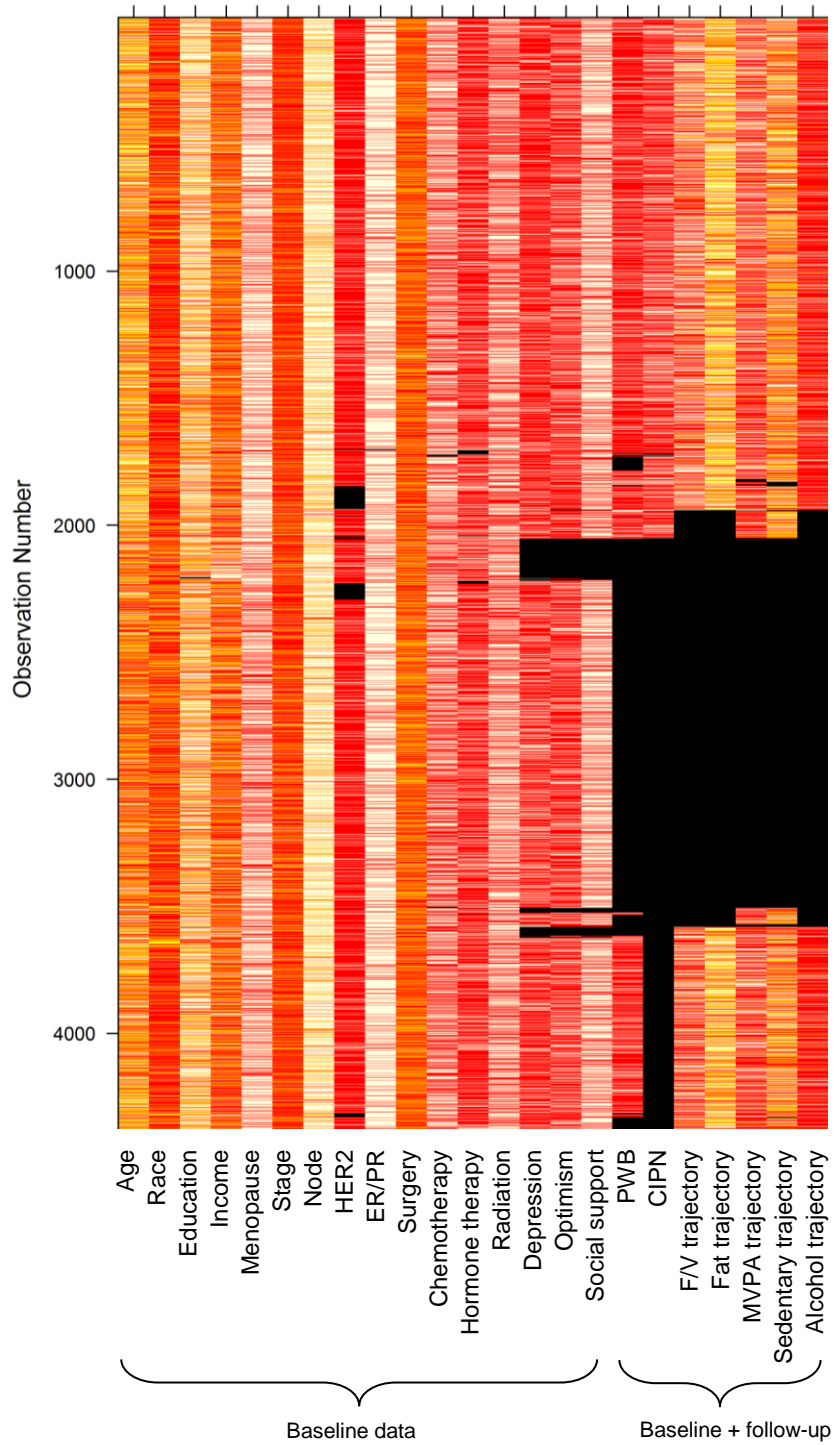
B

Change in time spent on each subcategory of sedentary activities (hours/week)



Appendix 13. Average change in subcategories of physical activity by behavior change trajectories.

The figure shows the mean and 95% CI of changes in each subcategory of moderate to vigorous physical activity (A) and sedentary behavior (B) by behavioral change trajectories.



Appendix 14. Missing data pattern for key analytical variables.

The figure displays the overall pattern of missing data for the 4505 participants in the Pathways Study. The color of each pixel represents the standardized values of each variable, with darker color indicating higher standardized value. Missing data points are shown as a black pixel. Observations are clustered by their missing data patterns.

Chapter 4 APPENDICES

Appendix 15. Linear regression analysis of BMI at 6 and 24 months following a breast cancer diagnosis

Behavior trajectory groups	6 months				24 months			
	Minimally adjusted ¹		Fully adjusted ²		Minimally adjusted ¹		Fully adjusted ²	
	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P	Difference (95% CI)	P
Fruit/vegetable (ref=Low increase-stable)								
High increase-stable	0.27 (-0.30, 0.84)	0.35	0.52 (-0.21, 1.25)	0.16	-0.33 (-1.14, 0.48)	0.42	-0.30 (-1.23, 0.64)	0.53
Medium increase-stable	-0.15 (-0.52, 0.22)	0.42	0.03 (-0.46, 0.53)	0.89	-0.43 (-0.97, 0.11)	0.12	-0.63 (-1.28, 0.02)	0.06
Dietary fat (ref=Low-stable)								
High-stable	0.65 (0.01, 1.29)	0.05	0.68 (-0.14, 1.50)	0.10	1.32 (0.41, 2.23)	<0.001	1.12 (0.06, 2.17)	0.04
Medium high-stable	0.50 (-0.01, 1.02)	0.05	0.42 (-0.25, 1.08)	0.22	0.93 (0.19, 1.67)	0.01	0.32 (-0.54, 1.19)	0.46
Medium low-stable	0.43 (-0.09, 0.95)	0.10	0.30 (-0.35, 0.96)	0.37	0.46 (-0.28, 1.20)	0.22	0.60 (-0.26, 1.45)	0.17
Moderate to vigorous physical activity (ref=Low-stable)								
High decrease-temporary	0.46 (-0.24, 1.17)	0.19	0.45 (-0.42, 1.33)	0.31	0.02 (-0.95, 1.00)	0.97	-0.14 (-1.26, 0.97)	0.80
Medium decrease-temporary	0.21 (-0.17, 0.60)	0.28	0.18 (-0.31, 0.67)	0.48	0.30 (-0.25, 0.86)	0.28	0.05 (-0.59, 0.68)	0.88
Sedentary activity (ref=Low-stable)								
High-stable	-0.02 (-0.54, 0.51)	0.95	0.26 (-0.42, 0.93)	0.46	0.57 (-0.19, 1.32)	0.14	0.89 (0.03, 1.75)	0.04
Medium high-stable	0.16 (-0.32, 0.63)	0.52	0.23 (-0.38, 0.84)	0.45	0.00 (-0.69, 0.70)	0.99	0.09 (-0.72, 0.90)	0.83
Medium low-stable	-0.11 (-0.57, 0.35)	0.64	0.00 (-0.58, 0.59)	1.00	0.45 (-0.21, 1.12)	0.18	0.29 (-0.47, 1.04)	0.45
Alcohol (ref=Low-stable)								
High decrease-temporary	0.18 (-0.63, 0.98)	0.67	0.01 (-1.06, 1.07)	0.99	-0.06 (-1.22, 1.10)	0.92	0.15 (-1.25, 1.56)	0.83
Medium decrease-temporary	-0.14 (-0.61, 0.33)	0.56	-0.11 (-0.71, 0.49)	0.72	0.08 (-0.59, 0.75)	0.81	0.01 (-0.76, 0.78)	0.99

Note

Abbreviations: CI, confidence interval

1. The minimally adjusted analysis controlled for baseline weight

2. The fully adjusted analysis controlled for age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline depressive symptom, worsening of physical well-being, and worsening of CIPN at 6 months

Appendix 16. Multinomial logistic regression of change in dietary trajectory and BMI trajectory after exclusion of extreme dietary data and adjusted for baseline total energy intake

Behavior trajectory groups	BMI trajectory groups (Referent=Healthy weight)			
	Severely obese		Overweight/obese	
	OR (95% CI)	P	OR (95% CI)	P
Fruit/vegetable (ref=Low increase-stable)				
High increase-stable	0.42 (0.37, 0.48)	<0.01	0.81 (0.58, 1.14)	0.23
High decrease-stable	0.62 (0.43, 0.91)	0.01	0.68 (0.54, 0.87)	<0.01
Dietary fat (ref=Low-stable)				
High increase-stable	2.34 (2.11, 2.60)	<0.01	2.24 (1.76, 2.86)	<0.01
Low increase-stable	2.14 (1.72, 2.66)	<0.01	1.51 (1.20, 1.90)	<0.01
High decrease-stable	1.30 (1.03, 1.64)	0.03	1.22 (0.97, 1.53)	0.09
Alcohol intake (ref=Low-stable)				
High increase-stable	0.18 (0.18, 0.18)	<0.01	0.51 (0.36, 0.73)	<0.01
High decrease-stable	0.33 (0.31, 0.35)	<0.01	0.57 (0.43, 0.78)	<0.01

Note

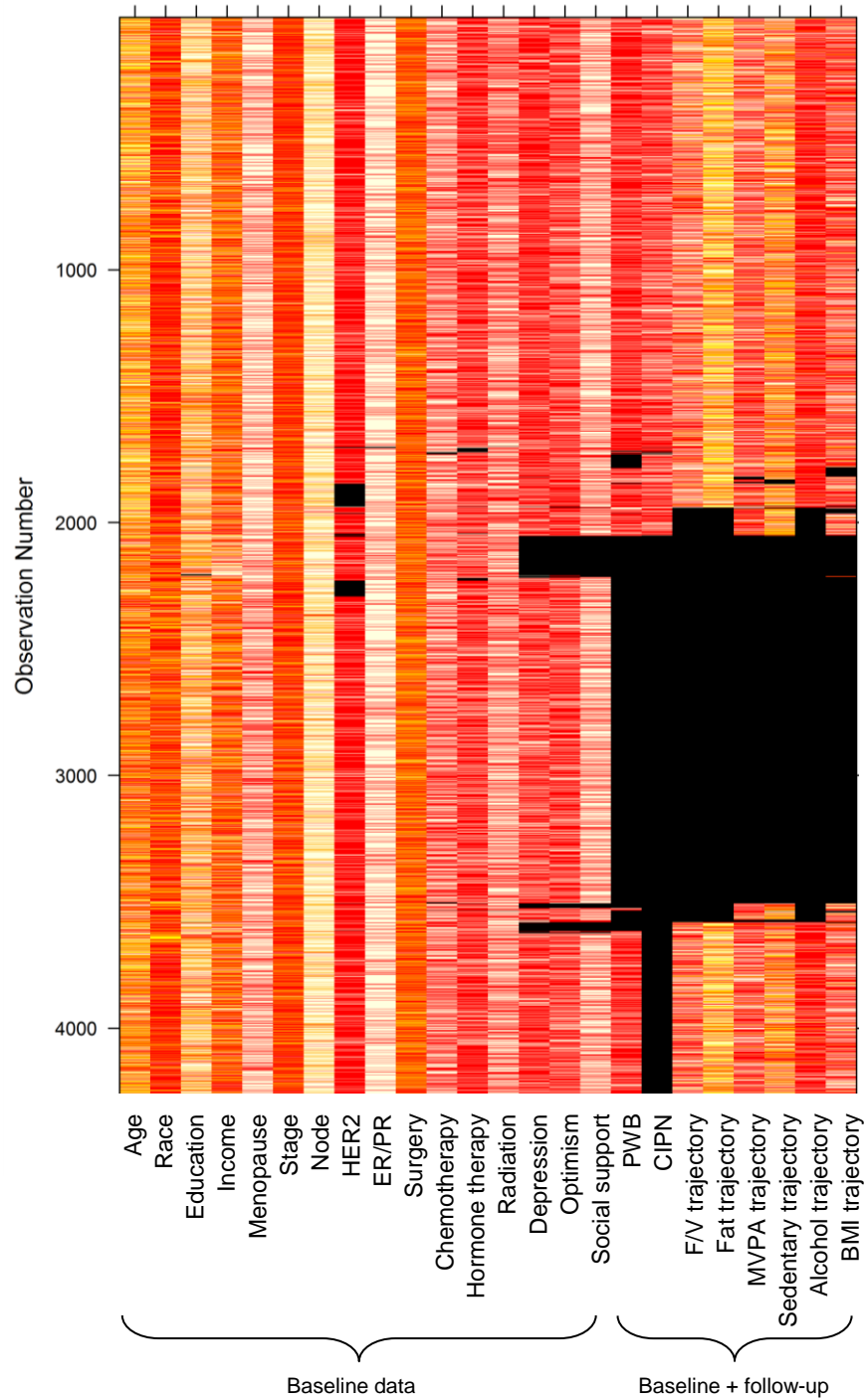
Abbreviations: OR, odds ratio; CI, confidence interval; NE, not estimable

These analyses were simultaneously controlled for group membership of all other health behaviors (moderate to vigorous physical activity and sedentary time), baseline energy intake, age, race/ethnicity, education, income, menopausal status, tumor stage, receipt of surgery, chemotherapy, hormonal therapy, radiation, baseline dispositional optimism, worsening of physical well-being, worsening of CIPN

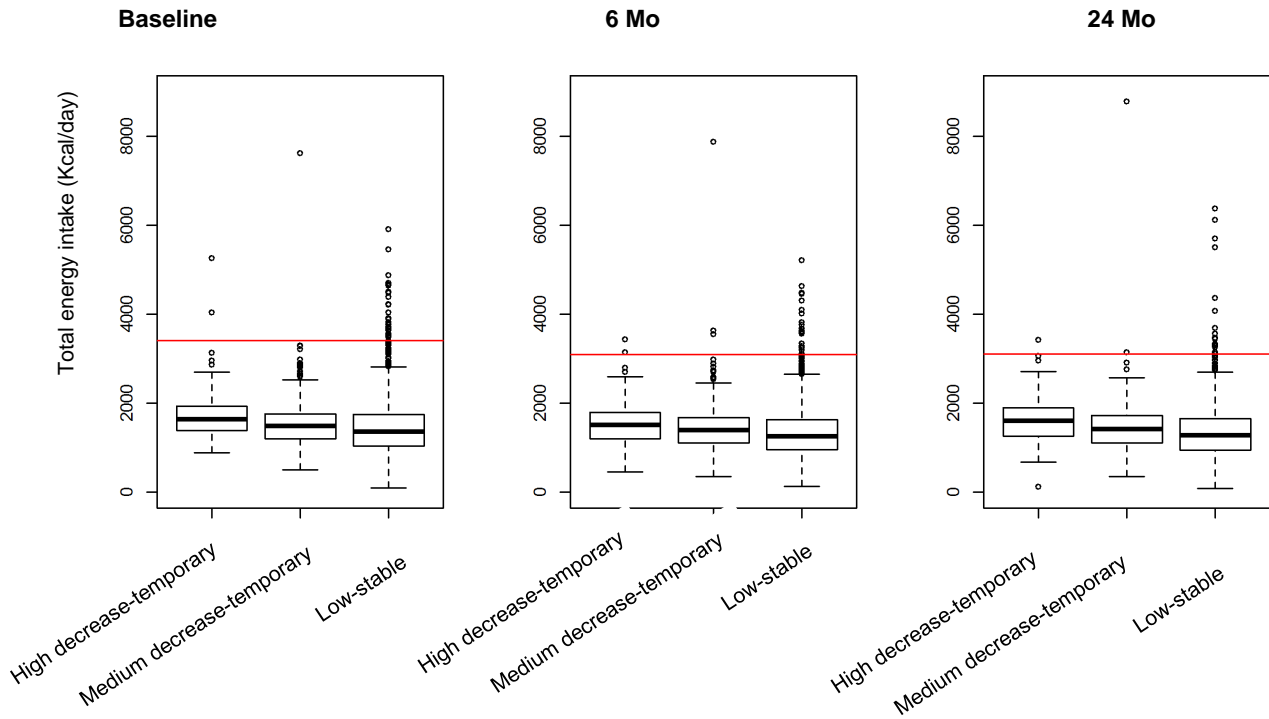
Appendix 17. Correlation between clinical classification of BMI and BMI trajectory groups

	BMI trajectory groups			Chi-squared test P
	High- stable	Medium- stable	Low- stable	
Clinical classification of BMI	Baseline			<0.01
	Normal	0	2	
	Overweight/obese	1	911	
	Class II obesity	242	145	0
	6 months			<0.01
	Normal	0	10	
	Overweight/obese	6	865	
	Class II obesity	214	111	0
	24 months			<0.01
	Normal	0	5	
Overweight/obese	6	632		
Class II obesity	142	84	0	

Clinical cutoff for BMI are as follows: normal: <25 kg/m², overweight: 25-30 kg/m², obese: ≥30 kg/m², Class II obesity: ≥35 kg/m²



Appendix 18. Missing data pattern for key analytical variables. The figure displays the overall pattern of missing data for the 4505 participants in the Pathways Study. The color of the pixels represents the standardized values of each variable, with darker color indicating higher standardized value. Missing data points are shown as a black pixel. Observations are clustered by their missing data patterns.



Appendix 19. Boxplot of total energy intake by alcohol intake trajectory. The boxplots show that the mean total energy intakes (the dark center bar within each box plot) were higher in women who maintained high alcohol intake vs. non-drinkers. However, extremely high energy intake was more frequent in women in the low-stable group, as evidenced by the number of data points greater than the mean+3 standard deviations of total energy intake (the red horizontal line).