The Associations between Dietary Supplement Use, Diet Quality, and Health-Related Quality of Life among Older Female Cancer Survivors

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Abstract

Background: Older cancer survivors report a high prevalence of dietary supplement use, specifically multivitamin (MVM), calcium, and vitamin D. Supplement intake is a modifiable health behavior that can impact overall diet quality and health-related quality of life (HRQoL).

Objective/Hypothesis: To identify the prevalence of supplement intake (MVM, calcium, vitamin D) in older female cancer survivors, and the association with diet quality and HRQoL.

Methods: Participants were female cancer survivors (≥65 years), who were ≤5 years post-cancer diagnosis, identified at the OSU-James Cancer Hospital. Participating women completed self-administered questionnaires assessing HRQoL (RAND-36), and diet quality and supplement intake (DHQ II converted to HEI-2015). Descriptive statistics, Pearson's correlations, and adjusted logistic regression models were used.

Results: Prevalence of MVM, calcium, and vitamin D supplementation was 61.4%, 76.9%, and 35.3%, respectively. The majority of participants that took in MVMs/calcium/vitamin D were white and received a college degree. Women that used MVM supplements had significantly higher mean scores for total vegetables (4.5±0.9 SD to 4.1±1.1), greens and beans (4.1±1.3 to 3.6±1.6), whole fruit (4.7± 0.8 to 4.3±1.3), and whole grains (2.9±1.8 to 2.3±1.6) than those who did not use these supplements. After controlling for demographic and clinical variables, participants with lower HRQoL were 4% more likely to take an MVM. Furthermore, the odds of taking an MVM was 1.07 times greater among those older women who had higher total HEI scores.

Conclusions: Although no evidence-based guidelines recommend dietary supplementation for cancer survivors, supplementation use among older female cancer survivors remains high. Participants with better diet quality were also more likely to be engaging in supplement use.

Understanding the prevalence of supplementation, associations with diet quality, and perceived benefits of supplementation may help health care providers in educating survivors and promoting dietary patterns that meet nutrient needs.

Dedication

I would like to thank my adviser, Dr. Jessica Krok-Schoen, for her expertise, guidance, and encouragement, and to all committee members for their commitment to my project's success. I would also like to thank my parents, Bonnie and Jeff, and my fiancé, Michael, for their constant support throughout my graduate program.

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Table of Contents

List of Tables

Chapter 1: Introduction

Background of the Problem

Cancer survival has increasingly improved since the 1970s for each of the most prevalent cancer sites, excluding uterine cervix and uterine corpus, leading to a growing cancer survivor population[1]. Cancer survivors are categorized as survivors from the time of diagnosis through the balance of his or her life[2]. As the U.S. population shifts towards an aging populace and life expectancies are rising, the number of older cancer survivors (age ≥65 years) increases[3]. Older adults represent the largest proportion of cancer survivors[3]. Due to this growing prevalence, researchers and clinicians need to investigate these older cancer survivors in order to provide effective healthcare. The most common cancer sites in survivors living today include female breast (23%, 3.9 million), prostate (22%, 3.7 million), colorectal (9%, 1.5 million), melanoma (8%, 1.4 million), and gynecologic (8%, 1.3 million)[4]. Furthermore, it is crucial to study females specifically, as cancer is the first or second leading cause of death for every age group shown among females, whereas, among males aged <40 years, accidents, suicide, and homicide predominate[1].

Older adults with a history of cancer may live with the fear of cancer recurrence or even a second primary cancer[5]. As this population is highly motivated to improve their health outcomes, many cancer survivors look to nutrition/dietary changes or other lifestyle changes (e.g., physical activity, stress reduction) as actionable behaviors to reduce their risk[6]. Current literature recognizes that a sizable amount of cancer diagnoses are related to a combination of risk factors including weight, physical activity, diet, and alcohol intake[7]. Although these are established risk factors, there is a lack of research surrounding dietary patterns and cancer, specifically in the older adult population.

The nutritional status and dietary requirements of older adults are multifactorial and related to both age-associated physiological changes and socioeconomic factors[8]. Furthermore, oral health affects almost everyone regardless of education, income, and location. Oral diseases may cause pain and infection, and also affect one's ability to chew, increasing an older person's risk for malnutrition, poor digestion, and weight loss[8].

Currently, there are many barriers (e.g., finances, access to Registered Dietitians, and insurance costs) to receiving nutrition education in this population, despite the evidence-based link between nutrition and health outcomes[8]. Research has found that in an outpatient oncology setting, there is one Registered Dietitian to 2,308 patients[9]. This staggering number further represents access barriers to evidence-based nutrition education to cancer survivors.

Health-related quality of life (HRQoL) is a meaningful and widely used assessment tool in the older adult population. HRQoL is frequently used to measure the effects of chronic illness like cancer, to better understand how an illness interferes with a person's daily life[8]. By investigating both physical and mental summary measures of HRQoL, researchers can investigate associations between HRQoL and nutritional health (e.g., dietary intake and dietary quality). This population is at risk for a decrease in HRQoL due to possible frailty, disability, and chronic illness with aging[8]. However, it should not be assumed that aging equates to an automatic decrease in HRQoL[8].

Diet quality is a key topic of importance in the aging cancer survivor population, as the connection between intake and health status is clear. To assess diet quality, questionnaires such as the food frequency questionnaire can be used to compare to the Dietary Guidelines for Americans (DGA). The DGA concentrates on foods and dietary patterns that promote health for individuals ≥2 years of age. Furthermore, the DGA provides a counsel on healthy aging through

dietary patterns and physical activity. Using Healthy Eating Index 2015 (HEI) scores can accurately assess a person's diet quality relative to the DGA[10]. Thus, it can be used to assess the conformity of any group of foods to the diet quality recommendations detailed in the DGA[11]. In an evaluation of the HEI 2015, each age group was investigated for diet quality scores. The oldest age groups (age ≥60 years) were found to have the highest mean score compared to younger age groups (20-39 years) indicating better diet quality[11].

An overwhelming proportion of older adults and cancer survivors utilize dietary supplements to improve health status[12]. A 2020 study found that survivors reported a higher prevalence of any supplement use (70.4% vs. 51.2%) and multivitamin (MVM)/mineral supplement use (48.9% vs. 36.6%) than individuals without cancer[12]. MVMs, vitamin D, and calcium are among the most commonly used supplements among older cancer survivors[13]. As so many older adults are relying on supplements, it is crucial to understand the association between their intake and diet quality.

There is a clear lack of data regarding older cancer survivors and dietary supplement usage. Furthermore, there is a lack of understanding on the relationship between diet quality and supplement use. The question remains: are survivors utilizing supplements while also eating a healthy balanced diet, or simply utilizing supplements as they are not closely following dietary guidelines? Moreover, there is a lack of research on HRQoL and supplement usage. Is supplementation with an MVM, vitamin D, or calcium associated with improved physical and mental health status?

Aim of the Study

The aim of this study was to explore potential associations of dietary supplementation with HRQoL as measured by the RAND-36, and diet quality as measured by the HEI 2015 among older (≥65 years) female cancer survivors.

Hypothesis

Dietary supplementation, specifically MVM, calcium, and vitamin D, will be associated with better HRQoL in both summary measures, physical and mental. Dietary supplementation will also be associated with better diet quality.

Objectives of the Study

The objectives of this study were as follows:

1. To determine the prevalence of MVM, vitamin D, and calcium supplementation in older female cancer survivors.
2. To explore potential associations between MVM, vitamin D, and calcium supplementation and HRQoL in older female cancer survivors.
3. To explore potential associations between MVM, vitamin D, and calcium supplementation and diet quality in older female cancer survivors.

Chapter 2: Literature Review

Adult Cancer Survivorship in the United States

Cancer continues to be a significant health concern nationwide, as it is the second-most cause of death in the United States. However, according to the Cancer Statistics 2020 released by the American Cancer Society (ACS), there has been a continuous decline in cancer mortality since 1991, with 3.2 million fewer cases or 31% fewer cancer deaths[1]. Furthermore, the number of cancer survivors is projected to grow to 21.7 million by 2029[4]. According to the National Cancer Institute (NCI), an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life[2]. This translates to any individual living with cancer or with a history of cancer diagnosis. Fortunately, cancer survival has steadily improved since the 1970s for most cancer types except for uterine. According to the ACS 2021 Cancer Statistics, men aged 60-69 have a 1 in 7 probability of developing invasive cancer, while men aged ≥70 have a 1 in 3 probability[1]. Women aged 60-69 have a 10% chance of developing invasive cancer, while women aged ≥70 have a 25% chance[1]. Furthermore, cancer is the number one leading cause of death in males and females aged 60-79 years in 2018[1].

Risk Factors for Cancer Recurrence and Second Primary Cancer

For cancer survivors, one major topic on their mind is a second primary cancer and cancer recurrence. Cancer recurrence is defined as a cancer that returns to the same area after treatment is complete, while a second primary cancer is defined as a cancer that occurs in a different part of the body[14]. Many cancer survivors live with the fear of recurrence, as the first diagnosis can be traumatizing both physically and psychologically[14]. This fear can take a large toll on both the survivors' mental health and their quality of life. A study completed in 2016 on newly diagnosed patients with early-stage breast cancer, evaluated cancer survivors' assessment

of their risk for cancer recurrence. Researchers found that 30.4% of breast cancer survivors with favorable prognoses overestimated the numeric risk of systemic recurrence to be more than twice their actual risk[5]. Furthermore, a third of women who had little to no risk of recurrence, considered their risk to be at 10% or higher[5]. This study indicates that many cancer survivors live in fear of recurrence and may not fully comprehend their exact risk. Furthermore, it is critical to understand the characteristics of those that have a higher likelihood of developing a fear of recurrence to properly address recurrence within this population. In 2018, researchers found that older adult female cancer survivors who were more likely to develop a fear of recurrence were younger in age at diagnosis, received chemotherapy, had a higher symptom score ($\geq$8) indicating occurrence and pain of symptoms experienced, and had a lower self-rated perceived health[15]. However, this study found no differences in fear of recurrence between cancer types (ovarian, breast, endometrial, colorectal)[15]. As the exact causes of second primary cancers or cancer recurrence is unknown, it is imperative for survivors to understand how to reduce or limit their risk.

The American Institute for Cancer Research (AICR) recommends that cancer survivors follow recommendations for overall cancer prevention. These recommendations include 10 key points: be a healthy weight; be physically active; eat a diet rich in whole grains, fruits, vegetables, and beans; limit consumption of fast foods or other processed foods that are high in fats, starches, or sugars; limit consumption of red and processed meat; limit sugar sweetened drinks; limit alcohol consumption; do not use supplements for cancer prevention; for mother's, breastfeed your baby if you can; follow the AICR recommendations if you can[16]. These guidelines target four major risk factors to reduce the cancer burden. According to the ACS, the combination of risk factors such as body weight, physical activity, alcohol intake, and diet,

account for at least 18.2% of cancer cases[7]. This combination of risks is the second highest percentage in both men and women[17]. This represents the magnitude that diet, physical activity, and body weight can have on future health outcomes and overall risk. However, it is important to note that these recommendations do not guarantee that cancer recurrence nor a second primary cancer will not occur.

Dietary Recommendations for Cancer

Six out of 10 of the AICR's recommendations for overall cancer prevention include lifestyle modifications surrounding diet. It is vital for cancer survivors to understand diet changes to improve their future health outcomes and reduce likelihood of recurrence/second primary cancer risk and comorbidities. According to the ACS, a healthy eating pattern includes: foods that are nutrient dense for maintenance of a healthy body weight and for achieving a healthy body weight, as an estimated 5% of cancers in men and 11% in women are attributed to excess body weight[1]. Recommended nutrient dense foods include a variety of vegetables, legumes; fruits, especially whole fruits, and whole grains[17]. While the USDA MyPlate Healthy Eating Guidelines recommends maintaining a healthy eating pattern throughout one's life, focusing on variety, amount, and nutrition. The food plate should be split into half fruits and vegetables, ¼ grains (half of which should be whole grains), and ¼ protein. In alignment with the USDA's MyPlate recommendations for healthy eating, the ACS is switching to cancer prevention guidelines that focus more on overall dietary patterns and healthy lifestyles rather than individual nutrients and foods. The message is to eat a diverse amount of healthy food, rather than focusing on which foods contain which vitamins and minerals. This holistic concept aids in people eating a variety of fruits, vegetables, and protein sources, which additionally aligns with MyPlate recommendations. Per the ACS, healthy overall dietary patterns are associated with a risk

reduction for cancer, this can especially be seen in colon and breast cancer risk[17]. This evidence further promotes the idea of overall healthy dietary eating rather than focusing on individual nutrients. Both the AICR and MyPlate recommendations, suggest obtaining nutrition through whole food sources rather than through dietary supplements. The ACS guidelines for cancer prevention further state to not use supplements for cancer prevention and to aim to meet nutritional needs through diet alone. Furthermore, the AICR notes that for the general population, eating and drinking a healthy diet is more likely to reduce risk of cancer than using dietary supplements[18]. However, it is essential to note that dietary supplement use was maintained at 52% of US adults from 2011-2012[19]. This represents a potential disconnect between the AICR recommendations and population use and belief.

The Dietary Guidelines for Americans (DGA) is released every five years and is created jointly through the U.S Departments of Health and Human Services and the USDA. This report contains nutritional and dietary information and guidelines for the general public based on evidence-based findings. Moderate evidence found in the 2015 DGA indicates that healthy eating patterns are associated with a reduced risk of type 2 diabetes, certain types of cancers (such as colorectal and postmenopausal breast cancers), overweight, and obesity[20]. As Americans do not eat food groups or nutrients in isolation, the DGA 2015-2020 focuses on overall dietary patterns and subsequent food and nutrient characteristics[20]. The DGA notes that it is important to follow a healthy eating pattern across one's lifespan to reduce the risk of chronic diseases and to support nutritional adequacy. Similar to the ACS guidelines and MyPlate, the DGA recommends limiting foods or beverages containing added sugars, sodium, and saturated fat[20]. Specifically geared towards the older adult population who are overweight or obese are encouraged to prevent additional weight gain. Among older adults who are obese, particularly those with

cardiovascular disease risk factors, intentional weight loss can be beneficial and result in improved quality of life and reduced risk of chronic diseases and associated disabilities[20]. It is important to note that the DGA recommends that nutrient and energy recommendations are first met through whole foods rather than dietary supplements when possible.

Age-Related Physiological Changes Impacting Diet

The older adult population is defined as persons aged 65 years and older and it is one of the fastest growing age groups in the United States[21]. In 2014, 46.3 million (14.5%) of the US population consisted of those aged 65 years and older. It is projected that in 2060, this age group will reach 98 million (23.5%)[21]. These numbers represent the need for further research on this population as it represents a large proportion of individuals living in the U.S. Aging is accompanied by many physiological changes and subsequent nutritional changes. These changes can make it more difficult for older adults to meet their nutritional needs. It can become challenging for older adults to balance their diet as calorie needs decline with age while nutrient needs either stay the same or increase, giving reason for supplement usage. The Nutrition Care Manual details that basal metabolic rate decreases due to a diminished lean body mass, which contributes to overall decreased energy requirements[22]. This translates to the increased need for nutrient dense foods rather than choosing energy dense foods. Older cancer survivors have unique qualities related to aging that place them at an elevated nutritional risk.

However, physiological age-related changes occur in the small intestine and in the liver, thus influencing digestion, absorption, and metabolism of nutrients. This affects nutrient availability in older adults. Vitamin D absorption is affected due to decreased sun exposure, possible food/drug interactions, and decreased skin synthesis of vitamin D. Furthermore, as the body matures, the intestinal mucosa loses the amount of vitamin D receptors. The kidneys are

also less efficient at converting vitamin D into its active form[22]. The Recommend Dietary Allowance (RDA) for vitamin D changes from 15 mcg/d to 20 mcg/d[23]. Similarly, calcium is poorly retained in the body therefore, causing an increase in the RDA from 1,000 mg/d to 1200 mg/d[23]. Vitamin B12 digestion and absorption is also affected through the aging process. Digestion can be affected due to a reduced secretion of gastric acid and intrinsic factor leading to a potential vitamin B_{12} or B_6 deficiency[22]. Furthermore, absorption may be affected by mucosal surface area decreases in the small intestine.

Constipation is one of the most common complaints among the aging population. Symptoms of constipation include difficult passage of hard stool, low frequency of stool, bloating, cramping, sensation of inadequate evacuation, and painful defecation. The aging process is associated with decreased colonic wall elasticity, impaired rectal sensation, and reduced colonic propulsion[24]. Bloating, cramping, and many other symptoms of constipation may lead to inadequate oral intake. Older adults eating diets lower in fiber, fluids, and excessive caffeine may also contribute to complications of constipation.

Oral health and mouth care are significant issues within the older adult population. The ability to chew and swallow can greatly affect whether older adults will be able to meet their nutritional needs[25]. With gum or tooth pain, appetite or the desire to eat can be detrimentally altered. Without the proper nutrition education, it can be difficult to cook food that is both palatable but also acceptable to control for pain while eating. Dysphagia is correlated with increasing age due to age-related physiologic changes in swallowing and illnesses[8]. Dysphagia may lead to a variety of serious conditions or complications including aspiration, hypovolemia, nutritional deficits, pneumonia, failure to thrive, airway obstruction, and depressive symptoms[8]. Pureeing food can be helpful to alleviate pain caused by swallowing or chewing, however, that

does require more work and tools in the kitchen. Furthermore, many older adults rely on dentures for chewing food. However, due to socioeconomic, social, or cognitive issues, older adults may have ill-fitting dentures that prohibit them from eating safely[25].

Xerostomia is a common condition in the older adult population and may lead to difficulty swallowing and lead to decreased food and beverage intake. Xerostomia is the lack of saliva which can greatly impair the ability to chew and digest carbohydrates. It is unclear whether age results in a decreased number of acinar cells in salivary glands or if this is caused by medications or diseases commonly associated with aging[22]. The decreased acinar cells can also lead to decreased taste sensation, reduced nutrient digestion, and increased discomfort while eating. Gustatory dysfunction may usually be perceived as a loss of taste, however, is often more correctly a defect in olfaction[25]. Reduced taste sensation may also result in decreased enjoyment and overcompensation with salt or sugar added to foods to improve taste[8]. Food may also digest slower through the gastrointestinal tract leading to decreased appetite and increased length of time feeling full[24]. For example, gastric emptying slows due to the aging process, leaving older adults feeling full for longer periods of time[24]. Furthermore, the decreased gastric motility then increases the nutrient requirements for fiber and water[8].

Of note, other physiological changes that consequently affect food and beverage intake include activities of daily living (ADL) like walking, eating, and transferring. A prospective cohort study found that disability in activities as household tasks, traveling, shopping, and continence had the highest risk and increased rapidly with age[26]. This study also notes that males had a higher risk of disability in preparing meals[26]. Instrumental ADLs such as shopping for groceries and cooking or preparing foods may be more cumbersome. Cooking the recommended small, frequent and nutrient dense meals for older adults can be exhausting or physically

demanding for some. Older adults may not possess the dexterity or muscle strength to open jars, cans, and boxes of food. If the older adult is wheelchair bound, this adds an extra element of difficulty in the kitchen. Furthermore, as one ages, older adults may lose the physical ability to grocery shop for themselves. Depending on health status, grocery shopping can be physically taxing to carry food items from the store to the car and from the car into your home. There are delivery options for groceries, however, these come with added fees that may be unaffordable to some older adults.

Barriers to Nutrition Care

Understanding any barriers to how this population obtains nutrition information or nutrition care is crucial. Approximately 90% of adult cancer survivors rely on outpatient treatment centers for a majority of their care[9]. Throughout care at these outpatient centers and comprehensive clinics, it is key to receive critical dietary information that can aid in treatment and future health outcomes. However, access to oncology nutrition information and care can be severely limited as it is left to the discretion of individual ambulatory entities or health care providers[9]. Due to this reason, the vast majority of oncology patients treated in outpatient centers do not have access to oncology nutrition services like working with a Registered Dietitian[9]. Without access to nutrition information and care, older adults can't be expected to fully understand healthy dietary patterns to alleviate symptoms, reduce risk of malnutrition, reduce risk of vitamin and mineral deficiency, and how to properly maintain a healthy weight. Furthermore, the patient to Registered Dietitian ratio was investigated and found to be 1 Registered Dietitian to 2,308 patients[9]. This staggering number further represents the limited access to nutrition care for oncology patients and signifies a barrier that needs to be acutely addressed.

Additional barriers to access include socioeconomic status, insurance, and out of pocket expenses[27]. Medical nutrition therapy services provided by RDNs are not currently covered by Medicare[28]. Lack of Medicare reimbursement for referral-based nutrition consultations can prevent countless older adult oncology patients from further pursuing nutrition care[29]. Additionally, Medicare does not currently cover dental care services further preventing access to oral care[8].

Social Factors and Diet

Many older adults make the decision to enter into retirement and may transition into a different, potentially, limited budget. In 2010, almost 3.5 million elderly persons were below the poverty level, while another 2.1 million older adults were considered near poor, demonstrating the potential for food insecurity[28]. This may affect the way older adults choose to buy food and what foods they are purchasing. For example, they may decide to purchase more processed foods to ensure the food lasts longer, or they may not purchase the same quantity of food due to budget constraints.

Mental health also plays a substantial role in health and diet. Older adults maintain similar life stressors to those in other age cohorts, however, they also experience a potential deficits in physical and cognitive functioning, loss of loved ones, and a decline in functional ability[9]. These stressors may lead to anxiety or depression. According to the World Health Organization, around 15% of adults aged 60 and over experience mental illness[30]. Depression, anxiety, and dementia are among the most common mental disorders that affect the older adult population. All three disorders may decrease food intake through decreased appetite, decreased quality of life, and decreased ability to obtain the food they need to be nutritionally adequate. Similarly, those who live alone may feel isolation and may not feel motivated to eat as many

individuals are social eaters. When a spouse is lost, an individual may feel immense grief, and many find it difficult to maintain a healthy lifestyle and their energy and nutrient requirements.

Dietary Recommendations in Older Adults

Diet recommendations slightly differ for older adults due to the aging process. However, older adults may not always be meeting these recommendations. When recommendations are no met, there are a variety of health outcomes that may be affected such as HRQoL, risk of comorbidities, physical fitness and mobility, and overall diet quality. It is important to note that nutrition is a major determinant of successful aging[28]. The precise nutrition requirements of an aging adult at any age are multi-factorial due to the high diversity within this population[28].

While protein requirements remain the same for the older adult population at 0.8 g/kg of protein, many people struggle to meet this recommended amount. According to a 2019 study, dietary protein intakes were significantly lower in older participants, with up to 46% of the oldest adults not meeting the 0.8/kg recommendation[31]. Furthermore, lower protein intake was associated with lower overall diet quality and physical functioning in the aging population. The study also found that those not meeting the protein recommendation were more likely to have intakes of other nutrients below recommended levels[31]. Not meeting recommended nutrient intakes may lead to vitamin or mineral deficiencies or malnutrition.

Nutrients of concern in the older adult population include calcium, vitamin D, vitamin B_{12}, vitamin B_6, and vitamin C. The Surgeon General's report on bone health and osteoporosis recommendations include consuming recommended amounts of calcium and vitamin D, maintaining a healthful body weight, and being physically active, along with minimizing the risk of falls[28]. Calcium and vitamin D from dietary or supplement sources are a main focus of therapy in this population for bone health[28]. Furthermore, there is increased wintertime parathyroid

hormone production and decreased calcium bioavailability, subsequently leading to an increased need for vitamin D[8]. As previously discussed, vitamin B_{12} absorption can be poorly affected in the aging process. An estimated 6-15% of older adults suffer from a vitamin B_{12} deficiency[28]. Vitamin B_6 has a higher metabolic turnover the older adults, making this a nutrient significant in this population[8]. It is important to note that there is a possible decreased absorption of vitamin C with age. Vitamin C tissue and plasma levels both decline with age and is seen more so in males than females[8]. These nutrients of concern call for a dietary pattern consuming nutrient dense foods rather than energy dense foods.

Furthermore, per the 2010 DGA, adults aged ≥51 years are recommended to reduce sodium in their diets to 1,500 mg daily in an effort to lower their risk of high blood pressure and associated consequences[28]. However, this reduction in sodium may be difficult for many older adults as loss of taste may occur during aging or with medications taken associated with aging. Also, processed foods that tend to be easier to cook and have a longer shelf life, typically contain more sodium. As discussed, some older adults may utilize these foods due to budget or physical constraints.

Health-Related Quality of Life

Quality of life is a significant and useful marker of a person's well-being and status, especially in the older adult population. Quality of Life (QoL) is defined by the World Health Organization as "a complete state of physical, mental, and social well-being and not merely the absence of disease or infirmity"[32]. Similar to QoL, HRQoL is a useful assessment to investigate further into a person's thoughts on their own status. HRQoL is defined as the personal sense of physical and mental health and the ability to react to factors in the physical and social environments[33]. To use this marker effectively in research, it is imperative to have a clear

operational definition. A common measure of HRQoL is the RAND-36, which is comprised of eight different areas: physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, energy/fatigue, pain, and general health perceptions[34]. Examining each facet of mental and physical health will help better assess this population's perception of their HRQoL and consequentially what factors affect their HRQoL. In the older adult population, HRQoL is likely to be impacted by physical activity, age related physical limitations, diet and nutrition, and living situation (including independence). A systematic review on dietary patterns and quality of life showed that the majority of studies found that subjects with a higher diet quality also had higher mean scores on the QoL scale[35]. While the association of diet quality and QoL scores have been investigated, only two of the studies reviewed used HEI scores to investigate diet quality. The World Cancer Research Fund found that HRQoL was positively associated with greater adherence to the WCRF/AICR guidelines in both the physical and the mental summary measures[36]. This finding reinforces the connection between dietary intake and HRQoL in both the physical and mental summary measures.

HEI Scores

The Healthy Eating Index (HEI) is a measure for assessing dietary quality, specifically whether a set of foods aligns with the Dietary Guidelines for Americans[37]. As the Dietary Guidelines for Americans change, so should the measures to assess them. The most recent available HEI score is the HEI 2015, which is reflective of the 2015-2020 DGA. The HEI yields a total score, which analyzes the overall dietary quality, and separate component scores that can be examined collectively to reveal a pattern of quality regarding multiple dietary dimensions[37]. The HEI has 13 components, and each component represents an important aspect of an overall

healthy dietary pattern. Nine components focus on adequacy or foods necessary to get the essential macronutrients and micronutrients[10]. Four components focus on moderation, dietary components that are recommended in small amounts[10]. All of the components are assessed on a density basis (typically intake per 1,000 calories). This is done to account for differing dietary recommendations, which vary based on age, sex, and activity level[10]. HEI-2015 is designed to be scored on a scale from 0-100 points, although the lower bound is difficult to reach[37]. HEI scores >80 indicate a "good" diet, scores ranging from 51 to 80 reflect a diet that "needs improvement," and HEI scores <51 imply a "poor" diet[38].

A 2018 study found that diet quality scores in older bladder cancer survivors were in the category of "needs improvement", similar to the results for Americans[39]. Older bladder cancer survivors represent an important target population of concern, and they typically represent the older adult population[39]. This population was also noted to be very representative of the overall population of individuals aged ≥65 years[39]. However, it is important to note, the use of dietary supplements is not assessed in regard to dietary quality in the HEI scores.

Overview of Multivitamins

Of the major dietary supplements that Americans take daily, an MVM is the most common, especially in older cancer survivors[13]. Americans have been consuming MVMs since the early 1940s[40]. According to the NIH State Science Panel, MVM refers to any supplement containing three or more vitamins and minerals, without herbs, hormones or drugs. The Dietary Supplement Health and Education Act of 1994 (DSHEA) defines and regulates dietary supplements[41]. Dietary supplement manufacturers and distributors firms are responsible for evaluating the safety and labeling of all of their products before marketing to ensure that they meet all the requirements of DSHEA and FDA regulations[42]. Furthermore, DSHEA requires the

FDA to monitor and taking action against any "adulterated or misbranded" dietary supplement product after it reaches the market[42]. However, there is no standard or regulatory definition of an MVM such as what nutrients, minerals to contain and at what amounts[40]. Each component of a once daily MVM is required at a dose less than the tolerable upper level determined by the Food and Nutrition Board, such that the maximum daily intake likely to pose no risk for adverse health effects[43]. However, it is noted that there is a subgroup of MVMs including: other MVMs contain vitamins and minerals at levels substantially higher than the recommended values or even tolerable upper intake level and may also include other nutritional and herbal ingredients[43]. Many Americans with poor diet quality struggle to reach the RDA for many vitamins and minerals through diet alone[43]. Furthermore, the MVM options provided to Americans in grocery stores and pharmacies can be extensive. According to research on MVMs from 2007-2010, results indicated that over half of Americans utilized MVM supplements containing ≥ 9 micronutrients[44]. Many of these MVMs are specialized and marketed to target specific health concerns that include heart healthy, improving hair skin and nails, gender specific, and vegan- or vegetarian-specific. This wide variety of MVM options may be confusing to consumers or misleading. Furthermore, it may be difficult to understand exactly what nutrients and minerals those who take MVMs are receiving as they do widely vary. As so many Americans are utilizing daily MVMs, it is imperative to understand the relationship between use and other health markers. Additionally, as overall supplement use rises, additional widely used supplements like calcium and vitamin D will be further explored.

Calcium and Vitamin D Supplements

As previously mentioned, both calcium and vitamin D absorption and metabolism are affected by the aging process. Therefore, it is critical to look at both dietary intake and dietary

supplement use of both calcium and vitamin D in this population to see how this population can meet their needs or is currently meeting their needs. In supplements and fortified foods, vitamin D is offered to consumers currently in two forms, D_2 (ergocalciferol) and D_3 (cholecalciferol), and they differ chemically only in their side-chain structure[45]. Currently, there are no recognized nutritional differences between D_2 and D_3 when it comes to supplementing with either. Several studies report a significantly greater effect of vitamin D_3 on increasing the levels of serum 25(OH)D, however, a more recent study found that the two forms of the vitamin were equally effective[46,47,48]. More research needs to be done on vitamin D form to provide appropriate supplementation guidance. As osteoporosis and loss of bone integrity is a common in the older adult population, calcium and vitamin D may be more utilized to ensure bone health. While Americans tend to maintain adequate vitamin D levels throughout the summer, levels decrease in the summertime due to the lack of sun exposure. Adequate intake of vitamin D is also necessary for calcium absorption, as it enhances gastrointestinal absorption and mineralization of the osteoid tissue. Furthermore, due to the short circulating half-life of vitamin D_2, vitamin is more physiological when it is administered on a daily basis, rather than infrequently[49]. It is also recommended to administrate daily at a moderate dose rather than a high dose for a shorter period of time. As with MVMs and numerous other supplements, calcium and vitamin D supplements should be taken as needed within the guideline[49]. Calcium supplementation is typically only recommended to supplement when adequate calcium consumption through the diet cannot be achieved. The two main forms of calcium in supplements are carbonate and citrate. Calcium citrate is also useful for people with achlorhydria, inflammatory bowel disease, or absorption disorders[50].

Dietary Supplement use in Adult Cancer Survivors

Many cancer survivors are instructed about the connection between diet, health status, and cancer risk. This may lead to many of these cancer survivors exploring ways to enhance their intake of nutrients like vitamins and minerals. According to a 2020 study adult cancer survivors reported a higher prevalence of supplement use and MVM/mineral supplement use than individuals without cancer, with an overall prevalence of 73% compared to 52% in the general population[12]. Overall, cancer survivors had significantly higher amounts of nutrient intake from supplements; however, cancer survivors also had lower nutrient intakes from their diet for the majority of the nutrients studied[12]. Dietary supplementation does not guarantee that individuals or cancer survivors will be meeting their nutrient requirements if their overall dietary pattern is not nutrient-dense. This study also found that compared with individuals without cancer, cancer survivors had a higher percentage of individuals with inadequate intake for folate, vitamin B_6, niacin, calcium, copper, and phosphorus, due to lower intakes of these nutrients from foods and beverages[12]. Therefore, indicating that without a balanced dietary intake, utilizing dietary supplements alone may not suffice. On the other hand, cancer survivors were also found to have exceeded certain nutrient recommendations through dietary supplementation for vitamin D, vitamin B_6, niacin, calcium, magnesium, and zinc[12]. Due to the high prevalence of cancer survivors utilizing dietary supplements, and the high prevalence of cancer survivors not meeting some nutrient recommendations while exceeding other recommendations, it is crucial to investigate dietary patterns and dietary supplements in the adult cancer population. However, it is important to note that this study utilized a 24-hour recall to assess overall dietary patterns in participants and cancer survivors aged 20 years and older.

Recent Literature on the Impact of Supplement Use and Adult Cancer Survivors

A 2019 meta-analysis studied dietary interventions for adult cancer survivors ranging from 23-85 years old[51]. Two of the aspects explored were the effects of dietary interventions on HRQoL and on the Diet Quality Index including 25 randomized controlled trials. Looking specifically at HRQoL, study results were highly varied and no conclusions could be drawn[51].

A 2008 cross sectional study investigated the older adult population aged ≥65 years in female breast, prostate, and colorectal survivors[13]. The purpose of this study was to investigate dietary supplement use and its association with micronutrient intakes and diet quality among older cancer survivors, whom were ≥5 years post diagnosis. Diet quality was assessed using HEI scores, however, these scores are not the most updated version available to research today. This study found that a majority of survivors (74%) reported taking supplements, with MVMs (60%), calcium/vitamin D (37%), and antioxidants (30%) as the most prevalent, thus reinforcing the prevalence of supplements being taken by cancer survivors[13]. In relation to diet quality, individuals scoring higher mean scores of Total Fruit, Whole Grain, and Oil components of the HEI were significantly more prone to utilize dietary supplements, while individuals with higher mean scores of Meat and Beans category were significantly less likely to take supplements[13]. Overall, supplement users were more likely to have higher mean HEI scores[13].

A 2019 study explored the effects of vitamin D supplementation on HRQoL. This study utilized 553 breast cancer patients/early survivors. Researchers found that approximately 30% of breast cancer patients that had blood levels recorded in the medical recorded, were potentially vitamin D deficient (<30 ng/mL)[52]. These results indicate a prospective need for increased dietary intake in this population or supplementation. The authors reported that vitamin D supplementation was associated with higher levels of self-reported HRQoL at enrollment

($p<0.05$) and that sufficient blood levels of vitamin D recorded between enrollment and follow-up were also associated with better HRQOL at follow-up ($p<0.05$)[52].

A 2016 study examined the association between vitamin D supplementation and quality of life in 453, stage 2 colorectal cancer patients[53]. To measure QoL, the FACT-C and the SF-12 were utilized. The SF-12 was used to assess the Mental Composite Score and the Physical Composite score in study participants. Additionally, calcium supplementation was also examined whether it modifies the associations between vitamin D supplementation and QoL. The study found that, compared to those not utilizing supplementation, those taking vitamin D tended to be older, female, attended some college, had a higher income, non-smokers, and also had dietary patterns including high amounts of fruits and vegetables and low amounts of fat[53]. While vitamin D blood levels were not assessed in participants, vitamin D supplementation was associated with a positive relationship with better symptom-related QoL over 24 months of follow-up[53]. Furthermore, calcium supplementation along with vitamin D supplementation, was shown to also have an association with better QoL[53].

Gaps in the Literature

There is a lack of quality studies in current literature exploring the potential association between dietary supplements, HRQoL, and overall dietary quality. There are even fewer studies specifically looking into the older adult population, noting that most studies include adults aged 20 years and older. Furthermore, the studies researching adult cancer survivors currently use a lack of various cancer sites in their research and more cancer sites and types are necessary to be further explored. Throughout the literature, it can be difficult to understand whether or not the cancer survivors are currently receiving treatment. Additionally, studies have not been completed on older female cancer survivors, with a variety of cancers looking at the relationship between

vitamin D, calcium, or MVM supplementation and diet quality (HEI scores) and HRQoL. There is currently a high prevalence of cancer survivors utilizing dietary supplementation. Providing more information on the association between this supplementation and their health status can be particularly beneficial, so that cancer survivors may make supplementation decisions that are right for them. Moreover, more information can aid healthcare providers in making evidence-based recommendations on supplementation for older cancer survivors. This research is imperative to add to the literature as there is a definitive gap in knowledge and research.

Conclusion

As cancer impacts 1 in 8 older Americans, it is imperative to further research this population, especially as this population continues to grow. The prevalence of older adults affected by cancer and seeking supplementation exemplifies the need for more quality research and education on this topic. Currently, the AICR nor the MyPlate guidelines recommend supplementation to aid cancer prevention, yet many survivors utilize supplements to obtain nutrient recommendations to improve their health status and HRQoL. Furthermore, supplementation does not guarantee that survivors will not obtain vitamin deficiencies. Therefore, it is of critical importance to explore the potential relationships between diet quality, health-related quality of life, and dietary supplementation.

Chapter 3: Methods

Study Overview

This study is a secondary data analysis of Dr. Krok-Schoen's project, Physical and Mental Well-being After Cancer Diagnosis: Examining the Influence of Nutrition Among Older Female Cancer Survivors. The study utilized a detailed one-time survey to obtain information on participant's nutritional intake and health and biopsychosocial factors that influence the association of nutrition and physical and mental well-being among older female cancer survivors[54].

Objectives of the Study

The objectives of this study are as follows:

1. To determine the prevalence of MVM, vitamin D, and calcium supplementation in older female cancer survivors.
2. To explore potential associations between MVM, vitamin D, and calcium supplementation and health-related quality of life in older female cancer survivors.
3. To explore potential associations between MVM, vitamin D, and calcium supplementation and diet quality in older female cancer survivors.

Participants and Recruitment

In order to be eligible for participation, prospective participants needed to be female cancer survivors, ≥65 years, who were willing and able to provide written informed consent. For the study's purposes, cancer survivors were defined as individuals who were diagnosed with cancer in the past five years and had completed primary cancer treatment (i.e., received chemotherapy, surgery, and/or radiation).

Women diagnosed with cancers at any anatomic sites and at any stage were eligible. Limiting participants to have up to five years post diagnosis was done to ensure the accuracy of reported dietary patterns and weight changes after cancer diagnosis.

Research Design

Participants were identified through one of two methods: 1) through OSUCCC clinic visits to the Blood Cancer and Longevity Clinic and Gastrointestinal Clinic and the Geriatric Oncology Clinic at the Stefanie Spielman Breast Center. Clinicians at each clinic provided prospective participants with a recruitment flyer including information surrounding the study and the PI's (Dr. Krok-Schoen) name and contact information. 2) through medical records obtained from the OSUCCC cancer registry. As eligible participants were identified, Dr. Krok-Schoen was provided with prospective participant's name and mailing address. A recruitment letter including information about the study was then mailed out to these potential participants. Women who contacted the study coordinator were screened to ensure they met all eligibility criteria and then informed of the study's goals. These women were then asked if they were willing to participate and if so, they could complete the survey online or request a survey via mail or telephone. Online surveys were taken via Research Electronic Data Capture (REDCap), a secure web application developed for clinical research. All participants provided informed consent. A HIPAA waiver was obtained to collect basic demographic, and clinical characteristics from participants' medical records. All participants received a $10 gift card for completing the survey. The Institutional Review Boards of the participating clinic and university approved the informed consent procedures and study protocols.

Measures

Health Related Quality of Life

The survey utilized a 36-Item Health Survey (RAND-36) to examine HRQoL in older adult female cancer survivors. The RAND-36 is one of the most widely used measures of HRQoL[34]. This 36-item survey is comprised of two summary measure of physical health and mental health, and eight subscales assessing the following aspects of HRQoL: physical functioning, role functioning physical, pain, general health, energy/fatigue, social functioning, role functioning emotional, and emotional well-being[34]. The survey uses a Likert scale to assess participant's responses. Responses to the individual items are transformed during data analysis to a scale ranging from 0-100, with 100 being the highest subscale score for each of the 8 subscales. In addition, two composite scores can be created from the 8 subscales concerning physical (PCS) and mental (MCS) health concerns. For the purposes of this study, the PCS and MCS were used as measures of the participants' physical and mental HRQoL.

Food Frequency and Healthy Eating Index-2015

A Diet History Questionnaire II (DHQ II), a validated food frequency questionnaire was used to investigate food and nutrient consumption among older adults in the study. The DHQ II has a food list that was updated based on more recent dietary data and consists of 134 food items and 8 dietary supplement questions[55]. The results of the DHQ II were used to estimate diet quality according to the Healthy Eating Index 2015 (HEI-2015). The HEI-2015 is the most recent version of HEI, which assesses diet quality, dietary patterns, and adherence to the 2015-2020 U.S. Dietary Guidelines for Americans[37]. The HEI uses a scoring system to evaluate a set of food components; the scores range from 0 to 100[37]. For each dietary component, the HEI assigns a certain amount as the standard. A maximum score of 5 or 10 points (depending on the component being assessed) is given to amounts that meet the standard recommendation[10]. The DHQ II was also used to assess dietary supplement intake among older female adults in this

study. The DHQ II included an extensive list of dietary supplements and herbals/botanicals that participants could mark if they were currently consuming and if so, what is the frequency. For the purposes of this study, MVM, vitamin D, and calcium supplementation (yes/no, frequency, and duration) will be investigated.

Demographics and Clinical Characteristics

Additional information regarding the participants' clinical (e.g., date of cancer diagnosis, cancer stage, treatments received, cancer recurrence, other chronic diseases, and prescription regimen) and demographic (e.g., age, gender, race, ethnicity) were collected through medical record review.

Data Analysis

Descriptive statistics (e.g., means, frequencies) were used for the demographic and health characteristics, HEI-2015 total score and subcomponent scores, dietary supplementation (vitamin D, calcium, and MVM), and HRQoL (PCS, MCS). DHQ II scores were converted to the HEI-2015 scores, per guidelines from the National Cancer Institute, utilizing SAS and Diet*Calc[56]. T-tests were used to assess potential differences between supplementation (yes/no) and RAND-36 scores and HEI scores. Pearson's correlations were used to assess potential associations among supplementation (yes/no), HEI total score, PCS, MCS, health-related quality of life, and demographic and clinical characteristics. Logistic regressions were conducted to assess potential associations between supplementation (yes/no), HEI total score, PCS, and MCS, while controlling for demographic (age, race, education, marital status, employment) and clinical (cancer type, AJCC stage, time since diagnosis, number of chronic conditions) characteristics. Factors were each mutually adjusted (i.e., age, retirement status, BMI) in logistic regression

models. IBM SPSS Statistics version 27.0 was used. All reported *P* values are two-sided, with a Type I error rate set at 0.05.

Chapter 4: Results and Discussion

Results

Demographic and Health Characteristics

Table 1 describes study participants' demographic and health characteristics. The study sample included 173 older female cancer survivors, with a mean age of 73.6 $\pm$ 6.1 years. The majority of participants were white (90%), married (54.7%), received a bachelor's, master's, or professional degree (50%), and were currently retired (82%). The majority of participants, 65%, had a normal BMI (18.5-24.9 kg/m^2) to overweight BMI (25-29.9 kg/m^2), with 56.9% reporting 1-2 chronic conditions in addition to their cancer diagnosis. The majority of participants were diagnosed with breast cancer (67.7%), followed by hematological (12.8%) and gynecological (12.0%) cancer. Cancer stage at diagnosis was most commonly stage 1A and 1B (44.2%), followed by stage 2A and 2B (36%). Household income was spread out between $20,000-50,000 (26.0%), $50,000-100,000 (27.8%), and $100,001+ (16.0%).

Prevalence of MVM usage was 61.4%, calcium usage was 76.9%, and vitamin D usage was 35.3%. Of the participants taking MVMs, the majority (85.4%) took their MVM every day. Of the participants taking calcium, 46.2% have been taking 10 years or more, 26.9% took calcium for 5-9 years, 16.3% took calcium 1-4 years, while 10.6% have been taking calcium for less than one year. The majority of participants supplementing calcium chose 1,000 mg or more (36.8%) or 600-999 mg (34.7%), followed by 500-599 mg (23.2%), and less than 500 mg (5.3%).

Demographic	N (%)
Age (mean (SD))	73.62 (6.1)
Age at diagnosis, mean (SD)	71.5 (5.9)
Race/Ethnicity	
White	144 (90.0)
Black	13 (8.1)
Asian	2 (1.3)
Other	1 (0.6)
Marital Status	
Married	93 (54.7)
Single/unmarried/unmarried couple	7 (4.2)
Divorced/widowed/separated	66 (38.8)
Education Level	
High School/GED or less	28 (16.5)
Some College/Associates	48 (28.2)
College graduate/Graduate degree	85 (50)
Doctoral	8 (4.7)
Employment Status	
Working full time	11 (6.5)
Working part-time	12 (7.1)
Retired/Homemaker/Disabled	146 (85.9)
Household Income	
Less than $20,000	17 (10.1)
$20,001-$50,000	44 (26.0)
$50,001-$100,000	47 (27.8)
$100,001+	27 (16.0)
Health Characteristics	
BMI (mean, SD)	27.7 (6.2)
Underweight	4 (2.4)
Normal/Overweight	109 (64.9)
Obese (1, 2, extreme)	55 (32.7)
Cancer type	
Breast	90 (67.7)
Hematological	17 (12.8)
Gynecological	16 (12.0)
Gastrointestinal	5 (3.8)
Other	5 (3.8)
AJCC stage at diagnosis	
0	8 (13.1)
1A/1B	27 (44.2)

Continued

Table 1: Demographics and Health Characteristics of Older Female Cancer Survivors

Table 1 continued

2A/2B	**22 (36)**
3B/3C	4 (6.5)
Number of Chronic Conditions	
0	8 (5.6)
1-2	82 (56.9)
3-4	34 (23.6)
5-6	14 (9.8)
7-10	6 (4.2)
Supplementation Usage	
Multivitamin	105 (61.4)
Calcium	133 (76.9)
Vitamin D	61 (35.3)

Table 1: Demographics and Health Characteristics of Older Female Cancer Survivors
Other cancers include kidney, skin, maxillary sinus, connective tissue, and lung.
AJCC= American Joint Committee on Cancer
*=Not all categories equal n=173 due to missing data

Dietary Intake

Table 2 details the mean HEI-2015 scores of older female cancer survivors in this study. Overall, the mean HEI score was 66.5 $\pm$ 10.1, which is 66% of the maximum possible score of 100. Table 2 shows the mean score for each component of the HEI 2015 in both the moderation and the adequacy categories. Highest mean component scores were in the total protein foods (4.6), seafood and plant proteins (4.5), and whole fruit (4.5). The lowest mean component score was whole grains (2.7), followed by fatty acids (4.7). With a higher score indicating lower consumption of the moderation foods, saturated fats at a mean score of 5.4 $\pm$ 3.2 and sodium at a mean score of 5.0 $\pm$ 2.9 should be noted.

Components	Maximum Points Possible	Mean Scores (SD)	Percent of Maximum Score
Adequacy:			
Total Vegetable	5	4.3 (1.0)	86%
Greens and Beans	5	3.9 (1.4)	78%
Total Fruit	5	4.2 (1.3)	84%
Whole Fruit	5	4.5 (1.0)	90%
Whole Grains	10	2.7 (1.8)	27%
Dairy	10	6.1 (2.7)	61%
Total Protein Foods	5	4.6 (0.8)	92%
Seafood and Plant Proteins	5	4.5 (0.9)	90%
Fatty Acids	10	4.7 (3.1)	47%
Moderation:			
Sodium	10	5.0 (2.9)	50%
Refined Grains	10	8.9 (1.7)	89%
Added Sugars	10	7.6 (3.0)	76%
Saturated Fats	10	5.4 (3.2)	54%
Total HEI Score	100	66.5 (10.1)	66%

Table 2: The Mean Healthy Eating Index 2015 (HEI) Scores of Older Female Cancer Survivors

Health-related Quality of Life

Table 3 shows the mean results of the RAND-36. Participants scored highest on social functioning (82.5) and role limitations due to emotional problems (81.3) out of the highest score of 100. Participants scored lowest on general health (59.4), energy/fatigue (42.7), and mental and physical composite scores (48.5 and 42.0).

Subscales	Mean (SD)
Physical Functioning	59.8 (24.1)
Role Limitations due to Physical Health	60.8 (42.0)

Continued

Table 3: The RAND-36 Scores of Older Female Cancer Survivors (n=173)

Table 3 continued

Role Limitations due to Emotional Problems	**81.3 (34.3)**
Emotional Well-being	65.0 (10.4)
Energy/fatigue	42.7 (10.0)
Social Functioning	82.5 (21.1)
Pain	72.7 (22.3)
General Health	59.4 (15.3)
Physical Composite Score (PCS)	42.0 (10.5)
Mental Composite Score (MCS)	48.5 (7.2)

Table 3: The RAND-36 Scores of Older Female Cancer Survivors (n=173)

Demographic and Health Characteristics of Supplement Users and Non-Users

Table 4 shows the demographic and health characteristics of participants stratified on their MVM, calcium, or vitamin D supplementation. The average age of MVM users was 74.2 $\pm$ 6.0, calcium users 73.4 $\pm$ 5.8, and vitamin D users 73.1 $\pm$ 5.8. The majority of participants that utilized MVMs were white (58.1%), married (33%), received at least a college degree (32.4%), and are retired/disabled/homemakers (54.1%). Participants utilizing calcium were white (68.1%), married (43.5%), have at least a college degree (38.8%), and be retired (66.5%). Vitamin D users were similarly white (33.8%), mostly married (21.8%), have a college degree (21.2%), and be retired (30%). Breast cancer survivors were the most likely to utilize MVM, calcium, and vitamin D.

Variables	Multivitamin		Calcium		Vitamin D	
	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)
Age (Mean (SD))	74.2 (6.0)	72.8 (6.2)	73.4 (5.8)	74.4 (7.0)	73.1 (5.8)	73.9 (6.3)
Race						
White	93 (58.1%)	51 (31.9%)	109 (68.1%)	35 (21.9%)	54 (33.8%)	90 (56.2%)
Black	8 (5.0%)	5 (3.1%)	12 (7.5%)	1 (0.6%)	3 (1.9%)	10 (6.2%)
Asian	0	2 (1.3%)	2 (1.3%)	0	0	2 (1.3%)
Other	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.6%)
Marital status						
Married	56 (33.0%)	37 (21.8%)	74 (43.5%)	19 (11.2%)	37 (21.8%)	56 (32.9%)
Single/Unmarried/ Unmarried couple	1 (0.6%)	6 (3.5%)	3 (1.8%)	4 (2.4%)	5 (2.9%)	2 (1.2%)
Divorced/widowed/ separated	46 (27.1%)	20 (11.8%)	49 (28.8%)	17 (10%)	18 (10.6%)	48 (28.2%)
Education Level						
High School/GED or less	15 (8.8%)	14 (8.2%)	23 (13.5%)	5 (2.9%)	8 (4.7%)	20 (11.8%)
Some College/ Associates	30 (17.6%)	18 (10.6)	36 (21.2%)	12 (7.1%)	14 (8.2%)	34 (20%)
College Graduate/ Graduate Degree	55 (32.4%)	30 (17.6%)	66 (38.8%)	19 (11.2%)	36 (21.2%)	49 (28.8%)
Doctoral	4 (2.4%)	4 (2.4%)	5 (2.9%)	3 (1.8%)	3 (1.8%)	5 (2.9%)
Employment Status						
Working full time	4 (2.4%)	7 (4.1%)	9 (5.3%)	2 (1.2%)	5 (2.9%)	6 (3.5%)

Continued

Table 4: Demographics and Health Characteristics of MVM, Calcium, and Vitamin D users

Table 4 continued

Working part time	8 (4.7%)	4 (2.4%)	7 (4.1%)	5 (2.9%)	5 (2.9%)	7 (4.1%)
Retired/Homemaker/Disabled	92 (54.1%)	54 (31.8%)	113 (66.5%)	33 (19.4)	51 (30%)	95 (55.9%)
Number of Chronic Conditions (Mean (SD))	2.4 (1.8)	2.5 (2.1)	2.3 (1.9)	2.8 (1.9)	2.7 (2.2)	2.3 (1.7)
BMI (Mean (SD))	27.8 (5.7)	27.6 (7.0)	27.5 (5.6)	28.5 (7.9)	27.8 (6.5)	27.7 (6.1)
Cancer Type						
Breast	53 (39.8%)	37 (27.8%)	74 (55.6%)	16 (12.0%)	35 (26.3%)	55 (41.4%)
Hematological	12 (9.0%)	5 (3.8%)	12 (9.0%)	5 (3.8%)	5 (3.8%)	12 (9.0%)
Gynecological	10 (7.5%)	6 (4.5)	11 (8.3%)	5 (3.8%)	5 (3.8%)	11 (8.3%)
Gastrointestinal	3 (2.3%)	2 (1.5%)	2 (1.5%)	3 (2.3%)	2 (1.5%)	3 (2.3%)
Other	4 (3.0%)	1 (0.8%)	3 (2.3%)	2 (1.5%)	1 (0.8%)	4 (3.0%)

Table 4: Demographics and Health Characteristics of MVM, Calcium, and Vitamin D users

Healthy Eating Index Scores by Supplement Use

Table 5 used independent samples t-tests to determine the differences in HEI component scores between participants that utilized dietary supplements and participants who did not. There were significantly higher mean scores for total vegetables, greens and beans, whole fruit, and whole grains among those that supplemented than those that did not supplement with MVM. There was a significant difference in those that supplemented with vitamin D in HEI scores as well. Those who supplemented with vitamin D had significantly higher mean scores for greens and beans, than those who did not supplement with vitamin D.

Components	MVM		Calcium		Vitamin D	
	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))
Total Vegetable	4.5 (0.9)*	4.1 (1.1)	4.3 (1.0)	4.4 (1.0)	4.5 (0.9)	4.2 (1.1)
Greens and Beans	4.1 (1.3)*	3.6 (1.6)	3.9 (1.5)	4.1 (1.3)	4.3 (1.2)*	3.7 (1.5)
Total Fruit	4.2 (1.2)	4.1 (1.4)	4.3 (1.2)	3.9 (1.4)	4.0 (1.4)	4.3 (1.2)
Whole Fruit	4.7 (0.8)*	4.3 (1.3)	4.6 (1.0)	4.3 (1.1)	4.6 (1.0)	4.5 (1.0)
Whole Grains	2.9 (1.8)*	2.3 (1.6)	2.8 (1.9)	2.5 (1.3)	2.6 (1.7)	2.8 (1.8)
Dairy	5.9 (2.7)	6.3 (2.8)	6.2 (2.8)	5.8 (2.4)	6.0 (2.4)	6.1 (2.9)
Total Protein Foods	4.6 (0.8)	4.5 (0.9)	4.6 (0.8)	4.5 (0.8)	4.6 (0.8)	4.5 (0.8)
Seafood and Plant Proteins	4.6 (0.9)	4.4 (1.0)	4.6 (0.9)	4.3 (1.1)	4.6 (0.8)	4.5 (1.0)
Fatty Acids	4.8 (3.1)	4.6 (3.2)	4.8 (3.1)	4.4 (3.3)	4.9 (3.2)	4.6 (3.1)
Sodium	4.8 (2.8)	5.4 (2.9)	5.0 (2.7)	4.9 (3.3)	4.7 (2.9)	5.2 (2.8)
Refined Grains	9.0 (1.7)	8.8 (1.9)	8.9 (1.8)	8.9 (1.7)	8.7 (2.1)	9.1 (1.5)
Added Sugars	7.7 (2.8)	7.7 (3.1)	7.7 (2.9)	7.6 (2.9)	8.0 (2.7)	7.5 (3.0)
Saturated Fat	5.6 (3.2)	4.9 (3.3)	5.5 (3.2)	4.9 (3.2)	5.1 (3.1)	5.5 (3.3)
Total HEI-2015 Score	67.5 (9.7)	64.9 (10.6)	67.2 (10.2)	64.5 (9.7)	66.4 (10.3)	66.6 (10)

*= $p<0.05$

Table 5: HEI-2015 Component Scores by Supplementation

Health-related Quality of Life by Supplement Use

Table 6 used independent samples t-tests to determine the difference in RAND-36 subscale scores for MVM, calcium, and vitamin D use. There were no significant differences in health-related quality of life scores by supplement usage.

Subscales	MVM		Calcium		Vitamin D	
	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))
Physical Functioning	59.4 (24.4)	60.3 (23.7)	61.5 (23.8)	53.8 (24.2)	61.0 (24.3)	59.1 (24.1)

Continued

Table 6: HRQoL Subscale Results by Supplementation

Table 6 continued

Role Limitations due to Physical Health	**59.1 (40.9)**	**63.5 (43.8)**	**60.8 (41.7)**	**60.8 (43.5)**	**58.3 (43.9)**	**62.1 (41.1)**
Role Limitations due to Emotional Problems	81.3 (33.9)	81.3 (35.1)	80.2 (35.1)	85.2 (31.3)	85.1 (30.7)	79.2 (36.1)
Emotional Well-being	65.5 (10.5)	64.1 (10.3)	65.3 (10.3)	64 (10.9)	64.1 (9.6)	65.5 (10.8)
Energy/fatigue	41.8 (10.4)	44.3 (8.9)	42.9 (9.9)	42.3 (9.9)	42.0 (10.6)	43.1 (9.6)
Social Functioning	82.3 (20.6)	82.8 (22)	83.2 (20.7)	80.1 (22.3)	83.5 (20.1)	81.9 (21.7)
Pain	71.2 (21.9)	75.2 (22.9)	73.6 (22.2)	69.8 (22.6)	73.8 (22.1)	72.2 (22.4)
General Health	59.1 (15.3)	59.9 (15.5)	59.9 (15.5)	57.8 (14.7)	58.6 (16.3)	59.9 (14.8)
Physical Composite Score (PCS)	42.4 (10.6)	41.3 (10.5)	42.7 (10.5)	39.9 (10.5)	41.9 (11.0)	42.1 (10.3)
Mental Composite Score (MCS)	48.6 (6.9)	48.3 (7.8)	48.6 (7.1)	48.1 (7.1)	48.0 (7.5)	48.8 (7.0)

Table 6: HRQoL Subscale Results by Supplementation

Demographic and Clinical Factors Associated with Supplement Use

Logistic regressions were utilized to examine participants' demographic and health characteristics with MVM, calcium, and vitamin D supplementation (Table 7). Regression results found that a single-unit increase in HRQoL was associated with 4% lower likelihood of using an MVM. Furthermore, single-unit increases in the HEI was associated with 7% greater likelihood of MVM use. For calcium supplementation, those who were retired were 82.5% less likely to take a calcium supplement. No significant associations were found with age, race, marital status, college education, number of chronic conditions, or having breast cancer in any supplement investigated. No significant associations were found in vitamin D supplementation.

Variables	MVM		Calcium		Vitamin D	
	OR	95% CI	OR	95% CI	OR	95% CI
Age	1.04	0.96-1.13	0.93	0.84-1.02	0.99	0.92-1.07
White	0.29	0.05-1.61	6.85	0.42-111.07	0.26	0.04-1.60
Married	0.88	0.33-2.36	0.80	0.27-2.35	0.77	0.31-1.94
College education	1.78	0.68-4.66	1.37	0.48-3.93	0.45	0.18-1.13
Retirement	0.54	0.15-2.02	0.18*	0.04-0.76	0.96	0.27-3.37
General health	0.96*	0.93-0.99	1.02	0.99-1.06	0.97	0.95-1.00
HEI score	1.07*	1.01-1.13	1.04	0.98-1.10	0.97	0.92-1.02
Number of chronic conditions	0.92	0.72-1.18	0.91	0.70-1.19	1.00	0.79-1.26
Breast cancer	0.88	0.32-2.38	2.73	0.93-8.02	1.58	0.61-4.09

Table 7: Demographic and Clinical Factors Associated with MVM, Calcium, and Vitamin D Supplementation among Older Female Cancer Survivors.
Variables are all mutually adjusted. OR=Odds Ratio
*= $p<0.05$

Discussion

This study sought to determine the potential associations of dietary supplementation with HRQoL, as measured by the RAND-36, and diet quality, as measured by the HEI 2015, among older (≥65 years) female cancer survivors. This study also investigated demographic and clinical factors associated with supplement use in this understudied population. Hypotheses included: 1) dietary supplementation, specifically MVM, calcium, and vitamin D, would be positively associated with physical and mental HRQoL; 2) dietary supplementation would be positively associated with diet quality.

Prevalence and Predictors of Dietary Supplementation

Despite AICR recommendations not to utilize supplementation for cancer prevention, dietary supplement usage remains high at 56% taking two or more high dosage vitamins or minerals in older female cancer survivors[16,57]. As many as 15–50% of cancer patients initiate new supplement use after diagnosis, providing rationale for the high prevalence of supplement use in this population[58,59]. MVM usage found in this study was high, with 64.1% of participants reporting MVM intake. However, calcium supplementation was the most prevalent supplement used in this study at 76.9%. Vitamin D was the third most prevalent supplement at 35.3%, similar to previous findings in the literature.

A 2008 study researching older cancer survivors, found that 74% of participants were utilizing supplements. Among these supplements, MVM was the most prevalent (60%), followed by calcium/vitamin D (37%)[13]. Increased prevalence of calcium supplementation may be explained by participant's knowledge of aging, bone health, and previous treatments received. Calcium is a main nutrient of concern in older female cancer survivors due to age-related physiological changes making this mineral poorly retained[28]. Thus, dietary or supplement sources are a main focus of therapy for bone health in this population[28]. Furthermore, the most prevalent cancer type in this study seen in participants is breast cancer. Breast cancer patients may take aromatase inhibitors, which can increase a patient's risk for osteoporosis, further increasing the importance for proper calcium intake[60].

A 2004 report from the Vitamins And Lifestyle (VITAL) study also found that participants with a history of breast cancer had higher use of multivitamins, vitamin E, and calcium than older adults without a previous cancer diagnosis[57]. As 68% of this study's participants had a breast cancer diagnosis, the results from the VITAL study is consistent with MVM and calcium prevalence found in the current study.

Relative to those not supplementing with calcium, calcium users were less likely to be retired, either working full-time or part-time. There is currently a scarcity of research on the potential association between retirement status and calcium supplementation. One 2013 study investigating retirement and changes in dietary intake found that intake of calcium-rich foods and milk was low among retired individuals compared to working individuals[61]. This study justifies results by a potential constraining food budget due to retirement[61]. While price can fluctuate depending on the form of calcium, a 300 mg calcium carbonate tablet was on average 11 cents, resulting in around 40 dollars a year[62]. Retired participants may not choose to add the expense of a calcium supplement. Conversely, one 2017 study found that dietary calcium intake did not change from employment to retirement in participants, however, transition to retirement was associated with unhealthier dietary intakes, such a decrease in the overall diet quality and intakes of recommended foods and nutrients[63]. This study notes that there should be targeted interventions before age of retirement to optimize diet quality, including calcium intake, with reduced budget could be of interest[63].

After adjustment, no significant associations were found for age, race, marital status, college education, number of chronic conditions, or having breast cancer with any supplement investigated. However, using unadjusted data, supplement users were more likely to be white, married, retired, and have at least a college degree. Similarly, studies have found that participants with a professional or graduate degree/a higher level of education were significantly more likely to use supplements[13,58]. Findings suggest that those with higher education levels are more likely to learn about and recognize the purpose of supplements. Furthermore, study findings may suggest that those with higher education have increased health literacy, thereby making supplement choices to support health concerns. Additionally, a 2020 study comparing cancer

survivors and individual adults without cancer, found that cancer survivors who used dietary supplements were older and more likely to be women and non-Hispanic whites, had higher levels of education, income, and better diet quality, and were less likely to be overweight/obese[12]. Conversely, a 2018 study found that older adult breast cancer survivors consumed more alcohol and more often used supplements than females in the control group[64]. Due to conflicting data and a growing population of older cancer survivors, more research is needed to verify the demographic characteristics and reasons why individuals are choosing to use supplements.

Healthy Eating Index and Diet Quality

According to NHANES data, the average total HEI score for older Americans in 2016 was 64[65]. While the mean total HEI scores from 1999-2002 for older females 67.6[66]. The average total HEI score for the older female participants of this study was 66.5, representing a slightly higher score compared to the national average. However, participants' average scores reflect a diet that "needs improvement"[38].

Compared to the older Americans, study participants reported higher intakes of adequacy total vegetable, greens and beans, total fruit, dairy, and fatty acids and lower intakes of whole fruit, whole grains, total protein, and seafood and plant proteins[65]. Of note, participants received a 2.7 out of a possible 10 points in the whole grains' component. The national average for the whole grains' component among older Americans was 4.0[65]. Study results represent consuming far less than 1.5 ounce equivalent per 1,000 kcal[67]. Participants, on average, scored higher than older Americans in every moderation subcomponent (sodium, refined grains, added sugar, and saturated fats), reflecting slightly lower intake of these foods[65]. The current sample's higher HEI scores compared to the national average could be attributed to higher education, as 50% of the participants are college graduates or have a graduate degree. In previous studies utilizing the HEI

2010, college graduates were more likely to have higher HEI scores than those with less education[68,69]. Another potential reason for higher HEI scores compared to the general older adult population is that participants were all women in this study. As reported in the 1999-2002 NHANES data, females had higher scores than males for the fruit, cholesterol, and sodium components, and the overall total HEI score[66].

The association between HEI 2015 scores and dietary supplement usage in participants was also investigated. A key question throughout this research was if older female cancer survivors were taking dietary supplements because they were already making healthier dietary choices, or were they taking dietary supplements to compensate for the gaps within their dietary intake. Participants supplementing with an MVM had significantly higher mean HEI component scores for total vegetables, greens and beans, whole fruits, and whole grains. Furthermore, single-unit increases in the HEI was associated with 7% greater likelihood of MVM use. Participants supplementing with vitamin D also had higher mean scores for greens and beans. These results suggest that older women with already higher mean HEI scores were also utilizing dietary supplements, rather than those with lower HEI scores filling in the gaps with MVM usage.

Results regarding HEI scores, and supplementation are similar to previous research on supplement use and older cancer survivors. Miller and colleagues determined that individuals scoring higher mean scores of total fruit, whole grain, and oil components of the HEI were significantly more prone to utilize dietary supplements[13]. While other studies utilized a prior HEI-2005, research has found supplement users to have higher diet quality scores[70,71]. While prior HEI subcomponents have been updated, previous studies support higher intakes of fruits, vegetables, and fiber, and lower intakes of saturated fat by supplement users[71,72].

As previously noted, participants who supplemented with vitamin D had higher mean greens and beans scores. The greens and beans subcomponent of the HEI contains dark green vegetables, peas, and legumes. None of the foods listed in this subcomponent are high food sources of vitamin D, however, they can be high in calcium. This finding may suggest that vitamin D supplement users are also aware of the relationship between calcium intake and bone health, as the risk of osteoporosis is increases with age[28]. Furthermore, cancer survivors may be at further risk of poor bone health due to cancer related treatments, further increasing the importance of eating calcium rich foods[73].

Health-related Quality of Life

Participants received an average of 42.0 out of a possible 100 in the PCS and a 48.5 in the MCS of the RAND-36. The average mean general health subscale was 59.4. There are mixed results comparing this study's results to previous research on older adults. In a 2018 study, older participants scored higher in the general health subscale, however they scored lower in the general health subscale in three additional studies[74,75,76,77]. Another study reported that older female cancer survivors have low HRQoL scores on average compared to older adults who were not cancer survivors[54].

There are a variety of factors that can influence study participants' HRQoL scores. A systematic review of HRQoL and dietary patterns in older adults found that adherence to healthy dietary patterns were associated with better HRQoL scores in at least one subscale[35]. Another study has also found that lower physical and mental HRQoL scores were associated with both demographic (age, race) and lifestyle characteristics (diet quality, physical activity)[54]. This current study was composed of older educated participants with higher than average HEI-scores in total vegetable, greens and beans, total fruit, dairy, and fatty acids; therefore, potentially

positively influencing HRQoL scores. In this study, regression results found that a single-unit increase in HRQoL was associated with 4% lower likelihood of using an MVM. Thus, demonstrating in this study that higher HRQoL is not associated with taking an MVM supplement.

This study found no significant correlations between HRQoL and MVM/calcium/vitamin D supplementation. MVMs contain a variety of vitamins and minerals that could potentially affect energy levels (vitamin B12, iron) and physical health (vitamin C, vitamin A), and thus HRQoL[78]. However, this association was not observed in this study. Participants' HRQoL may be more affected by their dietary quality rather than their supplementation use. Study results suggest that individual vitamin or mineral supplementation and multivitamin use do not positively affect HRQoL subscales. Findings suggest that more impact on HRQoL scores can be seen through positive changes to dietary intake. Contrary to current study's findings, previous studies have found that calcium and vitamin D supplementation have positively impacted HRQoL scores in cancer survivors[52,53]. Due to current contradictory results, future studies should further research the association between HRQoL and supplementation among older adults.

Study Strengths and Limitations

This study examined the associations between diet quality, HRQoL, and dietary supplementation in a population that is under researched, thus adding to the existing gap in the current literature. This study utilized the most recent and updated version of the HEI-2015 to better assess diet quality in participants. Furthermore, the sample size of 173 participants allowed for significant associations to be evaluated. Lastly, researching supplement intake adds to the literature as it is an under researched topic in older adults, particularly those with a history of cancer.

Despite these strengths, this study is limited due to the cross-sectional design, as it is not possible to assess a causal relationship between supplement use and health status. Future research should follow study participants longitudinally for the cause-and-effect relationships. The sample is not generalizable to males, different racial groups, and less educated older cancer survivors as the majority of the female participants have at least a college degree and are white. Furthermore, participants were recruited from one cancer center, potentially limiting generalizability. The data gathered in this study were collected from a self-report survey, which can lead to measurement error as participants may not feel comfortable answering questions candidly, they may exaggerate or understate health status, or they may not understand survey questions. Furthermore, the DHQ II is not robust in questions regarding supplementation. Questions regarding form of supplement, dosage, duration of supplement use, and for what reason supplements were initiated are lacking for every supplement included on the DHQ II. For example, study participants were asked if they took vitamin D, however, the form of vitamin D was not evaluated (i.e., D2 or D3).

Implications and Future Directions

It is crucial for Registered Dietitian Nutritionists (RDNs) and healthcare providers to ask if their patients are taking a dietary supplement, as the prevalence of supplement use remains high. Additionally, most older patients do not initiate supplement use under the advisement of an RDN or healthcare provider, or discuss supplement use during appointments, thus making it essential for RDNs to include supplement use in their nutrition assessment[79]. By considering supplement use, RDNs can understand potential medication interactions, reasons for supplementation use, and efficacy/accuracy of supplementation. Based on study results, older female cancer survivors utilizing MVM supplements were also more likely to have higher

average HEI scores. Therefore, it is important for RDNs to understand what variety of MVM their patient is taking and to address potential toxicities[80,81]. RDNs will be able to use dietary intake information to address whether the patient truly needs to utilize supplementation, as those with better diet quality were also the ones supplementing. RDNs can use supplementation as an opportunity to stress the importance of eating a whole foods balanced diet. This becomes especially important in the cancer survivor population, as many patients are looking for ways to reduce risk of recurrence or a second primary cancer. Furthermore, understanding the relationship between dietary quality and HRQoL will assist decisions on whether a patient should initiate use.

This study determined prevalence of supplementation in older female cancer survivors; however, future research should capture more specifics on dosage, frequency, brand, and reason for supplement utilization. Rather than focus on three supplements, studies moving forward should include a full list of herbal and dietary supplements. Future research could also utilize biomarkers to assess if supplementation aided in nutritional adequacy or possible toxicity among older cancer survivors. Furthermore, future research could utilize focus groups or semi-structured interviews to better assess when survivors are initiating supplements, for what reason, and to assess survivors' knowledge on the supplements being utilized.

Conclusion

The purpose of this study was to evaluate the associations between supplement use (MVM, calcium, vitamin D), diet quality, and HRQoL. Supplement usage in this population is high with MVM usage at 64% of participants, calcium supplementation at 77%, and vitamin D at 35%. Results found that MVM users had higher mean diet quality scores in total vegetables, greens and beans, whole fruits, and whole grains, while vitamin D users had higher mean scores

in greens and beans. Regression results found that retirees were 82.5% less likely to utilize calcium supplements. Regression results also found an association between higher HEI scores and MVM use. Lastly, participants with higher mean HRQoL scores were 4% less likely to utilize an MVM. To provide better healthcare to cancer survivors, it is crucial to also understand who is utilizing supplements and the nutritional necessity behind this behavior. As prevalence remains high in the cancer survivor population, RDNs should include supplement intake in their nutrition assessments to better evaluate patients' nutrition status, and ultimately improve patient health outcomes.

Chapter 5: Manuscript

Abstract

Background: Older cancer survivors report a high prevalence of dietary supplement use, specifically multivitamin (MVM), calcium, and vitamin D. Supplement intake is a modifiable health behavior that can impact overall diet quality and health-related quality of life (HRQoL).

Objective/Hypothesis: To identify the prevalence of supplement intake (MVM, calcium, vitamin D) in older female cancer survivors, and the association with diet quality and HRQoL.

Methods: Participants were female cancer survivors (≥65 years), who were ≤5 years post-cancer diagnosis, identified at the OSU-James Cancer Hospital. Participating women completed self-administered questionnaires assessing HRQoL (RAND-36), and diet quality and supplement intake (DHQ II converted to HEI-2015). Descriptive statistics, Pearson's correlations, and adjusted logistic regression models were used.

Results: Prevalence of MVM, calcium, and vitamin D supplementation was 61.4%, 76.9%, and 35.3%, respectively. The majority of participants that took in MVMs/calcium/vitamin D were white and received a college degree. Women that used MVM supplements had significantly higher mean scores for total vegetables (4.5±0.9 SD to 4.1±1.1), greens and beans (4.1±1.3 to 3.6±1.6), whole fruit (4.7± 0.8 to 4.3±1.3), and whole grains (2.9±1.8 to 2.3±1.6) than those who did not use these supplements. After controlling for demographic and clinical variables, participants with lower HRQoL were 4% more likely to take an MVM. Furthermore, the odds of taking an MVM was 1.07 times greater among those older women who had higher total HEI scores.

Conclusions: Although no evidence-based guidelines recommend dietary supplementation for cancer survivors, supplementation use among older female cancer survivors remains high.

Participants with better diet quality were also more likely to be engaging in supplement use. Understanding the prevalence of supplementation, associations with diet quality, and perceived benefits of supplementation may help health care providers in educating survivors and promoting dietary patterns that meet nutrient needs.

Introduction

Cancer survivors are categorized as survivors from the time of diagnosis through the balance of his or her life[2]. As the U.S. population shifts towards an aging populace and life expectancies are rising, the number of older cancer survivors (age ≥65 years) increases[3]. Older adults represent the largest proportion of cancer survivors[3]. Due to this growing prevalence, researchers and clinicians need to investigate these older cancer survivors in order to provide effective healthcare. Furthermore, it is crucial to study females specifically, as cancer is the first or second leading cause of death for every age group shown among females, whereas, among males aged <40 years, accidents, suicide, and homicide predominate[1].

Older adults with a history of cancer may live with the fear of cancer recurrence or even a second primary cancer[5]. As this population is highly motivated to improve their health outcomes, many cancer survivors look to nutrition/dietary changes or other lifestyle changes (e.g., physical activity, stress reduction) as actionable behaviors to reduce their risk[6].

Health-related quality of life (HRQoL) is a meaningful and widely used assessment tool in the older adult population. HRQoL is frequently used to measure the effects of chronic illness like cancer, to better understand how an illness interferes with a person's daily life[8]. By investigating both physical and mental summary measures of HRQoL, researchers can investigate associations between HRQoL and nutritional health (e.g., dietary intake and dietary quality). This population is at risk for a decrease in HRQoL due to possible frailty, disability, and chronic illness with aging[8]. However, it should not be assumed that aging equates to an automatic decrease in HRQoL[8]. To use this marker effectively in research, it is imperative to have a clear operational definition. The RAND-36 survey is comprised of eight different areas: physical functioning, role limitations caused by physical health problems, role limitations caused

by emotional problems, social functioning, emotional well-being, energy/fatigue, pain, and general health perceptions[34]. Examining each facet of mental and physical health will help better assess this population's perception of their HRQOL and consequentially what factors affect their HRQOL.

Diet quality is a key topic of importance in the aging cancer survivor population, as the connection between intake and health status is clear. To assess diet quality, questionnaires such as the food frequency questionnaire can be used to compare to the Dietary Guidelines for Americans (DGA). The DGA concentrates on foods and dietary patterns that promote health for individuals ≥2 years of age. Furthermore, the DGA provides a counsel on healthy aging through dietary patterns and physical activity. Using Healthy Eating Index 2015 (HEI) scores can accurately assess a person's diet quality relative to the 2015-2020 DGA[10]. Thus, it can be used to assess the conformity of any group of foods to the diet quality recommendations detailed in the DGA[11]. The HEI yields a total score, which analyzes the overall dietary quality, and separate component scores that can be examined collectively to reveal a pattern of quality regarding multiple dietary dimensions[37]. Nine components focus on adequacy or foods necessary to get the essential macronutrients and micronutrients[10]. Four components focus on moderation, dietary components that are recommended in small amounts[10]. In an evaluation of the HEI 2015, each age group was investigated for diet quality scores. The oldest age groups (age ≥60 years) were found to have the highest mean score compared to younger age groups (20-39 years) indicating better diet quality[11].

An overwhelming proportion of older adults and cancer survivors utilize dietary supplements to improve health status[12]. A 2020 study found that survivors reported a higher prevalence of any supplement use (70.4% vs. 51.2%) and multivitamin (MVM)/mineral

supplement use (48.9% vs. 36.6%) than individuals without cancer[12]. MVMs, vitamin D, and calcium are among the most commonly utilized supplements among the older cancer survivor population[13]. Dietary supplementation does not guarantee that individuals or cancer survivors will be meeting their nutrient requirements if their overall dietary pattern is not nutrient-dense. As so many older adults are relying on supplements, it is crucial to understand the association between intake and diet quality.

For this study, we hypothesized: 1) dietary supplementation, specifically MVM, calcium, and vitamin D, would be associated with better physical and mental HRQoL; 2) dietary supplementation would be associated with better diet quality.

Methods

Participants

In order to be eligible for participation, prospective participants needed to be female cancer survivors, ≥65 years, who were willing and able to provide written informed consent. For the study's purposes, cancer survivors were defined as individuals who were diagnosed with cancer in the past five years and had completed primary cancer treatment (i.e., received chemotherapy, surgery, and/or radiation). Women diagnosed with cancers at any anatomic sites and at any stage were eligible. Limiting participants to have up to five years post diagnosis was done to ensure the accuracy of reported dietary patterns and weight changes after cancer diagnosis.

Research Design

Participants were identified through one of two methods: 1) through OSUCCC clinic visits to the Blood Cancer and Longevity Clinic and Gastrointestinal Clinic and the Geriatric Oncology Clinic at the Stefanie Spielman Breast Center. Clinicians at each clinic provided prospective participants with a recruitment flyer including information surrounding the study and the PI's

(Dr. Krok-Schoen) name and contact information. 2) through medical records obtained from the OSUCCC cancer registry.

A recruitment letter including information about the study was then mailed out to these potential participants. Women who contacted the study coordinator were screened to ensure they met all eligibility criteria and then informed of the study's goals. These women were then asked if they were willing to participate and if so, they could complete the survey online or request a survey via mail or telephone. Online surveys were taken via Research Electronic Data Capture (REDCap), a secure web application developed for clinical research. Informed consent, as well as a HIPAA waiver, to collect basic demographic, and clinical characteristics from their medical records were obtained from all participants. All participants received a $10 gift card for completing the survey. The Institutional Review Boards of the participating clinic and University approved the informed consent procedures and study protocols.

Survey Measures

For the purposes of this study, the RAND-36, the DHQ II, and demographic and medical information was used.

Health-related Quality of Life

The survey utilized a 36-Item Health Survey (RAND-36) to examine health-related quality of life in older adult female cancer survivors. The RAND-36 is one of the most widely used health-related quality of life[34]. This 36-item survey is comprised of two summary measure of physical health and mental health, and eight subscales assessing the following aspects of HRQoL: physical functioning, role functioning physical, pain, general health, energy/fatigue, social functioning, role functioning emotional, and emotional well-being[34]. The survey uses a Likert scale to assess participant's responses. Responses to the individual items are transformed

during data analysis to a scale ranging from 0-100, with 100 being the highest subscale score for each of the 8 subscales. In addition, two composite scores can be created from the 8 subscales concerning physical (PCS) and mental (MCS) health concerns. For the purposes of this study, the PCS and MCS were used as measures of the participants' physical and mental HRQoL.

Food Frequency and Healthy Eating Index-2015

A Diet History Questionnaire II, a validated food frequency questionnaire was used to investigate food and nutrient consumption among older adults in the study. The DHQ II has a food list that was updated based on more recent dietary data and consists of 134 food items and 8 dietary supplement questions[55]. The results of the DHQ II were used to estimate diet quality according to the HEI-2015. The HEI-2015 is the most recent iteration of the HEI, which assesses diet quality, dietary patterns, and adherence to the 2015-2020 U.S. Dietary Guidelines for Americans[37]. The HEI uses a scoring system to evaluate a set of food components; the scores range from 0 to 100[37]. For each dietary component, the HEI assigns a certain amount as the standard. A maximum score of 5 or 10 points (depending on the component being assessed) is given to amounts that meet the standard recommendation[10]. The DHQ II was also used to assess dietary supplement intake among older female adults in this study. The DHQ II included an extensive list of dietary supplements and herbals/botanicals that participants could mark if they were currently consuming and if so, what is the frequency. For the purposes of this study, MVM, vitamin D, and calcium supplementation (yes/no, frequency, and duration) will be investigated.

Demographics and Clinical Characteristics

Additional information regarding the participants' clinical (e.g., date of cancer diagnosis, cancer stage, treatments received, cancer recurrence, other chronic diseases, and prescription

regimen) and demographic (e.g., age, gender, race, ethnicity) were collected through medical record review.

Data Analysis

Descriptive statistics (e.g., means, frequencies) were used for the demographic and health characteristics, HEI-2015 total score and subcomponent scores, dietary supplementation (vitamin D, calcium, and MVM), and HRQoL (PCS, MCS). DHQ II scores were converted to the HEI-2015 scores, per guidelines from the National Cancer Institute, utilizing SAS and Diet*Calc[56]. T-tests were used to assess potential differences between supplementation (yes/no) and RAND-36 scores and HEI scores. Pearson's correlations were used to assess potential associations among supplementation (yes/no), HEI total score, PCS, MCS, health-related quality of life, and demographic and clinical characteristics. Logistic regressions were conducted to assess potential associations between supplementation (yes/no), HEI total score, PCS, and MCS, while controlling for demographic (age, race, education, marital status, employment) and clinical (cancer type, AJCC stage, time since diagnosis, number of chronic conditions) characteristics. Factors were each mutually adjusted (i.e., age, retirement status, BMI) in logistic regression models. IBM SPSS Statistics version 27.0 was used. All reported *P* values are two-sided, with a Type I error rate set at 0.05.

Results

Demographic and Health Characteristics

Table 8 describes study participants' demographic and health characteristics. The study sample included 173 older female cancer survivors, with a mean age of 73.6 $\pm$ 6.1 years. The majority of participants were white (90%), married (54.7%), received a bachelor's, master's, or professional degree (50%), and were currently retired (82%). The majority of participants, 65%,

had a normal BMI (18.5-24.9 kg/m^2) to overweight BMI (25-29.9 kg/m^2), with 56.9% reporting 1-2 chronic conditions in addition to their cancer diagnosis. The majority of participants were diagnosed with breast cancer (67.7%), followed by hematological (12.8%) and gynecological (12.0%) cancer. Cancer stage at diagnosis was most commonly stage 1A and 1B (44.2%), followed by stage 2A and 2B (36%). Household income was spread out between $20,000-50,000 (26.0%), $50,000-100,000 (27.8%), and $100,001+ (16.0%).

Prevalence of MVM usage was 61.4%, calcium usage was 76.9%, and vitamin D usage was 35.3%. Of the participants taking MVMs, the majority (85.4%) took their MVM every day. Of the participants taking calcium, 46.2% have been taking 10 years or more, 26.9% took calcium for 5-9 years, 16.3% took calcium 1-4 years, while 10.6% have been taking calcium for less than one year. The majority of participants supplementing calcium chose 1,000 mg or more (36.8%) or 600-999 mg (34.7%), followed by 500-599 mg (23.2%), and less than 500 mg (5.3%).

Demographic	**N (%)**
Age (mean (SD))	73.62 (6.1)
Age at diagnosis, mean (SD)	71.5 (5.9)
Race/Ethnicity	
White	144 (90.0)
Black	13 (8.1)
Asian	2 (1.3)
Other	1 (0.6)
Marital Status	
Married	93 (54.7)
Single/unmarried/unmarried couple	7 (4.2)
Divorced/widowed/separated	66 (38.8)
Education Level	
High School/GED or less	28 (16.5)
Some College/Associates	48 (28.2)

Continued

Table 8: Demographics and Health Characteristics of Older Female Cancer Survivors

Table 8 continued

College graduate/Graduate degree	**85 (50)**
Doctoral	8 (4.7)
Employment Status	
Working full time	11 (6.5)
Working part-time	12 (7.1)
Retired/Homemaker/Disabled	146 (85.9)
Household Income	
Less than $20,000	17 (10.1)
$20,001-$50,000	44 (26.0)
$50,001-$100,000	47 (27.8)
$100,001+	27 (16.0)
Health Characteristics	
BMI (mean, SD)	27.7 (6.2)
Underweight	4 (2.4)
Normal/Overweight	109 (64.9)
Obese (1, 2, extreme)	55 (32.7)
Cancer type	
Breast	90 (67.7)
Hematological	17 (12.8)
Gynecological	16 (12.0)
Gastrointestinal	5 (3.8)
Other	5 (3.8)
AJCC stage at diagnosis	
0	8 (13.1)
1A/1B	27 (44.2)
2A/2B	22 (36)
3B/3C	4 (6.5)
Number of Chronic Conditions	
0	8 (5.6)
1-2	82 (56.9)
3-4	34 (23.6)
5-6	14 (9.8)
7-10	6 (4.2)
Supplementation Usage	
Multivitamin	105 (61.4)
Calcium	133 (76.9)
Vitamin D	61 (35.3)

Table 8: Demographics and Health Characteristics of Older Female Cancer Survivors
*=Not all categories equal n=173 due to missing data

Demographic and Health Characteristics of Supplement Users and Non-Users

Table 9 shows the demographic and health characteristics of participants stratified on their MVM, calcium, or vitamin D supplementation. The average age of MVM users was 74.2 $\pm$ 6.0, calcium users 73.4 $\pm$ 5.8, and vitamin D users 73.1 $\pm$ 5.8. The majority of participants that utilized MVMs/calcium/vitamin D were white (58.1%), married (33%), received at least a college degree (32.4%), and are retired/disabled/homemakers (54.1%). Breast cancer survivors were the cancer type to most likely utilize MVM, calcium, and vitamin D.

Variables	**Multivitamin**		**Calcium**		**Vitamin D**	
	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)	Yes Mean (SD) or n (%)	No Mean (SD) or n (%)
Age (Mean (SD))	74.2 (6.0)	72.8 (6.2)	73.4 (5.8)	74.4 (7.0)	73.1 (5.8)	73.9 (6.3)
Race						
White	93 (58.1%)	51 (31.9%)	109 (68.1%)	35 (21.9%)	54 (33.8%)	90 (56.2%)
Black	8 (5.0%)	5 (3.1%)	12 (7.5%)	1 (0.6%)	3 (1.9%)	10 (6.2%)
Asian	0	2 (1.3%)	2 (1.3%)	0	0	2 (1.3%)
Other	0	1 (0.6%)	1 (0.6%)	0	0	1 (0.6%)
Marital status						
Married	56 (33.0%)	37 (21.8%)	74 (43.5%)	19 (11.2%)	37 (21.8%)	56 (32.9%)
Single/Unmarried/ Unmarried couple	1 (0.6%)	6 (3.5%)	3 (1.8%)	4 (2.4%)	5 (2.9%)	2 (1.2%)
Divorced/widowed/ separated	46 (27.1%)	20 (11.8%)	49 (28.8%)	17 (10%)	18 (10.6%)	48 (28.2%)
Education Level						

Continued

Table 9: Demographics and Health Characteristics of MVM, Calcium, and Vitamin D users

Table 9 continued

High School/GED or less	15 (8.8%)	14 (8.2%)	23 (13.5%)	5 (2.9%)	8 (4.7%)	20 (11.8%)
Some College/ Associates	30 (17.6%)	18 (10.6)	36 (21.2%)	12 (7.1%)	14 (8.2%)	34 (20%)
College Graduate/ Graduate Degree	55 (32.4%)	30 (17.6%)	66 (38.8%)	19 (11.2%)	36 (21.2%)	49 (28.8%)
Doctoral	4 (2.4%)	4 (2.4%)	5 (2.9%)	3 (1.8%)	3 (1.8%)	5 (2.9%)
Employment Status						
Working full time	4 (2.4%)	7 (4.1%)	9 (5.3%)	2 (1.2%)	5 (2.9%)	6 (3.5%)
Working part time	8 (4.7%)	4 (2.4%)	7 (4.1%)	5 (2.9%)	5 (2.9%)	7 (4.1%)
Retired/Homemaker/Disabled	92 (54.1%)	54 (31.8%)	113 (66.5%)	33 (19.4)	51 (30%)	95 (55.9%)
Number of Chronic Conditions (Mean (SD))	2.4 (1.8)	2.5 (2.1)	2.3 (1.9)	2.8 (1.9)	2.7 (2.2)	2.3 (1.7)
BMI (Mean (SD))	27.8 (5.7)	27.6 (7.0)	27.5 (5.6)	28.5 (7.9)	27.8 (6.5)	27.7 (6.1)
Cancer Type						
Breast	53 (39.8%)	37 (27.8%)	74 (55.6%)	16 (12.0%)	35 (26.3%)	55 (41.4%)
Hematological	12 (9.0%)	5 (3.8%)	12 (9.0%)	5 (3.8%)	5 (3.8%)	12 (9.0%)
Gynecological	10 (7.5%)	6 (4.5)	11 (8.3%)	5 (3.8%)	5 (3.8%)	11 (8.3%)
Gastrointestinal	3 (2.3%)	2 (1.5%)	2 (1.5%)	3 (2.3%)	2 (1.5%)	3 (2.3%)
Other	4 (3.0%)	1 (0.8%)	3 (2.3%)	2 (1.5%)	1 (0.8%)	4 (3.0%)

Table 9: Demographics and Health Characteristics of MVM, Calcium, and Vitamin D users

Healthy Eating Index Scores by Supplement Use

Table 10 used independent samples t-tests to determine the differences in HEI component scores between participants that utilized dietary supplements and participants who did not. There were significantly higher mean scores for total vegetables, greens and beans, whole fruit, and whole grains among those that supplemented than those that did not supplement with MVM. Those who supplemented with vitamin D had significantly higher mean scores for greens and beans, than those who did not supplement with vitamin D.

Components	MVM		Calcium		Vitamin D	
	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))
Total Vegetable	4.5 (0.9)*	4.1 (1.1)	4.3 (1.0)	4.4 (1.0)	4.5 (0.9)	4.2 (1.1)
Greens and Beans	4.1 (1.3)*	3.6 (1.6)	3.9 (1.5)	4.1 (1.3)	4.3 (1.2)*	3.7 (1.5)
Total Fruit	4.2 (1.2)	4.1 (1.4)	4.3 (1.2)	3.9 (1.4)	4.0 (1.4)	4.3 (1.2)
Whole Fruit	4.7 (0.8)*	4.3 (1.3)	4.6 (1.0)	4.3 (1.1)	4.6 (1.0)	4.5 (1.0)
Whole Grains	2.9 (1.8)*	2.3 (1.6)	2.8 (1.9)	2.5 (1.3)	2.6 (1.7)	2.8 (1.8)
Dairy	5.9 (2.7)	6.3 (2.8)	6.2 (2.8)	5.8 (2.4)	6.0 (2.4)	6.1 (2.9)
Total Protein Foods	4.6 (0.8)	4.5 (0.9)	4.6 (0.8)	4.5 (0.8)	4.6 (0.8)	4.5 (0.8)
Seafood and Plant Proteins	4.6 (0.9)	4.4 (1.0)	4.6 (0.9)	4.3 (1.1)	4.6 (0.8)	4.5 (1.0)
Fatty Acids	4.8 (3.1)	4.6 (3.2)	4.8 (3.1)	4.4 (3.3)	4.9 (3.2)	4.6 (3.1)
Sodium	4.8 (2.8)	5.4 (2.9)	5.0 (2.7)	4.9 (3.3)	4.7 (2.9)	5.2 (2.8)
Refined Grains	9.0 (1.7)	8.8 (1.9)	8.9 (1.8)	8.9 (1.7)	8.7 (2.1)	9.1 (1.5)
Added Sugars	7.7 (2.8)	7.7 (3.1)	7.7 (2.9)	7.6 (2.9)	8.0 (2.7)	7.5 (3.0)
Saturated Fat	5.6 (3.2)	4.9 (3.3)	5.5 (3.2)	4.9 (3.2)	5.1 (3.1)	5.5 (3.3)
Total HEI-2015 Score	67.5 (9.7)	64.9 (10.6)	67.2 (10.2)	64.5 (9.7)	66.4 (10.3)	66.6 (10)

Table 10: HEI-2015 Component Scores by Supplementation
*= $p<0.05$

Health-related Quality of Life by Supplement Use

Table 11 used independent samples t-tests to determine the difference in RAND-36 subscale scores for MVM, calcium, and vitamin D use. There were no significant differences in health-related quality of life scores by supplement usage.

Subscales	MVM		Calcium		Vitamin D	
	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))	Yes (mean (SD))	No (mean (SD))
Physical Functioning	59.4 (24.4)	60.3 (23.7)	61.5 (23.8)	53.8 (24.2)	61.0 (24.3)	59.1 (24.1)
Role Limitations due to Physical Health	59.1 (40.9)	63.5 (43.8)	60.8 (41.7)	60.8 (43.5)	58.3 (43.9)	62.1 (41.1)
Role Limitations due to Emotional Problems	81.3 (33.9)	81.3 (35.1)	80.2 (35.1)	85.2 (31.3)	85.1 (30.7)	79.2 (36.1)
Emotional Well-being	65.5 (10.5)	64.1 (10.3)	65.3 (10.3)	64 (10.9)	64.1 (9.6)	65.5 (10.8)
Energy/fatigue	41.8 (10.4)	44.3 (8.9)	42.9 (9.9)	42.3 (9.9)	42.0 (10.6)	43.1 (9.6)
Social Functioning	82.3 (20.6)	82.8 (22)	83.2 (20.7)	80.1 (22.3)	83.5 (20.1)	81.9 (21.7)
Pain	71.2 (21.9)	75.2 (22.9)	73.6 (22.2)	69.8 (22.6)	73.8 (22.1)	72.2 (22.4)
General Health	59.1 (15.3)	59.9 (15.5)	59.9 (15.5)	57.8 (14.7)	58.6 (16.3)	59.9 (14.8)
Physical Composite Score (PCS)	42.4 (10.6)	41.3 (10.5)	42.7 (10.5)	39.9 (10.5)	41.9 (11.0)	42.1 (10.3)
Mental Composite Score (MCS)	48.6 (6.9)	48.3 (7.8)	48.6 (7.1)	48.1 (7.1)	48.0 (7.5)	48.8 (7.0)

Table 11: HRQoL Subscale Results by Supplementation

Demographic and Clinical Factors Associated with Supplement Use

Binary logistic regressions were utilized to find participant demographic and health characteristics associated with MVM, calcium, and vitamin D supplementation. Regression results found that a single-unit increase in HRQoL was associated with 4% lower likelihood of using an MVM. Furthermore, single-unit increases in the HEI was associated with 7% greater likelihood of MVM use. For calcium supplementation, those who were retired were 82.5% less likely to take a calcium supplement. No significant associations were found with age, race, marital status, college education, number of chronic conditions, or having breast cancer in any supplement investigated. No significant associations were found in vitamin D supplementation.

Variables	MVM		Calcium		Vitamin D	
	OR	95% CI	OR	95% CI	OR	95% CI
Age	1.04	0.96-1.13	0.93	0.84-1.02	0.99	0.92-1.07
White	0.29	0.05-1.61	6.85	0.42-111.07	0.26	0.04-1.60
Married	0.88	0.33-2.36	0.80	0.27-2.35	0.77	0.31-1.94
College education	1.78	0.68-4.66	1.37	0.48-3.93	0.45	0.18-1.13
Retirement	0.54	0.15-2.02	0.18*	0.04-0.76	0.96	0.27-3.37
General health	0.96*	0.93-0.99	1.02	0.99-1.06	0.97	0.95-1.00
HEI score	1.07*	1.01-1.13	1.04	0.98-1.10	0.97	0.92-1.02
Number of chronic conditions	0.92	0.72-1.18	0.91	0.70-1.19	1.00	0.79-1.26
Breast cancer	0.88	0.32-2.38	2.73	0.93-8.02	1.58	0.61-4.09

Table 12: Demographic and Clinical Factors Associated with MVM, Calcium, and Vitamin D Supplementation among Older Female Cancer Survivors.
Variables are all mutually adjusted. OR=Odds Ratio
*= $p<0.05$

Discussion

This study sought to determine the potential associations of dietary supplementation with HRQoL, as measured by the RAND-36, and diet quality, as measured by the HEI 2015, among older (≥65 years) female cancer survivors. This study also investigated demographic and clinical factors associated with supplement use in this understudied population. Despite AICR recommendations not to utilize supplementation for cancer prevention, dietary supplement usage remains high at 56% taking two or more high dosage vitamins or minerals in older female cancer survivors[16,57]. As many as 15–50% of cancer patients initiate new supplement use after diagnosis, providing rationale for the high prevalence of supplement use in this population[58,59]. MVM usage found in this study was high with 64.1% of participants. However, calcium supplementation was the most prevalent supplement used in this study at 76.9%. Vitamin D was the third most prevalent supplement at 35.3%, similar to previous findings in the literature.

A 2008 study researching older cancer survivors, found that 74% of participants were utilizing supplements. Among these supplements, MVM was the most prevalent (60%), followed by calcium/vitamin D (37%)[13]. Increased prevalence of calcium supplementation may be explained by participant's knowledge of aging, bone health, and previous treatments received. Calcium is a main nutrient of concern in older female cancer survivors due to age-related physiological changes making this mineral poorly retained[28]. Thus, dietary or supplement sources are a main focus of therapy for bone health in this population[28]. Furthermore, the most prevalent cancer type in this study seen in participants is breast cancer. Breast cancer patients may take aromatase inhibitors, which can increase a patient's risk for osteoporosis, further increasing the importance for proper calcium intake[60].

A 2004 report from the Vitamins And Lifestyle (VITAL) study also found that participants with a history of breast cancer had higher use of multivitamins, vitamin E, and calcium than older adults without a previous cancer diagnosis[57]. As 68% of this study's participants had a breast cancer diagnosis, the results from the VITAL study is consistent with MVM and calcium prevalence found in the current study.

Relative to those not supplementing with calcium, calcium users were less likely to be retired, either working full-time or part-time. There is currently a scarcity of research on the potential association between retirement status and calcium supplementation. One 2013 study investigating retirement and changes in dietary intake found that intake of calcium-rich foods and milk was low among retired individuals compared to other working individuals[61]. This study justifies results by a potential constraining food budget due to retirement[61]. While price can fluctuate depending on the form of calcium, a 300 mg calcium carbonate tablet was on average 11 cents, resulting in around 40 dollars a year[62]. Retired participants may not choose to add the expense of a calcium supplement. Conversely, one 2017 study found that dietary calcium intake did not change from employment to retirement in participants, however, transition to retirement was associated with unhealthier dietary intakes, such a decrease in the overall diet quality and intakes of recommended foods and nutrients[63]. This study notes that there should be targeted interventions before age of retirement on methods to optimize diet quality, including calcium intake, with reduced budget could be of interest[63]. Using adjusted data, no significant associations were found with age, race, marital status, college education, number of chronic conditions, or having breast cancer in any supplement investigated. However, using unadjusted data, supplement users were more likely to be white, married, retired, and have at least a college degree. Similarly, studies have found that participants with a professional or graduate degree/a

higher level of education were significantly more likely to use supplements[13,58]. Findings suggest that those with higher education levels are more likely to learn about and recognize the purpose of supplements. Furthermore, study findings may suggest that those with higher education have increased health literacy, thereby making supplement choices to support health concerns. Additionally, a 2020 study comparing cancer survivors and individual adults without cancer, found that cancer survivors who used dietary supplements were older and more likely to be women and non-Hispanic whites, had higher levels of education, income, and better diet quality, and were less likely to be overweight/obese[12]. Conversely, a 2018 study found that older adult breast cancer survivors consumed more alcohol and more often used supplements than females in the control group[64]. Due to conflicting data and a growing population of older cancer survivors, more research is needed to verify the demographic characteristics and reasons why individuals are choosing to use supplements.

According to NHANES data, the average total HEI score for older Americans in 2016 was 64[65]. While the mean total HEI scores from 1999-2002 for older females 67.6[66]. The average total HEI score for the older female participants of this study was 66.5, representing a slightly higher score compared to the national average. However, participants' average scores reflect a diet that "needs improvement"[38].

The association between HEI 2015 scores and dietary supplement usage in participants was also investigated. A key question throughout this research was if older female cancer survivors were taking dietary supplements because they were already making healthier dietary choices, or were they taking dietary supplements to compensate for the gaps within their dietary intake. Participants supplementing with an MVM had significantly higher mean HEI component scores for total vegetables, greens and beans, whole fruits, and whole grains. Furthermore,

single-unit increases in the HEI was associated with 7% greater likelihood of MVM use. Participants supplementing with vitamin D also had higher mean scores for greens and beans. These results suggest that older women with already higher mean HEI scores were also utilizing dietary supplements, rather than those with lower HEI scores filling in the gaps with MVM usage.

Participants received an average of 42.0 out of a possible 100 in the PCS and a 48.5 in the MCS of the RAND-36. The average mean general health subscale was 59.4. There are mixed results comparing this study's results to previous research on older adults. In a 2018 study, older participants scored higher in the general health subscale, however they scored lower in the general health subscale in three additional studies[74,75,76,77]. Another study reported that older female cancer survivors have low HRQoL scores on average compared to older adults who were not cancer survivors[54].

There are a variety of factors that can influence study participants' HRQoL scores. A systematic review of HRQoL and dietary patterns in older adults found that adherence to healthy dietary patterns were associated with better HRQoL scores in at least one subscale[35]. Another study has also found that lower physical and mental HRQoL scores were associated with both demographic (age, race) and lifestyle characteristics (diet quality, physical activity)[54]. This current study was composed of older educated participants with higher than average HEI-scores in total vegetable, greens and beans, total fruit, dairy, and fatty acids; therefore, potentially positively influencing HRQoL scores. In this study, regression results found that a single-unit increase in HRQoL was associated with 4% lower likelihood of using an MVM. Thus, demonstrating in this study that higher HRQoL is not associated with taking an MVM supplement.

Study Strengths & Limitations

This study examined the associations between diet quality, HRQoL, and dietary supplementation in a population that is under researched, thus adding to the existing gap in the current literature. Researching supplement intake adds to the literature as it is an under researched topic in older adults, particularly those with a history of cancer. Despite these strengths, this study is limited due to the cross-sectional design, as it is not possible to assess a causal relationship between supplement use and health status. Future research should follow study participants longitudinally for the cause-and-effect relationships. The sample is not generalizable to males, different racial groups, and less educated older cancer survivors as the majority of the female participants have at least a college degree and are white. Furthermore, participants were recruited from one cancer center, potentially limiting generalizability. The data gathered in this study were collected from a self-report survey, which can lead to measurement error as participants may not feel comfortable answering questions candidly, they may exaggerate or understate health status, or they may not understand survey questions. Furthermore, the DHQ II is not robust in questions regarding supplementation. Questions regarding form of supplement, dosage, duration of supplement use, and for what reason supplements were initiated are lacking for every supplement included on the DHQ II. For example, study participants were asked if they took vitamin D, however, the form of vitamin D was not evaluated (i.e., D2 or D3).

Implications and future directions

It is crucial for Registered Dietitian Nutritionists (RDNs) and healthcare providers to ask if their patients are taking a dietary supplement, as the prevalence of supplement use remains high. Additionally, most older patients do not initiate supplement use under the advisement of an

RDN or healthcare provider, or discuss supplement use during appointments, thus making it essential for RDNs to include supplement use in their nutrition assessment[79]. By considering supplement use, RDNs can understand potential medication interactions, reasons for supplementation use, and efficacy/accuracy of supplementation. Based on study results, older female cancer survivors utilizing MVM supplements were also more likely to have higher average HEI scores. Therefore, it is important for RDNs to understand what variety of MVM their patient is taking and to address potential toxicities[80,81]. RDNs will be able to use dietary intake information to address whether the patient truly needs to utilize supplementation, as those with better diet quality were also the ones supplementing.

This study determined prevalence of supplementation in older female cancer survivors; however, future research should capture more specifics on dosage, frequency, brand, and reason for supplement utilization. Rather than focus on three supplements, studies moving forward should include a full list of herbal and dietary supplements. Future research could also utilize biomarkers to assess if supplementation aided in nutritional adequacy or possible toxicity among older cancer survivors. Furthermore, future research could utilize focus groups or semi-structured interviews to better assess when survivors are initiating supplements, for what reason, and to assess survivors' knowledge on the supplements being utilized.

Conclusion

The purpose of this study was to evaluate the associations between supplement use (MVM, calcium, vitamin D), diet quality, and HRQoL. Supplement usage in this population is high with MVM usage at 64% of participants, calcium supplementation at 77%, and vitamin D at 35%. Results found that MVM users had higher mean diet quality scores in total vegetables, greens and beans, whole fruits, and whole grains, while vitamin D users had higher mean scores

in greens and beans. Regression results found that retirees were 82.5% less likely to utilize calcium supplements. Regression results also found an association between higher HEI scores and MVM use. Lastly, participants with higher mean HRQoL scores were 4% less likely to utilize an MVM. To provide better healthcare to cancer survivors, it is crucial to also understand who is utilizing supplements and the nutritional necessity behind this behavior. As prevalence remains high in the cancer survivor population, RDNs should include supplement intake in their nutrition assessments to better evaluate patients' nutrition status, and ultimately improve patient health outcomes.

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References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin*. 2021;71(1):7-33. doi:https://doi.org/10.3322/caac.21654

2. Denlinger CS, Carlson RW, Are M, et al. Survivorship: Introduction and Definition. *J Natl Compr Cancer Netw JNCCN*. 2014;12(1):34-45.

3. Survivorship in Older Adults with Cancer. ASCO. Published May 25, 2016. Accessed September 15, 2020. https://www.asco.org/practice-policy/cancer-care-initiatives/geriatric-oncology/survivorship-older-adults-cancer

4. Cancer Treatment| Survivor Facts & Figures| American Cancer Society. Accessed October 22, 2020. https://www.cancer.org/research/cancer-facts-statistics/survivor-facts-figures.html

5. Hawley ST, Janz NK, Griffith KA, et al. Recurrence risk perception and quality of life following treatment of breast cancer. *Breast Cancer Res Treat*. 2017;161(3):557-565. doi:10.1007/s10549-016-4082-7

6. Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin*. 2012;62(4):243-274. doi:10.3322/caac.21142

7. American Cancer Society Guideline for Diet and Physical Activity. Accessed September 15, 2020. https://www.cancer.org/healthy/eat-healthy-get-active/acs-guidelines-nutrition-physical-activity-cancer-prevention/guidelines.html

8. Bernstein M, Munoz N. *Nutrition for the Older Adult*. Second Edition.

9. Trujillo EB, Claghorn K, Dixon SW, et al. Inadequate Nutrition Coverage in Outpatient Cancer Centers: Results of a National Survey. *J Oncol*. 2019;2019:7462940. doi:10.1155/2019/7462940

10. Overview & Background of Healthy Eating Index (HEI) | EGRP/DCCPS/NCI/NIH. Accessed September 10, 2020. https://epi.grants.cancer.gov/hei/

11. Reedy J, Lerman JL, Krebs-Smith SM, et al. Evaluation of the Healthy Eating Index-2015. *J Acad Nutr Diet*. 2018;118(9):1622-1633. doi:10.1016/j.jand.2018.05.019

12. Du M, Luo H, Blumberg JB, et al. Dietary Supplement Use among Adult Cancer Survivors in the United States. *J Nutr*. 2020;150(6):1499-1508. doi:10.1093/jn/nxaa040

13. Miller P, Demark-Wahnefried W, Snyder DC, et al. Dietary supplement use among elderly, long-term cancer survivors. *J Cancer Surviv Res Pract*. 2008;2(3):138-148. doi:10.1007/s11764-008-0060-3

14. After Treatment. American Institute for Cancer Research. Accessed July 22, 2020. https://www.aicr.org/cancer-survival/treatment-tips/after-treatment/

15. Krok-Schoen JL, Naughton MJ, Bernardo BM, Young GS, Paskett ED. Fear of recurrence among older breast, ovarian, endometrial, and colorectal cancer survivors: Findings from the WHI LILAC study. *Psychooncology*. 2018;27(7):1810-1815. doi:10.1002/pon.4731

16. Cancer Prevention. American Institute for Cancer Research. Accessed July 22, 2020. https://www.aicr.org/cancer-prevention/

17. American Cancer Society guideline for diet and physical activity for cancer prevention - Rock - - CA: A Cancer Journal for Clinicians - Wiley Online Library. Accessed July 22, 2020. https://acsjournals-onlinelibrary-wiley-com.proxy.lib.ohio-state.edu/doi/full/10.3322/caac.21591

18. Do not use supplements for cancer prevention. World Cancer Research Fund. Published April 24, 2018. Accessed July 24, 2020. https://www.wcrf.org/dietandcancer/recommendations/dont-rely-supplements

19. Kantor ED, Rehm CD, Du M, White E, Giovannucci EL. Trends in Dietary Supplement Use Among US Adults From 1999-2012. *JAMA*. 2016;316(14):1464-1474. doi:10.1001/jama.2016.14403

20. 2015-2020 Dietary Guidelines | Dietary Guidelines for Americans. Accessed September 10, 2020. https://www.dietaryguidelines.gov/current-dietary-guidelines/2015-2020-dietary-guidelines

21. Older Adults | Healthy People 2020. Accessed July 24, 2020. https://www.healthypeople.gov/2020/topics-objectives/topic/older-adults

22. Physical Changes With Age - Nutrition Care Manual. Accessed July 24, 2020. https://www.nutritioncaremanual.org/topic.cfm?ncm_category_id=31&lv1=255614&lv2=255648&lv3=268685&ncm_toc_id=268685&ncm_heading=Older%20Adult%20Nutrition

23. National Academies of Sciences E, Oria M, Harrison M, Stallings VA. Dietary Reference Intakes (DRIs): Recommended Dietary Allowances and Adequate Intakes, Elements, Food and Nutrition Board, National Academies. Published March 5, 2019. Accessed July 24, 2020. https://www.ncbi.nlm.nih.gov/books/NBK545442/table/appJ_tab3/

24. Bales C, Ritchie C. *Handbook of Clinical Nutrition and Aging*. Second Edition. Humana Press

25. Oral Health, Smell, and Taste - Nutrition Care Manual. Accessed August 30, 2020. https://www.nutritioncaremanual.org/topic.cfm?ncm_category_id=31&lv1=255616&lv2=255640&lv3=272431&ncm_toc_id=272431&ncm_heading=Older%20Adult%20Nutrition

26. Bleijenberg N, Zuithoff NPA, Smith AK, de Wit NJ, Schuurmans MJ. Disability in the Individual ADL, IADL, and Mobility among Older Adults: A Prospective Cohort Study. *J Nutr Health Aging*. 2017;21(8):897-903. doi:10.1007/s12603-017-0891-6

27. McMaughan DJ, Oloruntoba O, Smith ML. Socioeconomic Status and Access to Healthcare: Interrelated Drivers for Healthy Aging. *Front Public Health*. 2020;8. doi:10.3389/fpubh.2020.00231

28. Position of the Academy of Nutrition and Dietetics: Food and Nutrition for Older Adults: Promoting Health and Wellness. *J Acad Nutr Diet*. 2012;112(8):1255-1277. doi:10.1016/j.jand.2012.06.015

29. Trujillo EB, Dixon SW, Claghorn K, Levin RM, Mills JB, Spees CK. Closing the Gap in Nutrition Care at Outpatient Cancer Centers: Ongoing Initiatives of the Oncology Nutrition Dietetic Practice Group. *J Acad Nutr Diet*. 2018;118(4):749-760. doi:10.1016/j.jand.2018.02.010

30. Mental health of older adults. Accessed July 28, 2020. https://www.who.int/news-room/fact-sheets/detail/mental-health-of-older-adults

31. Krok-Schoen JL, Archdeacon Price A, Luo M, Kelly OJ, Taylor CA. Low Dietary Protein Intakes and Associated Dietary Patterns and Functional Limitations in an Aging Population: A NHANES Analysis. *J Nutr Health Aging*. 2019;23(4):338-347. doi:10.1007/s12603-019-1174-1

32. WHO | WHOQOL: Measuring Quality of Life. WHO. Accessed August 6, 2020. https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/

33. Quality of Life - Nutrition Care Manual. Accessed August 6, 2020. https://www.nutritioncaremanual.org/topic.cfm?ncm_category_id=31&lv1=255614&lv2=255650&lv3=268687&ncm_toc_id=268687&ncm_heading=Older%20Adult%20Nutrition

34. Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. *Ann Med*. 2001;33(5):350-357. doi:10.3109/07853890109002089

35. Govindaraju T, Sahle BW, McCaffrey TA, McNeil JJ, Owen AJ. Dietary Patterns and Quality of Life in Older Adults: A Systematic Review. *Nutrients*. 2018;10(8). doi:10.3390/nu10080971

36. Inoue-Choi M, Lazovich D, Prizment AE, Robien K. Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention is associated with better health-related quality of life among elderly female cancer survivors. *J Clin Oncol Off J Am Soc Clin Oncol*. 2013;31(14):1758-1766. doi:10.1200/JCO.2012.45.4462

37. Krebs-Smith SM, Pannucci TE, Subar AF, et al. Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet*. 2018;118(9):1591-1602. doi:10.1016/j.jand.2018.05.021

38. (PDF) The Healthy Eating Index 1994-96. ResearchGate. Accessed September 16, 2020. https://www.researchgate.net/publication/242508135_The_Healthy_Eating_Index_1994-96

39. Gopalakrishna A, Chang A, Longo TA, et al. Dietary patterns and health-related quality of life in bladder cancer survivors. *Urol Oncol Semin Orig Investig*. 2018;36(10):469.e21-469.e29. doi:10.1016/j.urolonc.2018.06.001

40. Office of Dietary Supplements - Multivitamin/mineral Supplements. Accessed September 10, 2020. https://ods.od.nih.gov/factsheets/MVMS-HealthProfessional/

41. Summary of S. 784 (103rd): Dietary Supplement Health and Education Act of 1994. GovTrack.us. Accessed October 27, 2020. https://www.govtrack.us/congress/bills/103/s784/summary

42. Nutrition C for FS and A. Dietary Supplements. FDA. Published February 4, 2020. Accessed October 27, 2020. https://www.fda.gov/food/dietary-supplements

43. Biesalski HK, Tinz J. Multivitamin/mineral supplements: Rationale and safety. *Nutrition*. 2017;36:60-66. doi:10.1016/j.nut.2016.06.003

44. Full article: Multivitamin/Mineral Supplement Contribution to Micronutrient Intakes in the United States, 2007–2010. Accessed August 6, 2020. https://www-tandfonline-com.proxy.lib.ohio-state.edu/doi/full/10.1080/07315724.2013.846806

45. Office of Dietary Supplements - Vitamin D. Accessed September 11, 2020. https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/

46. Armas LAG, Hollis BW, Heaney RP. Vitamin D2 is much less effective than vitamin D3 in humans. *J Clin Endocrinol Metab*. 2004;89(11):5387-5391. doi:10.1210/jc.2004-0360

47. Cranney A, Horsley T, O'Donnell S, et al. Effectiveness and safety of vitamin D in relation to bone health. *Evid ReportTechnology Assess*. 2007;(158):1-235.

48. Holick MF, Biancuzzo RM, Chen TC, et al. Vitamin D2 is as effective as vitamin D3 in maintaining circulating concentrations of 25-hydroxyvitamin D. *J Clin Endocrinol Metab*. 2008;93(3):677-681. doi:10.1210/jc.2007-2308

49. Wimalawansa SJ, Razzaque MS, Al-Daghri NM. Calcium and vitamin D in human health: Hype or real? *J Steroid Biochem Mol Biol*. 2018;180:4-14. doi:10.1016/j.jsbmb.2017.12.009

50. Office of Dietary Supplements - Calcium. Accessed September 11, 2020. https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/

51. Burden S, Jones DJ, Sremanakova J, et al. Dietary interventions for adult cancer survivors. *Cochrane Database Syst Rev*. 2019;2019(11). doi:10.1002/14651858.CD011287.pub2

52. Andersen MR, Sweet E, Hager S, Gaul M, Dowd F, Standish LJ. Effects of Vitamin D Use on Health-Related Quality of Life of Breast Cancer Patients in Early Survivorship. *Integr Cancer Ther*. 2019;18. doi:10.1177/1534735418822056

53. Lewis C, Xun P, He K. Vitamin D supplementation and quality of life following diagnosis in stage II colorectal cancer patients: a 24-month prospective study. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer*. 2016;24(4):1655-1661. doi:10.1007/s00520-015-2945-9

54. Krok-Schoen JL, Pisegna J, Arthur E, Ridgway E, Stephens C, Rosko AE. Prevalence of lifestyle behaviors and associations with health-related quality of life among older female cancer survivors. *Support Care Cancer*. Published online October 11, 2020. doi:10.1007/s00520-020-05812-3

55. Background on Diet History Questionnaire II (DHQ II) | EGRP/DCCPS/NCI/NIH. Accessed September 10, 2020. https://epi.grants.cancer.gov/dhq2/about/

56. Diet History Questionnaire II: Calculating HEI Scores | EGRP/DCCPS/NCI/NIH. Accessed September 16, 2020. https://epi.grants.cancer.gov/dhq2/dietcalc/output.html

57. Greenlee H, White E, Patterson RE, Kristal AR, Vitamins and Lifestyle (VITAL) Study Cohort. Supplement use among cancer survivors in the Vitamins and Lifestyle (VITAL) study cohort. *J Altern Complement Med N Y N*. 2004;10(4):660-666. doi:10.1089/acm.2004.10.660

58. Velicer CM, Ulrich CM. Vitamin and mineral supplement use among US adults after cancer diagnosis: a systematic review. *J Clin Oncol Off J Am Soc Clin Oncol*. 2008;26(4):665-673. doi:10.1200/JCO.2007.13.5905

59. Patterson RE, Neuhouser ML, Hedderson MM, Schwartz SM, Standish LJ, Bowen DJ. Changes in diet, physical activity, and supplement use among adults diagnosed with cancer. *J Am Diet Assoc*. 2003;103(3):323-328. doi:10.1053/jada.2003.50045

60. Calcium Supplements | Memorial Sloan Kettering Cancer Center. Accessed January 25, 2021. https://www.mskcc.org/cancer-care/patient-education/calcium-supplements

61. Bhurosy T, Jeewon R. Effectiveness of a Theory-Driven Nutritional Education Program in Improving Calcium Intake among Older Mauritian Adults. *Sci World J*. 2013;2013:1-16. doi:10.1155/2013/750128

62. Keller JL, Lanou AJ, Barnard ND. The Consumer Cost of Calcium From Food and Supplements. *J Am Diet Assoc*. 2002;102(11):1669-1671. doi:10.1016/S0002-8223(02)90355-X

63. Si Hassen W, Castetbon K, Lelièvre E, Lampuré A, Hercberg S, Méjean C. Associations between transition to retirement and changes in dietary intakes in French adults (NutriNet-Santé cohort study). *Int J Behav Nutr Phys Act*. 2017;14. doi:10.1186/s12966-017-0527-6

64. Kałędkiewicz E, Szostak-Węgierek D. Dietary practices and nutritional status in survivors of breast cancer. *Rocz Panstw Zakl Hig*. 2018;69(2):175-182.

65. Age Group HEI. Accessed January 6, 2021. https://fns-prod.azureedge.net/sites/default/files/media/file/FinalE_Draft_HEI_web_table_by_Age_Groups_jf_citation_rev.pdf

66. Ervin RB. Healthy Eating Index Scores Among Adults, 60 Years of Age and Over, by Sociodemographic and Health Characteristics: United States, 1999–2002. 2008;(395):17.

67. How the HEI Is Scored | USDA-FNS. Accessed January 6, 2021. https://www.fns.usda.gov/how-hei-scored

68. George SM, Ballard-Barbash R, Manson JE, et al. Comparing indices of diet quality with chronic disease mortality risk in postmenopausal women in the Women's Health Initiative Observational Study: evidence to inform national dietary guidance. *Am J Epidemiol*. 2014;180(6):616-625. doi:10.1093/aje/kwu173

69. Reedy J, Krebs-Smith SM, Miller PE, et al. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. *J Nutr*. 2014;144(6):881-889. doi:10.3945/jn.113.189407

70. Hann CS, Rock CL, King I, Drewnowski A. Validation of the Healthy Eating Index with use of plasma biomarkers in a clinical sample of women. *Am J Clin Nutr*. 2001;74(4):479-486. doi:10.1093/ajcn/74.4.479

71. Weinstein SJ, Vogt TM, Gerrior SA. Healthy Eating Index scores are associated with blood nutrient concentrations in the third National Health And Nutrition Examination Survey. *J Am Diet Assoc*. 2004;104(4):576-584. doi:10.1016/j.jada.2004.01.005

72. Demark-Wahnefried W, Peterson B, McBride C, Lipkus I, Clipp E. Current health behaviors and readiness to pursue life-style changes among men and women diagnosed with early stage prostate and breast carcinomas. *Cancer*. 2000;88(3):674-684.

73. What Breast Cancer Survivors Need To Know About Osteoporosis | NIH Osteoporosis and Related Bone Diseases National Resource Center. Accessed March 3, 2021. https://www.bones.nih.gov/health-info/bone/osteoporosis/conditions-behaviors/osteoporosis-breast-cancer

74. Hoeksema AR, Peters LL, Raghoebar GM, Meijer HJA, Vissink A, Visser A. Health and quality of life differ between community living older people with and without remaining teeth who recently received formal home care: a cross sectional study. *Clin Oral Investig*. 2018;22(7):2615-2622. doi:10.1007/s00784-018-2360-y

75. Pinheiro LC, Wheeler SB, Chen RC, Mayer DK, Lyons JC, Reeve BB. The effects of cancer and racial disparities in health-related quality of life among older Americans: A

case-control, population-based study. *Cancer*. 2015;121(8):1312-1320. doi:https://doi.org/10.1002/cncr.29205

76. Ramocha LM, Louw QA, Tshabalala MD. Quality of life and physical activity among older adults living in institutions compared to the community. *South Afr J Physiother*. 2017;73(1):342. doi:10.4102/sajp.v73i1.342

77. Assaf AR, Beresford SAA, Risica PM, et al. Low-fat dietary pattern intervention and health-related quality of life: The WHI randomized controlled Dietary Modification trial. *J Acad Nutr Diet*. 2016;116(2):259-271. doi:10.1016/j.jand.2015.07.016

78. Tardy A-L, Pouteau E, Marquez D, Yilmaz C, Scholey A. Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence. *Nutrients*. 2020;12(1). doi:10.3390/nu12010228

79. Gahche JJ, Bailey RL, Potischman N, Dwyer JT. Dietary Supplement Use Was Very High among Older Adults in the United States in 2011–2014. *J Nutr*. 2017;147(10):1968-1976. doi:10.3945/jn.117.255984

80. Phua DH, Zosel A, Heard K. Dietary supplements and herbal medicine toxicities—when to anticipate them and how to manage them. *Int J Emerg Med*. 2009;2(2):69-76. doi:10.1007/s12245-009-0105-z

81. Mulholland CA, Benford DJ. What is known about the safety of multivitamin-multimineral supplements for the generally healthy population? Theoretical basis for harm. *Am J Clin Nutr*. 2007;85(1):318S-322S. doi:10.1093/ajcn/85.1.318S