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Effects Of A Plant-Based Vegan Diet On The Risk Of Cancer: An Integrative Review Of The Literature

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EFFECTS OF A PLANT-BASED VEGAN DIET ON THE RISK OF CANCER: AN
INTEGRATIVE REVIEW OF THE LITERATURE

by

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A thesis submitted in partial fulfillment of the requirements
for the Honors in the Major Program in Nursing
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Abstract

Cancer, an aggressive chronic disease, impacts the lives of millions of people every day. There are numerous proposed triggers related to the diagnosis and much remains to be learned about the causes. Associated with this disease's variability is the challenge to identify a single causative agent that lead to its prevention. Specific topics that need additional evidence relate to environmental factors and lifestyle behaviors in the development, treatment and, in some instances, even suppression of disease progression. Specifically, a diet that excludes animal-based products but consists of a variety of fruits and vegetables (i.e., plant-based vegan diet) is reported to retard disease progression among some individuals diagnosed with cancer. The purpose of this thesis was to examine the effects of a plant-based vegan diet as a treatment approach with individuals who have been diagnosed with cancer. The methodology included a systematic review of literature focusing on use of a plant-based vegan diet on cancer risks in research articles published in peer reviewed journals from 2006 to 2018. Consistent findings include evidence that a diet high in fruits, vegetables, whole grains, and minimal amounts of animal products showed a decrease risk of the development of various types of cancer. Recommendations for nursing education, practice, policy and research are discussed.

Dedications

In remembrance of my grandmother, whom I saw fight and struggle with signet cell carcinoma and breast cancer. Your unconditional love and support will forever carry me through every endeavor. You will forever be with me.

(July 14, 1953 - March 31, 2017)

To my parents, who have encouraged me every step of the way. I am incredibly grateful for your love and support throughout this experience. I will always cherish the bond we have.

Table of Contents

***Introduction* 1**

***Purpose* 4**

***Problem Statement* 5**

***Background and Review of Literature* 6**

***Methodology*..... 11**

***Results & Discussion* 12**

***Vegan Diet*12**

***Increased Fruit and Vegetable Consumption*.....14**

***Meat Consumption*16**

***Increased Fiber Intake*.....18**

***Implications for Nursing & Study Limitations* 22**

***Practice*.....22**

***Policy*23**

***Research*24**

***Limitations*24**

***Appendix A*..... 26**

***Figure 1: Consort chart describing article selection process*27**

***Appendix B*..... 28**

***Figure 2: Table of Evidence*29**

***References*..... 37**

Introduction

Cancer is an aggressive chronic disease that affects the lives of millions of people in the world. It is estimated there are nearly 1.7 million new cancer diagnoses in the United States (US) each year and cancer related deaths account for 13% of all deaths worldwide. Additionally, in the US medical costs for cancer related treatments in 2010 exceeded 124 billion dollars and are estimated to increase to 157 billion dollars in 2020 (Gapstur et al., 2018). These statistics are truly overwhelming, reinforcing the necessity for research on potential mechanisms to successfully manage and even eradicate this disease all the more important. Even though some progress has been made in the past decade, much remains to be learned in regard to cancer formation, progression and effective treatments. Currently, research indicates that lifestyle behaviors play a crucial part in the development of cancer including obesity, tobacco use, exposure to ultraviolet (UV) radiation and dietary patterns consisting of consumption of red and processed meats, low consumption of fruits/vegetables, dietary fiber, and calcium (Gapstur et al., 2018). Surprisingly, dietary patterns account for an estimated 30% risk for developing a cancer (Tantamango-Bartley, Jaceldo-Siegl, Fan, & Fraser, 2012).

Unfortunately, it is challenging to isolate the precise cause of specific types of cancer. There are multiple types of cancer developing in various parts of the human body, with different metabolic processes which, in turn, require different treatment options. While there has been a degree of success in treating some types of cancer, many of the interventions have debilitating side effects that seriously impact the individual's quality of life. The various types and stages of cancer pose challenges in selecting the most effective course of treatment. For example, the treatment plan for woman diagnosed with stage one breast cancer may require the surgical

PLANT-BASED VEGAN DIET AND CANCER RISK

removal of the breast (mastectomy) along with extensive chemotherapy and radiation. However, a person diagnosed with tumor which has metastasized extending into the lymph nodes and body organs may require more extensive surgeries, multiple chemotherapies and radiation regimens (Arruebo et al., 2011).

The treatment goal is to eliminate tumor growth by preventing angiogenesis as well as shrink the number of cells affected by the disease process. Therapies, for the most part, often involve toxic interventions in the form of chemotherapy, radiation, and often times invasive surgical procedures. Drugs used to accompany these therapies often include; antimetabolites, such as methotrexate, antitubulin drugs, such as taxanes, and DNA-interactive agents, such as cisplatin. However, it is important to emphasize, these chemotherapies and drug combinations have highly potent adverse side effects. The most notable adverse effects being blood dyscrasias, vomiting, nausea, fatigue, compromised immune systems, suppression of bone marrow, hair loss, and emotional and metabolic changes (Hosseini and Ghorbani, 2015). Essentially, chemotherapy interventions, with the accompanying side effects, often leave the person in worse condition and with a poorer quality of life than before the treatments were started. Consequently, it is important to evaluate the evidence related to 'natural' and less invasive treatment options to prevent and treat individuals who have been diagnosed with cancer. There is some evidence supporting the association of nutrition in promoting health and the management of certain illnesses.

For cancer cells, or neoplasms to grow and metastasize, the process of angiogenesis, or the creation of new blood vessels must be active. Increasing the uptake and consuming a variety of foods containing phytochemicals and angiogenesis inhibitors could potentially be an option for cancer prevention and treatment. This nutritional goal can be achieved by maintaining a

PLANT-BASED VEGAN DIET AND CANCER RISK

plant-based vegan diet which emphasizes the intake of fruits and vegetables while avoiding animal-based proteins (Pham, 2006). Consequently, maintaining a lifestyle could prevent this abnormal cellular process from occurring and offers potential benefits for treating cancer (Hosseini and Ghorbani, 2015).

Purpose

The purpose of this integrated literature is to examine the effects of a plant-based vegan diet as a preventative approach for individuals who have high risk incidence with cancer. Also, to discover where further research can be done in order to discover the potential for diet as an adjunctive treatment for individuals with cancer.

Problem Statement

What are the effects of a plant-based vegan diet as a preventative approach with individuals who have high risk incidence with cancer? Is there potential for adjunctive treatment options with a plant-based vegan diet?

Background and Review of Literature

Angiogenesis is the physiological process by which new vascularization occurs in a body site which, in turn, allows more nutrients and oxygen to be delivered to the tumor (i.e. neoplasm). Without angiogenesis, a neoplasm cannot grow which results in the tumor remaining dormant. (Sagar, Yance, & Wong, 2006). Cells in the body naturally perform this process by secreting polypeptides which increases nutrients during growth, healing, and tissue renewal. However, neoplasms also induce the development of polypeptides via the secretion of vascular endothelial growth factor (VEGF) and angiopoietins (APNS). While this process is effective in utero and during muscle growth, it can have life-threatening negative repercussions when occurring in cancer progression. Interestingly, there are regulators in the body that can stimulate or inhibit angiogenesis. Consequently, in order for the VEGF and APNS processes to be successful, there must be more stimulators than inhibitors present in the body (Bignold, 2006). Therefore, it is essential for researchers and healthcare professionals to identify the stimulators and inhibitors related to angiogenesis in order to prevent the occurrence of cancer cell development.

Some natural products may act as direct and indirect inhibitors of angiogenic activity, such as phytochemicals and phytoestrogens. Both phytochemicals and phytoestrogens are chemicals derived from certain plants, including some fruits, vegetables, legumes and grains. Specific phytochemicals that may act in this manner include; curcuma longa (found in turmeric), carotenoids (found in orange plants), polyphenols and phytoestrogens. Phytoestrogens, which mimic estrogen, include chemicals such as; isoflavins (found in legumes such as red lentils and soybeans), Resveratrol (found in grapes), stilbenes, coumestans, and ligans (found in flax seed,

PLANT-BASED VEGAN DIET AND CANCER RISK

whole grains etc.) (Hwang and Choi, 2015). These plants provide chemopreventative properties in the body that could potentially function as inhibitors of angiogenesis in the body. According to Hosseini and Ghorbani, Curcumin, Camptothecin, *Allium sativum*, green tea, and *Panax ginseng* have specific phytochemicals studied which showed general positive effects in regard to cancer whether in the form of prevention, or regression (2015).

The amount of fiber in a person's diet could be a risk factor in the end for the development of certain types of cancer according to Xu, Ding, Xin, Wang, & Zhang (2018). This metabolic process reduces the availability of steroid hormones, lower serum levels of estrogen, increase the protection of certain phytoestrogens, as well as regulate Insulin-like growth factor-1 (IGF-1) (2018). More specifically, insulin and IGF-1 promote the growth normal and abnormal pre-neoplastic tissue by increasing cell production (Tantamango-Barley et al., 2014). Furthermore, IGF-1 is responsible for inhibiting apoptosis, a mechanism by which cells die thereby avoiding the replication of mutated DNA (Xu et al., 2018); thus, enhancing the likelihood for cancer cell development (McCarty, 2014). Increased dietary fiber intake has been associated with decreased risk of breast, endometrial, and colorectal cancer. A meta-analysis of the effects of dietary fiber on ovarian cancer concluded there was a significant association with increased fiber intake and decreased ovarian cancer rates. It was noted that for every additional 5 grams increased of dietary fiber intake, the risk of ovarian cancer decreased by 3% (Xu et al., 2018).

Consequently, populations who consume diets high in plant products, such as in some Asian countries, are reported to have a lower incidence of cancer compared with cultures where less plant foods are consumed. Consuming foods that are high in phytochemicals have recently

PLANT-BASED VEGAN DIET AND CANCER RISK

been used in conjunction with chemotherapies, which enhanced the medicinal effects. Specifically, equol, a type of isoflavinoid, enhanced the effects of tamoxifen for breast cancer and was associated with decreased risk of death and recurrence. This outcome was also achieved with use of hormonal therapy combined with phytoestrogens, which are associated with the estrogen-like effect in regard to breast cancer. As such, Asian women are reported to be three times less likely to experience mortality from breast cancer compared to Americans. This finding is attributed to Asian populations consuming from 20 mg to 50 mg of phytoestrogens in their daily diet compared to Americans who typically consume from 0.153 mg to 0.491 mg of phytoestrogens (Hwang & Choi, 2015).

It is generally recommended that people consume at least 5 servings of vegetables and fruits per day, limit red and processed meat, and choose whole grains food versus those which are refined. In the US few people achieve these dietary recommendations. In 2015 about 16% of U.S. adults consumed 3 or more servings of vegetables and fruit in their daily diet (Gapstur et al., 2018). When adapting specifically to a vegan diet, defined as the complete exclusion of any animal-derived substance, the intake of angiogenic inhibitors increased (Dinu, Abbate, Gensini, Casini, & Sofi, 2017). A true plant-based vegan diet excludes all animal derived milk products eggs, and meat, along with foods that have animal-based products in the process; and *only* includes the consumption of plant-based nutrients. A vegetarian diet specifically excludes meat and meat products. With the exclusion of animal products in the person's diet, there is a corresponding increased intake of plant-based products; thus, increasing the ingestion of products acting as angiogenetic inhibitors.

PLANT-BASED VEGAN DIET AND CANCER RISK

Alternatively, recent research suggests that animal product-based diets may be associated with an increased risk of developing cancer, especially with the consumption of processed meats (bacon, sausage, hot dogs, deli meat, etc.) In 2015 processed meats were identified as carcinogenic or considered risk factors for cancer (Gapstur et al., 2018). Subsequently, when people relocated to regions in which the population increased consumption of animal-based proteins, their cancer rates increased to reflect the local incidence of cancers (Pham, 2006). For example, one article compared the incidence of prostate cancer in Japanese men before and after moving to the US (Saxe, Major, Westerberg, Khandrika, & Downs. 2008). The researchers found that the relocated first generation Japanese men had from four to nine times increased incidence of prostate cancer. Subsequently, the second generation of Japanese men experienced from eleven to fourteen times higher incidence of prostate cancer. The most significant contributing factor was associated with nutritional changes, from a diet primarily focused on plants to a high animal-based protein diet. (Saxe et al., 2008).

Processed meat consumption has specifically been linked to the development of colorectal cancer (CRC). For each 100 grams of red meat or 50 grams of processed meat consumed, the risk of colorectal cancer increased from 17 to 18% (Gapstur et al., 2018). This is a particular when the meat is prepared at high temperatures, such as during grilling, causing the creation of heterocyclic aromatic amines (HCA) and polycyclic aromatic hydrocarbons (PAHs), which causes a mutation in the DNA.

Heme is another chemical contained in meat with potential cancer-causing abilities. Four large prospective studies concluded that a diet containing high amounts of heme was linked to a higher rate of CRC (Demeyer, Mertens, De Smet, Ulens, & Ulens, 2016). When red meat is

PLANT-BASED VEGAN DIET AND CANCER RISK

processed at a high temperature and cured with salt containing nitrates are associated with development of CRC (Bastide, 2011).

Likewise, a recent (2017) meta-analysis focusing on a review of eighty-six cross-sectional studies and ten cohort prospective studies, reported that populations who maintained a vegetarian diet showed a reduced risk of about 8% in the incidence of cancer while those adhering to a vegan diet had a 15% reduction in the incidence of cancer (Dinu et al., 2017). Decreased consumption of certain amino acids may also play a role in the reduction in the incidence of cancer. A particular enzyme, kinase GCN2, has the ability to detect when amino acids are scarce in the liver. In turn, this metabolic process leads to an increased production of fibroblast growth factor 21 (FGF21). More specifically, FGF21 opposes the stimulation of growth hormone production from the hypothalamus; thus, decreasing the amount of circulating insulin-like growth factor-1 (IGF-1) in the body. As previously mentioned IGF-1 is responsible for increasing cell growth throughout the body (McCarty, 2014). Consequently, the decreased amount of amino-acids consumed in a plant-based vegan diet is associated with decreased amount of amino acids and protein, which could contribute to cancer regression in the body.

Methodology

This thesis review of present research regarding the effectiveness of vegan plant-based diets on cancer risk. Databases that were researched include CINAHL Plus, MEDLINE and PubMed.

Search terms included; vegan* or plant-based* or *plant-based vegan or phytoestrogens* or phytochemicals* AND cancer* or neoplasms*. Inclusion criteria include peer reviewed research articles published from 2006 to 2018, written in the English language, and conducted with human subjects. Exclusion criteria include non-peer reviewed articles, peer reviewed articles published outside of the specified time frame, those written in other than the English language, and those that studied non-human subjects.

Initially, using the search terms, 512 articles were found using CINAHL, CINAHL Plus, MEDLINE and PubMed. In a way to narrow results, articles which included meat products in their definition of “plant-based diet”, which were not in English, conducted on humans, peer-reviewed and published outside of the time frame of 2006-2019, bringing the total to 21 studies. After that, further in-depth analysis of the abstracts and results brought the total articles reviewed to 7 with exclusions made for those that did not focus on cancer as the primary medical diagnosis and those that did not completely meet the inclusion criteria.

Other relevant sources were identified and used in the review process; resulting in a total for articles reviewed for this literature review to N=11. Subsequently, each article was critiqued, analyzed and synthesized by the researcher. Consistent and inconsistent findings along with gaps in the literature were noted and are summarized in the results and discussion of this thesis. (See Appendices, Figure 1: Consort Chart: Article selection process; Table 1: Table of Evidence).

Results & Discussion

Based on the review of the articles this section highlights the findings based on dietary food groups; specifically, vegan diet, increased fruit and vegetable intake, meat consumption, and increased fiber intake. Based on the synthesis of the research, consistent and inconsistent findings, along with gaps in the literature are noted.

Vegan Diet

Four studies specifically studied the effects of a different diets on cancer progression in this review. The first study is based on the Adventist Health Study-2 (AHS-2) including N=96,000 subjects from the U.S. and Canada conducted by Tantamango-Bartley et al (2012). The study used a self-administered food frequency questionnaire that contained a list of over 200 food items for subjects to mark off if they consumed, and how often ranging from “never” to “6+ times/day”; and, amount ranging from “1/2 or less” to “1/2 or more”. Subsequently, cancer cases were identified by computer-matching of AHS-2 subjects to state tumor registries and categorized by anatomical location, including digestive, respiratory/intra-thoracic, urinary tract, female cancers, and male cancers (N=69,120). The results showed an overall decreased risk for female associated cancers as well as in overall cancers (HR=0.84; 95% CI: 0.72, 0.99) for subjects utilizing a vegan diet (Tantamango-Bartley et al., 2012).

Another study by Tantamango-Bartley et al. focused on the AHS-2 and its effects of a vegan diet on subjects diagnosed with prostate cancer (2014). This study was based on a self-administered food frequency questionnaire. Cancer cases were again identified by using computer-matching identifying information within the AHS-2 study. A total of N=1,079 cases

PLANT-BASED VEGAN DIET AND CANCER RISK

were observed; of these, 8% reported adherence to a vegan diet. Other variables considered in the study included alcohol consumption, physical activity, smoking, BMI, sociodemographic characteristics, prevalence of diabetes mellitus, and prostatic hypertrophy. Overall, there was a strong inverse relationship between dietary intake and prostate cancer (HR: 0.65; 95% CI: 0.49, 0.85) suggesting a protective association for those adhering to a vegan diet (Tantamango-Bartley et al., 2014).

The third study specifically examined the effects of a vegan diet compared to non-vegetarian diets by Key et al. (2012) in Britain by analyzing the Oxford Vegetarian Study and the EPIC-Oxford cohort (2012). Participants for the Oxford Vegetarian Study were recruited between 1980 and 1984 in the United Kingdom (UK) with a total of N=11,140. Subjects were administered a food frequency questionnaire regarding their lifestyle and dietary habits. Dietary habits were measured based on 4 questions focusing on whether or not they consumed meat, fish, eggs or dairy products. The EPIC-Oxford Study recruited participants between 1993 and 1999 in the UK and data were collected using a questionnaire. Participants were longitudinally followed until December 31, 2010 with the recording of the incidences of cancer diagnoses during that time. Adjustments were made for those who smoked, consumed alcohol, and participated in physical activity. Cancers of the lymphatic and hematopoietic tissues was 36% lower for subjects maintaining a vegan diet compared to those who consumed meat. Observing all cancers combined, subjects who consumed a vegan diet had a 19% lower cancer development risk compared to meat eaters (Key et al., 2014).

The fourth study conducted by Nguyen et al. (2006) specifically addressed how a plant-based diet affects individuals having a high PSA level, which can be an indicator for prostate

PLANT-BASED VEGAN DIET AND CANCER RISK

cancer. The study was conducted using participants from the University of California, San Diego (UCSD) Healthy Men Study in which each subject served as their own control. There were ten subjects with a rising PSA in at least 3 diagnostic tests, each being at least a month apart. Subjects did not receive any hormonal treatment in the previous 12 months leading up to the experiment. Each subject had a designated support person to assist in implementing the expected dietary change. Subjects were followed up with weekly telephone calls by a dietician along with participating in weekly cooking classes and group meetings. The goal for each subject was to increase the amount of plant-based food ingested, specifically whole grains, vegetables, fruit and legumes and decreasing the intake of meat. Findings from this study showed that as the PSA level decreased, there was an inverse relationship with an increased intake of both whole grains and vegetable. The findings from this study suggested that an increase in plant-based food consumption resulted in declining PSA levels. Within the first 3-month period of the study, whole grain and vegetable consumption increased dramatically, as PSA levels notably declined; and, for several subjects even returned to normal ranges. During the second half of the study, the intake of whole grains and vegetables by subjects, while greater than before the study started, was lower than during the first half of the study. Consequently, some subjects' PSA levels again began rising (Nguyen et al., 2006).

Increased Fruit and Vegetable Consumption

The first study by Tang, Lee, Su, & Binns, specifically focused on the association between fruit and vegetable consumption and risk of epithelial ovarian cancer in women. (2014). In this study, the N=500 participants in a hospital-based case-control study in Guangzhou,

PLANT-BASED VEGAN DIET AND CANCER RISK

southern China participated in a face-to-face interview using a food frequency questionnaire. Vegetables were categorized according to green leafy (e.g. spinach), cruciferous (e.g. broccoli), yellow orange (e.g. carrots), allium (e.g. leeks), and other vegetables. Fruit intake was categorized as yellow orange (e.g. peaches), and other fruits. Confounding variables included age at interview, education level, BMI, physical activity, fresh meat consumption, total energy intake, smoking/drinking status, etc. The ratios for increased fruit and vegetable intake and risk of cancer were found to be 0.30 (95% confidence interval (CI) 0.21 to 0.44) and 0.07 (95% CI 0.04 to 0.12) for daily consumption of more than 490 grams of fruits and 970 grams of vegetables. Conclusion from this study indicated fruits and vegetables seemed to have protective features in developing ovarian cancer (Tang et al., 2014)

Another study focused on different dietary habits and the effects on the risk of breast and ovarian cancer (Edefonti et al., 2009). The researchers observed five different dietary patterns including, high fruit and vegetable intake (G1), meat, eggs and dairy products and sugar/desserts (G2), low intake of food and nutrients (G3), high intakes of vegetables with olive or other seed oils (G4), and high intake of bread and pasta dishes (G5). Overall, the researchers found that a dietary pattern that was rich in fruits and vegetables was moderately associated with a reduced risk of ovarian cancer (Edefonti et al., 2009).

Catsburg et al. studied dietary patterns and the effect on breast cancer risk (2015). They focused on three nutritional patterns; healthy, ethnic, and meat and potatoes. A total of N=1,097 subjects were administered a food-frequency questionnaire which addressed dietary ingestion of certain foods, portion sizes and frequency. The findings revealed that women who consumed the diet based on meat and potatoes were more likely to have a higher BMI along with significantly

PLANT-BASED VEGAN DIET AND CANCER RISK

lower level of physical activity compared with subjects engaging in the other dietary patterns. The dietary pattern was also associated with a decreased risk of breast cancer compared to subjects engaging in the meat and potato dietary pattern (post-menopausal women only) who had an increased risk of developing breast cancer. The researchers concluded that adherence to a plant-based diet, which limits red meat consumption, may be associated with a decreased risk for breast cancer (Catsburg et al., 2015).

Gonzalez and Riboli conducted a study based on examining the EPIC Oxford Study which included N=519,978 subjects (2010). Their results showed that gastric cancer risk was inversely associated with phytochemical consumption (high plasma vitamin C, some carotenoids, retinol, and α -tocopherol) as well as high intake of fiber (Gonzalez and Riboli 2010). Likewise, Navarro Silvera et al., (2010) found supporting evidence of an inverse relationship with increased fruit and vegetable consumption and risk of esophageal adenocarcinoma. They concluded there is a potential protective effect that fruits and vegetables have in regard to esophageal cancer risk due to them being higher in antioxidants, phytosterols and other substances that may inhibit carcinogenesis (Navarro Silvera et al, 2010).

Meat Consumption

Two studies that were reviewed specifically addressed the impact meat consumption has on cancer risk. Both concluded that increased meat consumption was associated with increased risk of cancer (specifically CRC, esophageal, BC, and gastric).

Orlich et al. observed the effects that the vegetarian diet has on the risk of colorectal cancer (CRC) (2015). Their study was carried out by utilizing the AHS-2 Study, assessing food

PLANT-BASED VEGAN DIET AND CANCER RISK

frequency questionnaire by diet category including meat (semivegetarian, pescovegetarian, lacto-ovo vegetarian, and vegan). Their results showed it may be adventitious for people to consume a vegetarian diet in order to decrease their risk of developing CRC as well as with some types of colon cancers. They also found that pescovegetarians (consuming fish in the diet and omitting red meat and poultry) decreased the risk for developing these cancers (Orlich et al., 2015).

Another study conducted by Navarro Silvera et al. and focused on non-cardia gastric adenocarcinoma and esophageal squamous cell carcinoma (2010) with subjects from Connecticut, New Jersey, and Washington state. The study was a multi-center, population-based, control-study. Professionals administered an expanded version of the food frequency questionnaire focusing on subjects' usual food intake from 3 to 5 years before being diagnosed with cancer. This version of the questionnaire was validated by investigators at the Fred Hutchinson Cancer Research Center. After exclusions for being seriously ill or not reporting enough energy intake (<600 kcal/day or >5000Kcal/day) N=1,782 participants were observed. This study found a higher intake of meats, specifically red meat, and decreased intake of vegetables was associated with an increased risk of esophageal adenocarcinoma. Higher intake of meats, in this case, specifically poultry was associated with increased risk of gastric cardia adenocarcinoma. High-fat dairy consumption was associated with an increased risk in both cancer types mentioned above (Navarro Silvera et al., 2010).

Gonzalez and Riboli, also found a positive association between total intake of meat (red and processed) and non-cardia gastric cancer. This relationship was especially strong for subjects who were infected with *Helicobacter pylori* (Gonzalez and Riboli 2010). They further examined the risk of developing CRC when consuming 160 grams/day of red and processed meat

PLANT-BASED VEGAN DIET AND CANCER RISK

compared to ingesting less than 20 grams/day which increased the risk 35%. The also noted when fiber intake is lower, along with consuming high red and processed meat, there was an increased risk of being diagnosed with CRC (Gonzalez and Riboli 2010).

Increased Fiber Intake

A study conducted by Daniel et al. were involved in the NIH-AARP Diet and Health Study in the US which included N=491,841 subjects (2013). Data were collected using a self-administered food frequency questionnaire which included items related to demographics, dietary intake and lifestyle. Researchers followed up after 9 years, an found that N=1,816 had been diagnosed with renal cell carcinoma (RCC). The found that a higher total dietary fiber intake was associated with a significant 15% to 20% lower risk of developing RCC compared to subjects having a BMI <30 and had never smoked. When incorporating legumes, whole grains, and cruciferous vegetables into the diet, there was a 16% to 18% decreased risk of being diagnosed with RCC. Conversely, this study noted an increased risk of RCC with the increased consumption of refined grain intake (Daniel et al., 2013). Additionally, Gonzalez and Riboli found a significant negative association with colorectal cancer and dietary fiber intake in their research regarding CRC (2015).

Of the 11 studies that were reviewed, while not all specifically addressed a vegan diet, the research consistently showed the benefits surrounding the maintenance of a diet that is focused around plant-based options. All of articles focused on the effects of these food groups on the risk of developing cancer or the risk of recurrence. Other benefits noted that were included

PLANT-BASED VEGAN DIET AND CANCER RISK

were increased satiety, more effective weight management, and decreased risk of diabetes (Daniel et al., 2013).

As plant foods are full of fiber, which is processed more slowly, the consumption leads to an increased absorption of nutrients. Other benefits of fiber consumption include reducing lowering serum levels of estrogen, increasing the protection of certain phytoestrogens, and regulating Insulin-like growth factor-1 (IGF-1) (Xu et al., 2018). Xu et al. also observed that when people increased their fiber intake, for every 5 grams increased per day, their risk of ovarian cancer decreased by 3% (2018). Combining high fiber intake with high fruit and vegetable consumption which nutrient dense in vitamins and minerals, increases the absorption of micronutrients.

Plant-based food items have phytochemicals that have been shown to have chemopreventative properties, such as phytochemicals, which may lead to cancer-cell regression. Specifically, equol, a type of isoflavonoid, has been used to enhance the effects of tamoxifen in patients with breast cancer. There was a decreased risk of death or recurrence with this nutritional treatment approach (Hwang & Choi, 2015). This leads to the notion that including other types of phytochemicals may provide enhancing effects as well. There was also a connection seen with high consumption of meat, especially processed and red meat but also sometime poultry, and the increase in cancer diagnosis (Navarro, Silvera et al., 2010).

Five major prospective studies that were reviewed observed the incidence for cancer between non-vegetarians, vegetarians, and vegans; the Adventist Health Study, the Adventist Health Study-2, the EPIC-Oxford Study, the Oxford Vegetarian Study, and the UK Women's Cohort Study. The Adventist Health Study-2 (AHS-2) was a major source of information on this

PLANT-BASED VEGAN DIET AND CANCER RISK

topic as the study participants all reside in North America, maintain similar lifestyles including omitting cigarettes and alcohol, while eating similar diets including the plant-based vegan diet. As there are people in AHS-2 who did not adhere to this diet plan, comparisons were to health outcomes for the two groups. The European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) study used a similar approach and had similar outcomes as the AHS-2.

In all of the studies, it was recorded that there was an overall decreased risk for cancer in vegetarians (including vegans) compared to meat consuming counterparts (Key et al., 2014). In a large sample taken from the United Kingdom which pooled two prospective studies including EPIC-Oxford and the Oxford Vegetarian Study found that the total cancer incidence was 12% lower in fish eaters, 11% lower in vegetarians, and 19% lower in vegans compared with meat eaters, which are comparable results found in the Adventist Health Study II where cancer risk in vegetarians was 8% less than nonvegetarians and 16% less in vegans (Key et al., 2014).

In the majority of these studies a food frequency questionnaire or some adapted variation was used to collect the data. Some studies reported giving the questionnaire and determining which diet group each participant belonged to instead of asking the participants outright or having a professional administrator administer the questionnaire. By using the same measurement tool, more accurate comparisons can be made on analyzing the data and supporting the findings in other research articles.

Several inconsistent findings were further identified in this integrative literature review focusing on dietary patterns with a diagnosis of cancer. Orlich et al. (2012) concluded that pescovegetarians (consuming only fish as meat in the diet and omitting red meat and poultry) decreased the risk for developing certain types of cancers (2015). While, Tantamango-Bartely et

PLANT-BASED VEGAN DIET AND CANCER RISK

al. found there was protection noted for cancers of the gastrointestinal tract when consuming a lacto-ovo-vegetarian diet (inclusion of dairy and eggs) (2012). Additionally, this researcher noted a significant gap in the literature on this topic during some decades. For example, research was conducted during the 1980's; then, little was published during 1990s; but more was published during the early 2000's. Definitely, additional research is needed focusing on plant-based diets in the treatment of invasive types of cancer in various populations and settings.

Implications for Nursing & Study Limitations

The next section of this thesis discusses the implications for nursing education, practice, policy and research of this integrative review focusing on the effects of plant based vegan diets in the treatment of cancer; concluding with study limitations.

Education

Students in health professional disciplines, along with practicing nurses, need information about the effects of diet on the prevention and treatment of diseases. Nurses are incredibly influential in patient's care as they are the ones regularly teaching during their stay, explaining discharge orders and providing daily care. In this role, when appropriate there is an increased opportunity for nurses to inform oncology patients about potential adjunctive treatment options that have less severe adverse effects compared to chemo and radiation treatment regimens. Lifestyle and dietary modifications empower a patient to take some degree of control of their health, which could also affect the treatment and progression. Nutrition and dietary choices increasingly is recognized as a treatment option in western medicine. Unfortunately, few providers in general, nurses in particular, are familiar with the evidence related to the benefits of nutritional modifications, specifically, adopting a plant-based vegan diet. Empowering nurses and providers with this information could contribute to enhanced therapeutic benefits of medications with improved quality of life especially in individuals having a cancer diagnosis.

Practice

In many cases, nurses are the healthcare providers giving information about specific dietary needs or lifestyle changes to combat processes. Frequently, patients are advised by their care providers to modify their lifestyle, in particular their dietary intake, in conjunction with

PLANT-BASED VEGAN DIET AND CANCER RISK

prescribed medication for various medical conditions. For example, the Mayo Clinic (2018) suggests those diagnosed with hypertension to adhere to a Dietary Approaches to Stop Hypertension (DASH) diet with low sodium foods in addition to the prescribed medications. Likewise, those diagnosed with type 2 diabetes are recommended to adhere to a diet low in refined carbohydrates and saturated fats along with prescribed insulin (Type 2 diabetes, 2019). More specifically for those with a diagnosis of cancer, dietary modifications are recommended to prevent and treat side effects such as nausea, fatigue, and anorexia.

There is some evidence to suggest that plant-based diets may prevent or enhance treatment effects of cancer therapies. In general, the public perceive plant-based vegan diets as extreme and require numerous supplements to meet the recommended minimum daily nutrient requirements. While there may be some nutrient deficits with this type of diet, there is an increased intake of other vitamins and minerals which may be beneficial in the treatment of cancer. Nurses need to be informed about the benefits for some diagnosis, in particular cancer, associated with adopting a plant-based vegan diet. Or, perhaps, adapting one's current dietary pattern by increasing the number of servings of fruits and vegetables one ingests while decreasing meat consumption every day there is a major opportunity for change.

Policy

Institutional and organizational policies must be implemented to effectively implement a plant-based vegan dietary therapeutic intervention for patients with cancer. For example, official dietary guidelines focusing on these diets must be used to develop agency specific educational materials for both care givers and the patients. Official information also is essential for the sake of consistency among nurses when providing information to patients, to minimize the risk

PLANT-BASED VEGAN DIET AND CANCER RISK

nutrient deficiencies and to appropriately achieve therapeutic effects. Support groups are another strategy to assist individuals to adhere to this prescribed this nutritional approach as a treatment modality. Reimbursement policies also should take into consideration patient education, nutritional counseling and follow-up assessments of as nutritional therapeutic treatment modalities, specifically vegan and other plant-based diets for oncology patients.

Research

Based on this integrative review of the literature additional studies are needed in the following areas.

Further research should be conducted specifically focusing on the effects a vegan diet on various types of cancer and on quantitative evidence-based effects for specific stages of cancer. Studies are also needed to determine which foods contain the essential nutrients to most effectively prevent or manage various cancers, such as PSA levels related to prostate cancer. Longitudinal studies are needed to examine the most effective nutrients and foods, to prevent and manage the side effects of cancer progression and treatment modalities. Finally, the interaction of genomics and nutrients must be investigated to effectively tailor and individualize interventions to prevent and treat cancer.

Limitations

Several limitations are noted with this limited integrative review of research. This thesis only examined 11 articles published in peer reviewed journals, published from 2006 to 2018, in the English language that focused on plant-based diets in the treatment of cancer. Another limitation is that the existing research used self-reported questionnaires and dietary journals which may be impacted by the subjects' level of accurate recall. Lastly, there were not many

PLANT-BASED VEGAN DIET AND CANCER RISK

articles that specifically addressed plant-based vegan diets, which limits our knowledge on the topic.

In summary, this thesis highlighted findings from N=11 research articles focusing how a plant-based vegan diet effects the risk of cancer. The literature suggests there may be benefits of adopting a plant-based vegan diet to preventing or treat certain cancer types that can improve quality of life. Additional research is needed to examine the most effective approach to integrate nutrition to augment oncology interventions.

APPENDIX A

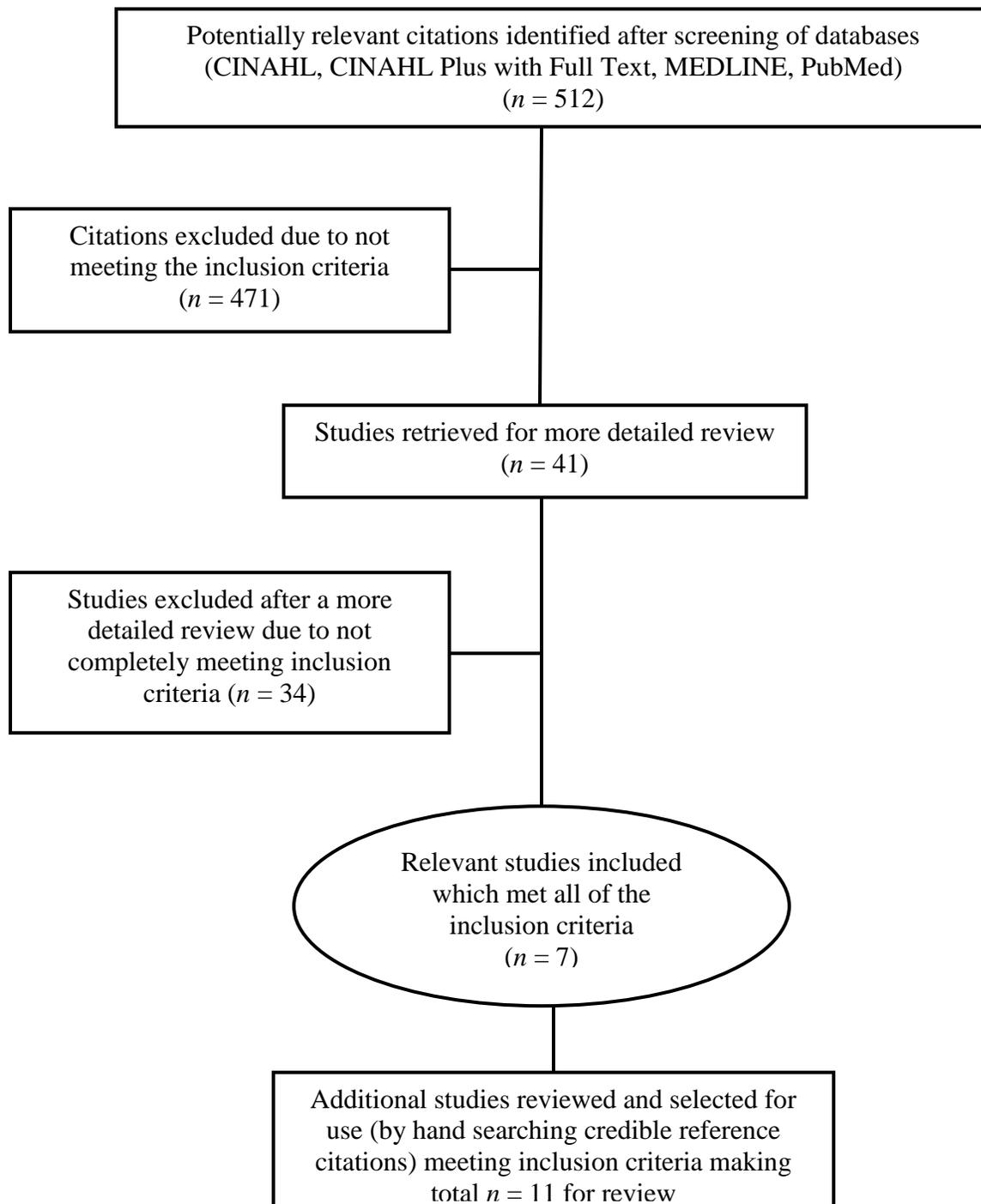
Figure 1: Consort chart describing article selection process

PLANT-BASED VEGAN DIET AND CANCER RISK

Figure 1: Consort chart describing article selection process

Key Search Terms = Plant-based/vegan and cancer/neoplasms or phytoestrogens/phytochemicals and cancer

Limiters = English language, humans, peer-reviewed, 2006-2019, meat included in plant-based diet definition



APPENDIX B

Figure 2: Table of Evidence

PLANT-BASED VEGAN DIET AND CANCER RISK

Figure 2: Table of Evidence Plant-based vegan diet and cancer

Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other
Carrie R Daniel, Yikyung Park, Wong-Ho Chow, Barry I Graubard, Albert R Hollenbeck, and Rashmi Sinha / California, Florida, Louisiana, New Jersey, North Carolina, Pennsylvania, Atlanta, GA, and Detroit, MI	Intake of fiber and fiber-rich plant foods is associated with a lower risk of renal cell carcinoma in a large US cohort/ (2013)	Prospective cohort/ 491,841	To investigate dietary intake and food sources of fiber in relation to renal cell carcinoma (RCC) risk.	<ul style="list-style-type: none"> - Dietary fiber intake was associated with a significantly lower risk of RCC. - A high-fiber diet, by altering gut metabolism, may decrease the generation and absorption of potential toxins. - A pooled analysis of 13 cohorts reported that total fruit and vegetable intake was associated with an ~30% reduced risk of RCC. - Specific types of vegetables, including broccoli and carrots, were also inversely associated with RCC risk. 						X

PLANT-BASED VEGAN DIET AND CANCER RISK

Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other
Michael J. Orlich, MD, PhD; Pramil N. Singh, Dr PH; Joan Sabaté, MD, Dr PH; Jing Fan, MS; Lars Sveen; Hannelore Bennett, MS; Synnove F. Knutsen, MD, PhD; W. Lawrence Beeson, Dr PH; Karen Jaceldo-Siegl, Dr PH, MS; Terry L. Butler, Dr PH; R. Patti Herring, PhD; Gary E. Fraser, PhD, MD / Adventist Church members in U.S. and Canada	Vegetarian Dietary Patterns and the Risk of Colorectal Cancers (2015)	Prospective cohort trial/ 77, 659	To evaluate the association between vegetarian dietary patterns and incident colorectal cancers.	- Vegetarian diets are associated with an overall lower incidence of colorectal cancers. - The consumption of red meat, especially processed meats, is related to an increased risk of colorectal cancers. - Reduction in meat intake may be a primary reason for the reduced risk demonstrated in vegetarians, an increase in the consumption of various whole plant foods might also contribute to the reduction.		X				
Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other

PLANT-BASED VEGAN DIET AND CANCER RISK

Yessenia Tantamango-Bartley, Karen Jaceldo-Siegl, Jing Fan, and Gary Fraser / Adventist church members in U.S. and Canada	Vegetarian Diets and the Incidence of Cancer in a Low-Risk Population (2012)	Prospective -cohort study/ 69,120	To evaluate the effects of vegetarian style diets and the incidence of cancer in a low-risk population	- Vegan diet seems to confer lower risk for overall and female-specific cancer compared to other dietary patterns. - The lacto-ovo-vegetarian diets seem to confer protection from cancers of the gastrointestinal tract.					X	
Yessenia Tantamango-Bartley, Synnove F Knutsen, Raymond Knutsen, Bjarne K Jacobsen, Jing Fan, W Lawrence Beeson, Joan Sabate, David Hadley, Karen Jaceldo -Siegl, Jason Penniecook, Patti Herring, Terry Butler, Hanni Bennett, Gary Fraser / Adventist church members in U.S. and Canada	Are Strict Vegetarians Protected Against Prostate Cancer? (2015)	Prospective cohort study/ 26,346	To evaluate if strict vegetarians protected against prostate cancer	Vegan diets showed a statistically significant protective association with prostate cancer risk.				X		
Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other

PLANT-BASED VEGAN DIET AND CANCER RISK

<p>Key TJ, Appleby PN, Crowe FL, Bradbury KE, Schmidt JA, Travis RC / United Kingdom</p>	<p>Cancer in British vegetarians: updated analyses of 4998 incident cancers in a cohort of 32,491 meat eaters, 8612 fish eaters, 18,298 vegetarians, and 2246 vegans (2014)</p>	<p>Pooled analysis of 2 prospective studies including analysis of EPIC-Oxford and the Oxford Vegetarian Study / 61,647</p>	<p>Use a large sample in the United Kingdom and compare the incidence of cancer based on diet.</p>	<p>- The risk of some cancers is lower in vegetarians than in meat eaters. - When vegans were examined as a separate group for the 3 commonest cancers, with meat eaters as the reference group, there were no significant associations with risk of colorectal, breast, or prostate cancer, but vegans had a 19% lower risk than did meat eaters for all cancers combined. - Stomach cancer risk was 63% lower in vegetarians (including vegans) compared with meat eaters.</p>					<p>X</p>	
<p>Author(s)/ Location/</p>	<p>Title/ Year</p>	<p>Study design/ sample size</p>	<p>Purpose</p>	<p>Key findings</p>	<p>BC</p>	<p>CRC</p>	<p>OC</p>	<p>PC</p>	<p>All</p>	<p>Other</p>

PLANT-BASED VEGAN DIET AND CANCER RISK

Li Tang, Andy H.Lee, Dada Su, Colin W.Binns / Guangzhou, Guangdong Province	Fruit and vegetable consumption associated with reduced risk of epithelial ovarian cancer in southern Chinese women (2013)	Case-control study/ 1,000	To examine the effects of increased fruit and vegetable intake on ovarian cancer.	- Consumption of fruits and vegetables was inversely associated with the incidence of epithelial ovarian cancer in southern Chinese women. - With the exception of lycopene, high intakes of these nutrients (dietary fiber, vitamin C and E, niacin, folate, α -carotene, β -carotene, β -cryptoxanthin, lutein + zeaxanthin, potassium, magnesium, calcium, and iron) were associated with reduced risk of ovarian cancer.			X			
V. Edefonti G. Randi A. Decarli C. La Vecchia C. Bosetti S. Franceschi L. Dal MasoM. Ferraroni / Italy	Clustering dietary habits and the risk of breast and ovarian cancers (2008)	Case-control study/ 3,600	Examining the association of dietary habits and the risk for breast and ovarian cancers.	A diet rich in fruits and vegetables may be associated with a reduced risk of ovarian cancer.	X		X		X	

Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other
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PLANT-BASED VEGAN DIET AND CANCER RISK

Nguyen JY, Major JM, Knott CJ, Freeman KM, Downs TM, Saxe GA/UCSD and San Diego Veterans Affairs Medical Centers	Adoption of a plant-based diet by patients with recurrent prostate cancer (2006)	Pre-post pilot clinical trial/ 14	To determine whether a plant-based dietary intervention, reinforced by stress reduction, could effect a major dietary change and influence the progression of recurrent prostate cancer	Changes in the rate of rise in PSA, an indicator of disease progression, were in the opposite direction as changes in the intake of plant-based food groups (specifically regarding whole grains and vegetables), suggesting that adoption of a plant-based diet may have therapeutic potential in the management of prostate cancer.				X		
Navarro Silvera SA, Mayne ST, Risch H, Gammon MD, Vaughan T, Chow W-H, Dubrow R, Schoenberg J, Stanford JL, West AB, Rotterdam H, Blot WJ, and Fraumeni JF, Jr./ Connecticut, New Jersey, and western Washington State	Food group intake and risk of subtypes of esophageal and gastric cancer/ (2008)	Multi-center, population-based, case-control study/ 1,782	To examine food group intake as a risk factor for subtypes of esophageal and gastric cancers.	<ul style="list-style-type: none"> - Higher intake of meats, particularly red meats, and lower intake of vegetables were associated with an increased risk of esophageal adenocarcinoma. - Higher intake of meats, particularly poultry, and high-fat dairy was associated with increased risk of gastric cardia adenocarcinoma. 						X

PLANT-BASED VEGAN DIET AND CANCER RISK

Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other
Carlos A.Gonzalez and Elio Riboli / Denmark, France Germany, Greece, Italy, the Netherlands, Norway, Spain, and the U.K.	Diet and cancer prevention: Contributions from the <i>European Prospective Investigation into Cancer and Nutrition</i> (EPIC) study (2010)	European Prospective Investigation into Cancer and Nutrition (EPIC) study/ 519, 978	To summarize the initial findings published regarding the EPIC study.	- Gastric cancer was inversely related with high plasma vitamin C, carotenoids, and more while red and processed meat were associated with increased risk. - High intake of fruit and vegetables in current smokers was associated with decreased risk of lung cancer. - High intake of dairy protein and calcium from dairy products was associated with increased risk of PC.	X	X		X	X	

PLANT-BASED VEGAN DIET AND CANCER RISK

Author(s)/ Location/	Title/ Year	Study design/ sample size	Purpose	Key findings	BC	CRC	OC	PC	All	Other
Chelsea Catsburg, Ryung S Kim, Victoria A Kirsh, Colin L Soskolne, Nancy Kreiger, Thomas E Rohan/ Canada	Dietary patterns and breast cancer risk: a study in 2 cohorts/ (2015)	Prospective cohort study: Canadian Study of Diet, Lifestyle and Health (CSDLH) and National Breast Screening Study (NBSS) / 3,659	To identify and confirm associations between dietary patterns and breast cancer risk.	- In the CSDLH (Canadian Study of Diet, Lifestyle and Health) cohort, the healthy dietary pattern comprised of vegetable and legume food groups, was associated with reduced risk of breast cancer. - Dietary patterns characterized by high vegetable intake were inversely associated with risk of breast cancer. - Adherence to a plant-based diet that limits red meat intake may be associated with reduced risk of breast cancer, particularly in postmenopausal women.	X					

Key

BC- Breast cancer **CRC-** Colorectal cancer **OC-** Ovarian cancer **PC-** Prostate cancer **All-** Multiple cancers

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