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Review

Examining the Role of Nutrition in Cancer Survivorship and Female Fertility: A Narrative Review

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ABSTRACT

Female cancer survivors have a higher chance of experiencing infertility than females without a history of cancer diagnosis. This risk remains high despite advances in fertility treatments. There is a need to augment fertility treatments with cost-effective methods such as nutritional guidance to improve fertility chances. The aim of this review article is to connect the current literature on cancer survivorship nutrition and fertility nutrition, focusing on the importance of integrating nutritional guidance into fertility counseling, assessment, and treatment for female cancer survivors. Consuming a healthful diet comprising whole grains, soy, fruits, vegetables, seafood, and unsaturated fats has improved both female fertility and cancer survivorship. Similarly, maintaining a healthy body weight also improves female fertility and cancer survivorship. Therefore, dietary interventions to support female cancer survivors with fertility challenges are of immense importance. The period of follow-up fertility counseling and assessment after cancer treatment may provide a unique opportunity for implementing nutritional guidance for female cancer survivors. Dietary interventions are a promising strategy to improve pregnancy chances and overall quality of life among female cancer survivors; thus, researchers should investigate perceptions regarding fertility, barriers, and challenges to changing nutrition-related behaviors, and preferences for nutritional guidance to support fertility treatments in this population.

Keywords: female cancer survivors, diet, fertility counseling, infertility

Introduction

The effects of cancer and cancer treatments on female fertility cannot be over-emphasized. The likelihood for females of reproductive age to get pregnant after cancer treatment is almost 40% lower than the general population, with female cancer survivors achieving fewer pregnancies across all cancer types and having a lower chance of attaining first pregnancy [1]. Cancer treatments such as surgery, chemotherapy, and radiation negatively impact many biological systems by disrupting the neuroendocrine system, ovarian function, and other reproductive organs in females [2]. Despite this problem, research examining fertility challenges faced by young females after cancer is sparse, and there has been little opportunity to extend understanding, adequately acknowledge, or effectively manage the unique reproductive insecurities of this population of females [3]. Although fertility treatment in the 21st century has evolved, and there are several methods to preserve fertility before cancer

Abbreviations: AGE, advanced glycation end-products; ACS, American Cancer Society; ACOG, American College of Obstetricians and Gynecologists; AICR, American Institute for Cancer Research; ASCO, American Society of Clinical Oncology; ASRM, American Society for Reproductive Medicine; ART, assisted reproductive technology; CVD, cardiovascular disease; DGA, Dietary Guidelines for Americans; EARTH, Environmental and Reproductive Health; FFQ, food frequency questionnaire; IARC, International Agency for Research on Cancer; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; LACE, Life After Cancer Epidemiology; LIFE, Longitudinal Investigation of Fertility and Environment; NHS, Nurses' Health Study (NHS) II; PREPARE, Preconception Dietary Supplements in Assisted Reproduction (PREPARE) Trial; RDA, recommended dietary allowances; VDR, vitamin D receptor; WCRF, World Cancer Research Fund.

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treatment and assist reproduction after treatment, infertility remains a significant source of distress for cancer survivors, especially young female survivors [4].

Several factors may influence the success of fertility treatment. For females, factors such as quality of eggs, embryo, age, and type of cancer treatment are typically nonmodifiable fixed factors that are known determinants of fertility outcomes [5,6]. In contrast, healthful nutrition and engagement in healthy lifestyle behaviors, such as physical activity and stress reduction, are factors that can favorably affect fertility outcomes for females undergoing fertility treatments [7]. However, these factors are subject to unmet information needs and misinformation, warranting the need for evidence-based guidance.

Integrating evidence-based nutrition guidance into fertility assessment, counseling, and treatment may be particularly important for female cancer survivors due to the potential double benefit of improving both cancer survivorship and fertility outcomes. In this review, we explore how cancer survivorship nutrition intersects with fertility nutrition. By incorporating nutritional guidance into fertility assessment, counseling, and treatment, we can develop effective interventions. Evidence supports the consumption of foods that align with the Dietary Guidelines for Americans (DGA) 2020-2025.

Methods

Literature was sourced from PubMed, Ovid, Google Scholar, and social media (for new articles). Data were also sourced from reputable websites such as the American Institute for Cancer Research (AICR), the World Cancer Research Fund (WCRF), and the National Cancer Institute (NCI) to understand current recommendations and practices. Search terms in the listed search engines included "red meat," "processed meat," "fatty acids," "seafood," "whole grains," "soy," "legumes," "dairy," "sugar," "coffee," "fruits," "vegetables," "alcohol," and "body weight" combined with the following terms: "fertility," "cancer," and "assisted reproductive technologies." The search included both human and animal studies that were published in English. No limits were set for the date of publication. Gray literature and sources not published in English were excluded. A total of 144 research articles were included in this review, excluding website articles. We acknowledge that this might not be an exhaustive list, and additional relevant literature and research in this field may exist.

The Impact of Infertility Diagnosis and Fertility Treatment on Cancer Survivorship

The diagnosis of infertility is higher for female cancer survivors compared with females without a history of cancer diagnosis [8]. Many cancer survivors express intense negative emotions concerning the possibility of missing the opportunity to have children after cancer and consider cancer to have "robbed" or "stolen" a natural right of parenthood [9]. The potential of losing one's fertility could also be as painful as the cancer diagnosis itself. Thus, fertility preservation and treatment presents an opportunity to cope with the burden of cancer treatment [10]. However, the fertility treatment process is wrought with uncertainties and unmet information needs [3,10].

Despite advances in fertility treatment and assisted reproductive technologies, infertility remains high among female cancer survivors, who have a 30% higher relative risk of infertility than females without a cancer diagnosis [8,11]. Determining an individual's possibility of pregnancy with fertility therapies is difficult and often unreliable. Fertility-preserving treatments for females are complicated and expensive, requiring invasive procedures at or soon after cancer diagnosis while awaiting a definitive plan for cancer therapy [12]. Consequently, this period can be emotionally and medically complex for female cancer survivors [13]. Many perceive fertility preservation and treatment as one of the most difficult decisions they will ever make, which may potentially delay cancer treatment [13,14].

The exorbitant costs involved in female fertility preservation and treatment hinder the reproductive autonomy of many females, especially female cancer survivors, and are identified as major constraining factors impacting the fertility treatment decision-making process [15,16]. Insurance coverage for infertility treatment in the United States is not comprehensive. When coverage is available, the process is fraught with complexity. Often, coverage is denied based on technical errors, leaving patients to navigate billing codes and appeal procedures, imposing major roadblocks for couples [15]. Thus, patients often pay $\leq$100% of in vitro fertilization (IVF) costs out of pocket. Many young cancer survivors consider the cost of building a family as a "financial toxicity" of cancer, compounded by the depletion of savings and assets to cover medical care amidst reduced work and income due to attending cancer treatment sessions [9].

Given the psychological and socioeconomic challenges of assisted reproductive technologies (ARTs) and the unique challenges of cancer survivorship, there is a need to augment fertility treatment with evidence-based methods that are also economical. Incorporating nutrition-related guidance into fertility counseling and treatment is an approach to support fertility and may ultimately improve pregnancy chances for female cancer survivors, thereby helping them to "move forward beyond cancer" [9].

The Influence of Diet on Cancer Survivorship and Female Fertility

Data on nutritional factors influencing cancer recurrence are still evolving [17]. However, the same factors that influence cancer risk may also increase the chance of recurrence after treatment. Thus, the American Cancer Society (ACS) and other expert bodies recommend that cancer survivors in stable health after treatment adhere to the same nutrition guidelines as recommended to prevent cancer [18–20]. Increasing the consumption of fruits, vegetables, whole grains, nuts, legumes, and seafood and limiting red meat, added sugar, alcohol, and processed meat has been associated with improved cancer survivorship [17,19].

Similarly, much evidence has accrued over the years regarding the role nutrition plays in fertility. Periconception nutritional status of both the mother and father affects the entire trajectory of the fertility process, including early fetal development and perinatal and long-term health of children [21]. For females, a low body weight or obesity may impair fertility and adversely affect fertility treatment success, whereas healthful eating, maintaining a healthy body weight, and being physically active have positive effects on embryo implantation and pregnancy chances among females [11]. In the following sections, we will examine the existing scientific evidence that illustrates the connections between food, dietary patterns, and body weight and their effects on cancer survivorship and female fertility.

Red and processed meat

Influence on cancer survivorship

Current evidence suggests that consuming high amounts of red (all types of mammalian muscle meat including beef, veal, pork, lamb, mutton, horse, and goat) and processed meat (meat transformed through salting, curing, fermentation, smoking, or other processes to enhance flavor or improve preservation) may increase risk of developing certain cancers such as colorectal, pancreatic and lung cancers, with the strongest evidence for colorectal cancer [22]. Compared to lean meat like poultry or seafood, red meat has higher levels of heme iron and saturated fat. This can lead to DNA and cellular damage, chronic inflammation in the gut, and the proliferation of gut bacteria that promote inflammation [22]. Curing, smoking, salting, and high-temperature cooking of meat result in the production of carcinogenic compounds such as nitroso-compounds and polycyclic aromatic hydrocarbons [23]. If processed meat includes red meat like beef or pork, risk of developing cancer increases.

After reviewing over 800 articles on red and processed meat consumption and cancer risk to humans, an expert panel of the International Agency for Research on Cancer (IARC), which is the cancer agency of the WHO, classified red meat consumption to be "probably carcinogenic to humans" and processed meat consumption as "carcinogenic to humans" [24]. This finding is supported by strong evidence from the WCRF and the AICR's Continuous Update Project, which has also reported that consuming red and processed meat could lead to colorectal cancer after reviewing evidence from 18 systematic reviews [25]. The IARC expert group found that eating even small portions of processed meats regularly increased risk of colorectal cancer. For example, each 50-g portion of processed meat (equivalent to 1 hot dog or 2 ham slices) eaten daily increases colorectal cancer risk by ~18% [22,24]. It is not necessary for cancer survivors to eliminate meat from their diet completely due to its valuable source of nutrients such as protein, iron, zinc, and vitamin B12 [26]. However, choosing lean animal-based protein sources like chicken, turkey, seafood, or eggs and plant-based sources like beans, lentils, and dried peas are healthful options that could reduce cancer risk [26].

Influence on fertility

The most up-to-date information on red meat consumption and female fertility suggests poorer outcomes in relation to pregnancy and live births. Consuming red meat has been found to reduce the chances of blastocyst (fertilized egg at day 5 or 6) formation during embryo development [11]. Increased intake of meat in general negatively affects ovulation [27,28]. For example, an extensive study by Gaskins and colleagues, which tracked over 18,000 females for 8 y, discovered that 1 additional serving of meat led to a 32% higher risk of ovulatory infertility. This correlation remained even after accounting for other factors such as age, parity, smoking history, oral contraceptive use, and physical activity [29]. Likewise, increased red meat consumption has been linked to an increased risk of developing endometriosis, a condition where the endometrial lining grows outside of the uterus, which can lead to infertility [30,31].

Red meat consumption also negatively affects ART success. Among females undergoing IVF with intracytoplasmic sperm injection (ICSI), which is a technique combined with IVF to treat male factor infertility, a prospective cohort study in Brazil involving 269 couples found that consuming red meat had a negative influence on the likelihood of blastocyst formation and the likelihood of pregnancy [32]. The authors attributed this finding to the increased levels of endocrine-disrupting compounds in processed foods such as red meat which in turn could lead to increased levels of sex steroids in the body. Additionally, they cited the possibility of high contents of advanced glycation end-products (AGE) in red meat, which has been correlated with poor follicular and embryonic development. A limitation of this study, however, is that dietary intake was measured only once before the start of treatment and no nutritional biomarkers were assessed to confirm intake [32]. Similarly, other studies have also reported associations between high AGE in foods such as red and processed meat, lower pregnancy chances, and lower ART success [33–35].

Unsaturated fatty acids and seafood

Influence on cancer survivorship

Foods rich in Ω-3 polyunsaturated fatty acids (PUFAs) such as fish and seafood are associated with improved quality of life of cancer survivors, reduced risk of cardiovascular diseases, and decreased overall cancer-related mortality [17]. Omega-3 fatty acids PUFAs negatively affect the replication of cancer cells and promote cancer cell death [36,37]. They also sensitize tumor cells to anticancer drugs and therefore are used as adjuvants in anticancer therapy [36,37]. Additionally, Ω-3 PUFAs suppress systemic inflammation, and modulate membrane-associated signal transduction and gene expression, all of which have been implicated in cancer pathogenesis and progression [38]. For example, a large prospective cohort study in the United States involving 1600 patients diagnosed with colorectal cancer observed for 10 y found that a higher intake of Ω-3 PUFAs from fish was associated with a lower risk of colorectal cancer-specific mortality [39]. Similarly, a meta-analysis of 21 independent prospective cohort studies on breast cancer found higher marine Ω-3 PUFA, EPA, and DHA are often referred to as marine Ω-3 PUFAs due to their significant quantities in seafood) consumption reduced breast cancer risk by ≤14% and dose–response analysis indicated that breast cancer risk was reduced by 5% per 0.1 g/d or 0.1% increment of dietary marine Ω-3 PUFA intake [40]. Omega-3 PUFAs have also been found to be beneficial against other cancers such as leukemia, pancreatic, head and neck, and gastric cancers [38].

Influence on fertility

Fatty acids in general are required during oocyte maturation and for early embryo development as energy substrates and serve as precursor molecules for prostaglandins and steroid hormones, which are key for implantation and maintaining pregnancy [27]. Specifically, a 1% increase in long-chain Ω-3 PUFAs was found to increase the probability of clinical pregnancy and live birth by 8% in the environmental and reproductive health (EARTH) study [41]. The EARTH study is an ongoing prospective cohort study conducted at the Massachusetts General Hospital Fertility Center with the aim of evaluating the relationships between environmental and nutritional factors with fertility. For this research, food frequency questionnaires (FFQ) and blood samples were analyzed from a random sample of 100 females undergoing ART prior to egg retrieval. Although a positive association was found between pregnancy and live birth with serum Ω-3 PUFA concentrations, Ω-6 concentrations were not associated with ART outcomes. A similar study conducted earlier by Hammiche et al. [42] in the Netherlands among 235 females undergoing IVF/ICSI also found positive associations between Ω-3 PUFA intake and embryo quality and morphology. However, this study relied on FFQs only to determine PUFA concentrations among participants and lacked information on Ω-6 PUFA intake [42]. Regarding Ω-6 PUFA intake, in a small, randomized control trial in Australia involving 46 females with overweight and obesity, those who became pregnant had high levels of PUFA, especially Ω-6 and linoleic acid. Aside from the small sample size, the limitation of this study is that dietary intake was self-reported and FFQs were designed to capture dietary intake 12 mo prior to treatment [43]. Notwithstanding, increased intake of PUFAs, specifically long-chain Ω-3, may be beneficial for improving female fertility.

Despite the benefits of consuming seafood as a source of fatty acids, there have been concerns about consuming fish that contain high levels of mercury [44]. The presence of mercury in fish has been associated with interference in the endocrine system, which subsequently impairs fertility [45]. However, more recent studies have been unable to prove this association but have instead found that fish and seafood intake reduces time to pregnancy and increases the probability of live birth by increasing Ω-3 PUFA levels in the body [41,46]. Additionally, strong correlations have been found between fish consumption and blastocyst formation among females undergoing ART, which is likely mediated by high Ω-3 PUFA concentrations [32]. Furthermore, recent prospective studies have found no associations between mercury concentrations, IVF endpoints, and time to pregnancy as reported in the review by Chiu et al. [27], 2018. Subsequently, experts have come to a consensus that the benefits of consuming fish outweigh risks posed by environmental contaminants they may carry. The American College of Obstetricians and Gynecologists (ACOG) encourages females who are pregnant or who intend to become pregnant to consume ≥2 servings of a variety of fish per week and to avoid fish with high mercury content such as bigeye tuna and king mackerel [47].

Whole grains

Influence on cancer survivorship

Whole grains are high in fiber content and have a variety of compounds that possess important hormonal and antioxidant effects [17]. Antioxidant compounds in whole grains such as phenolic acids, flavonoids, tocopherol, and lignans may influence lipid metabolism, thereby reducing risk and progression of cancer as well as cardiovascular disease [48]. There is strong evidence that consuming whole grains protects against colorectal cancer. Further, regular consumption of high-fiber foods, such as whole grains, reduces risk of unhealthy weight gain, overweight, and obesity, all of which have negative effects on cancer risk and cancer survivorship [49]. Likewise, a meta-analysis involving 45 studies found that consuming 90 g/d (equivalent to 3 servings) of whole grains reduced the relative risk of mortality from all cancers by 11% [50]. Further reductions in risk of mortality from cancer were found with intakes as high as 210 to 225 g/d of whole grains (equivalent to 7.5 servings per d) [50]. Additionally, the meta-analysis reported reductions in risk of mortality from cardiovascular disease (CVD) and type 2 diabetes mellitus with increasing whole grain consumption [50]. This finding is particularly important because cancer survivors have a higher probability of developing chronic diseases such as CVD, type 2 diabetes, and class 3 obesity [BMI (kg/m^2) of 40 or higher] due to treatment side effects, suboptimal diets, and reduced physical activity [51,52]. Thus, consuming whole grains could also be protective against these chronic diseases [50,53].

Influence on fertility

Whole grains have antioxidant and anti-inflammatory properties, which are beneficial for glucose metabolism and potentially enhance fertility because insulin resistance and oxidative damage are culprits in the pathogenesis of subfertility [27]. Additionally, lignan, a substance found in whole grains, can be metabolized into phytoestrogens that are tissue selective, producing both pro-estrogenic (enabling or possessing estrogen-like activity) and antiestrogenic (inhibiting or suppressing estrogen) effects through complex signaling pathways, which may cumulatively exert reproductive benefits for females [54]. This assertion is supported by a study by Mumford et al. [51] investigating the association between male and female urinary phytoestrogen concentrations and time to pregnancy among 501 couples in the Longitudinal Investigation of Fertility and the Environment (LIFE) study, a large, population-based cohort measuring phytoestrogen concentrations before conception, which found that females with higher urinary lignan concentrations had shorter time to pregnancy. This finding was made after controlling for age, BMI, race, research site, creatinine, supplement use, and physical activity. Similarly, the EARTH study, a prospective preconception cohort study investigating the impact of environmental, nutritional, and lifestyle factors among both females and males on fertility and pregnancy outcomes, found higher consumption of whole grains (>52.4 g/d, 3 or more servings) to be associated with a 50% higher probability of live birth among females undergoing ART [27,55]. This higher probability was attributed to increased endometrial thickness, which resulted in improved embryo receptivity. Thus, a diet with a low glycemic load containing high amounts of whole grains could improve fecundity in females [55].

Soy

Influence on cancer survivorship

Foods like soy and flaxseed are rich sources of phytoestrogen called isoflavones, which are also pro-estrogenic and anti-estrogenic [17]. Because circulating high levels of estrogens are a risk factor for breast cancer recurrence and soy isoflavones have been shown to promote in vitro growth of breast tumor cells in animal studies, the consumption of soy has often been associated with poor prognosis among breast cancer survivors [56]. However, large epidemiological studies have neither found adverse effects nor increased mortality between soy consumption and breast cancer recurrence, even when soy is consumed alone or in combination with *tamoxifen* (a drug that treats hormone receptor-positive breast cancer) [17]. In fact, soy consumption consistent with a traditional Japanese diet of 2 to 3 servings (25–50 mg isoflavones) is associated with a reduced risk of breast cancer incidence, recurrence, and mortality [57]. Moreover, the beneficial effect of soy consumption against breast cancer risk is present for both estrogen receptor-positive and negative breast cancers [58]. Among a cohort of almost 2000 female breast cancer survivors participating in the Life After Cancer Epidemiology (LACE) study in the United States, which included a 6-y follow-up, soy isoflavone consumption comparable to lower levels of intake (1.5 servings or 22.6 mg) among Asian populations was found to reduce the risk of breast cancer recurrence by ≤60% among postmenopausal tamoxifen users and did not interfere with tamoxifen efficacy [59]. Likewise, in a combined cohort of over 9000 Chinese and American breast cancer survivors with an average of 7-y follow-up, increased consumption of soy isoflavones was associated with a statistically significant reduced risk of breast cancer recurrence, a nonsignificant risk of breast cancer-associated mortality, and a nonsignificant risk of all-cause mortality [60].

Influence on fertility

Soy consumption among females attempting pregnancy has been hypothesized to have negative effects due to the presence of phytoestrogens in soy potentially influencing estrogen-dependent pathways [27,28]. However, soy isoflavone supplements have been found to be beneficial in females undergoing fertility treatments, resulting in increased live births after ovulation induction, higher endometrial thickness, and increased ongoing pregnancy rates after ART. Additionally, dietary soy intake has been positively linked to the probability of live birth after ART among the EARTH study cohort [27,61]. Soy food intakes of ≤1 serving/d and isoflavone (measured separately) intake of ≤28 mg/d were associated with higher odds of live birth than in females who did not consume soy, adjusting for factors such as age, BMI, infertility diagnosis, protocol type, folate and B12 intake, dietary patterns, and race [61].

Legumes

Influence on cancer survivorship

Other legumes in general, such as pulses, contain dietary fiber, resistant starch, and several phenolic compounds. These compounds may prevent cancer risk and improve survivorship by promoting a healthy microbiome and healthy body weight [62]. A 4-wk randomized controlled trial study conducted in Colorado among 18 older adult cancer survivors (60+ y) with overweight and obesity found that consuming 35 g of navy beans daily improved stool metabolome across several metabolic pathways relevant to improving colon health and reducing colorectal cancer risk [63]. Consuming navy beans improved metabolic pathways involving sterol, lysine, fatty acid, amino acid, and inositol metabolism, which are protective against colorectal cancer [63]. Similarly, a meta-analysis involving a total of 29 observational studies reported that consuming >1 serving of legumes per day was associated with a 21% risk reduction for colorectal cancer [64]. Other studies have also investigated and found beneficial effects of legume consumption on breast and prostate cancer risk reduction [65–67].

Although legumes have beneficial effects on cancer risk reduction and survivorship, the AICR's Third Expert Report found limited evidence regarding legume consumption and the risk for cancers including colorectal, prostate, and breast cancer [68]. This could be because assessing legume consumption particularly pulses, among the United States population is quite challenging given that this staple is not typically part of the American diet. However, the potential health benefits they convey cannot be overlooked. More research is needed to determine the true impact of legumes on cancer risk and survivorship in the United States context.

Influence on fertility

Legumes including pulses are high in plant-based protein, fiber, and micronutrients including zinc, folate, iron, B vitamins, and magnesium, which are important for female fertility [69]. Although the amount of dietary protein consumed affects fertility and IVF success, with low amounts affecting activation of the primordial follicle in animal studies, the quality of protein consumed also affects female fertility [70,71]. Animal protein intake among healthy participants in the Nurses Health Study (NHS) II was associated with ovulatory disorders compared with plant protein intake [29]. Substituting 5% of energy intake for plant proteins was associated with a 50% reduction in ovulatory infertility risk among females aged >32 y [29]. Another study investigating the effects of a pulse-based diet on cardio-metabolic effects in reproductive-aged females with polycystic ovarian syndrome in Canada found improved insulin response, blood pressure, and lipid profiles among the intervention pulse-based diet group compared with the group on an isocaloric diet without pulses [72]. Both insulin resistance and dyslipidemia can negatively impact egg quality and development [73,74]. Consuming legumes and pulses could enhance female fertility by mitigating the negative effects of insulin resistance and dyslipidemia on ovulation.

Dairy

Influence on cancer survivorship

Dairy products and milk are sources of several important micronutrients such as calcium and bioactive constituents such as microbes that could reduce cancer risk and progression [75]. Strong evidence suggests that dairy consumption reduces the risk of colorectal cancer [76]. For example, a dose–response meta-analysis involving 14 studies found a 13% reduction in colorectal cancer risk for every 400-g increase in dairy consumption, controlling for BMI, physical activity, alcohol consumption, tobacco smoking, red meat, and menopausal hormone therapy [76]. In another meta-analysis involving 29 studies, consumption of total dairy products was associated with a reduced relative risk of developing colorectal cancer, however, specific dairy products including low-fat dairy, whole milk, fermented dairy, and cultured milk had no associations with colorectal cancer risk [77]. Pertaining to other cancers, studies have found high dairy consumption to increase the risk for prostate cancer, whereas data are inconclusive for other sites including breast, oral, and bladder cancers [76,78]. In conclusion, dairy products may only be protective against colorectal cancer risk, and further studies are warranted to determine whether consuming dairy products affects the risk of other cancers.

Influence on female fertility

Although dairy products have several components such as calcium, vitamin D, magnesium, and probiotics, which have hypoglycemic activity that could mitigate ovulation disorders, there are currently mixed findings regarding dairy products and female fertility [79]. The NHS II study found no relationship between dairy intake and the risk for ovulatory infertility, although low-fat milk was associated with anovulation [27,28]. However, a prospective cohort of females ≥ 35 y in the United States undergoing ART had a higher probability of live birth with high intakes of pretreatment dairy than females with lower intakes [28]. In contrast, the BioCycle study which was designed to determine the relationship between oxidative stress and endogenous reproductive hormone and antioxidant concentrations across the menstrual cycle, found sporadic anovulation among females consuming high amounts of cream and yogurt [80]. Moreover, Danish and other North American fertility cohorts also report inconsistent findings pertaining to dairy intake, with total milk and dairy consumption increasing fecundity in a study in Denmark (Foraeldre cohort) but having little association in a United States study (PRESTO cohort) [27]. No strong conclusions can be drawn regarding periconceptional dairy intake and female fertility.

Sugar

Influence on cancer survivorship

Convincing evidence suggests that sugar-sweetened drinks like soda increase the risk of weight gain, overweight, and obesity, which increase the risk of developing several cancers such as breast, ovarian, and colorectal cancers [81,82]. Contrary to previous theories about sugar consumption feeding cancer cells, evidence supports that excess sugar provides a high concentration of calories and a limited amount of nutrients that can promote excessive weight gain [81]. Additionally, excess sugar consumption may increase cancer risk by stimulating the synthesis of insulin and insulin-like growth factor-1 and inducing oxidative stress [83,84]. Therefore, sugar both directly and indirectly increases cancer risk, progression, and recurrence by increasing weight gain, body anabolic processes, and free radical formation [17,81,83].

Owing to the deleterious effects of excessive sugar consumption on human health, food manufacturers and consumers have made a shift toward artificial sweetener usage. Concerns about the safety of artificial sweeteners have been raised due to their synthetic or artificial nature, particularly the increased risk of cancers. For example, a large French adult cohort study involving over 100,000 adults found higher consumption of aspartame (>14.45 mg/d in males and >15.39 mg/d in females) and acesulfame -K (>5.06 mg/d in males and >5.50 mg/d in females), 2 common artificial sweeteners used in several food and beverages, increased overall cancer risk, adjusting for factors including age, sex (except for breast and prostate cancer), BMI, height, weight gain, physical activity, and diabetes [85]. Similarly, a recent in vitro study found that sucralose-6-phosphate, a metabolite of sucralose digestion in the gut, significantly damages cellular DNA and increases the expression of genes linked to inflammation, oxidative stress, and cancer [86]. However, a large study conducted by the NCI among American older adults found no association between artificial sweetener consumption and cancer risk [87]. Other studies with large sample sizes have also found mixed associations between artificial sweetener consumption and cancer risk [88].

Influence on fertility. High sugar consumption among females intending to get pregnant has been reported to reduce pregnancy chances [89]. For example, among a prospective cohort of over 3,000 females undergoing ART in Denmark followed for a period of 3 y, consumption of any type or amount (< 1 to 3+ servings) of sugar-sweetened soda reduced pregnancy chances, indicating a possible adverse effect of sugar on female fertility [90]. Another study that compared 2 preconception cohorts in the United States and Denmark found a higher intake of added sugars to be associated with a reduced probability of pregnancy in a dose–response pattern [91].

Pertaining to artificial sweetener consumption, a cross-sectional study among over 500 females undergoing IVF/ICSI in Brazil, found decreased blastocyst formation, implantation, and pregnancy chances among females who consumed 2 or more servings per day of artificially sweetened coffee or soft drinks [92]. Another study in Taiwan, which included over 800 females, found that aspartame consumption was associated with increased oxidative stress and reduced mitochondrial function in the ovary and granulosa cells of the female reproductive system, resulting in fewer follicles in the ovary and disrupted steroidogenesis in granulosa cells [93]. Given these reasons, females intending to get pregnant should consider limiting their consumption of artificial sweeteners.

Coffee

Influence on cancer survivorship

Coffee contains several protective antioxidants and phytochemicals, such as phenolic acids, that may reduce cancer development by reducing inflammation, cellular oxidation, and cancer cell growth [94]. Emerging evidence suggests that consuming ≥1 cup of coffee per day reduces the risk of endometrial and liver cancers [94,95]. Coffee consumption is also linked to a reduced risk of developing prostate cancer, with a 1% decrease in risk for each additional cup per day [96]. Furthermore, both regular and decaf coffee have the same effect on endometrial and liver cancer [94]. However, the link between coffee consumption and the risk of developing other cancers such as esophageal, pancreatic, breast, and colorectal cancers is less clear [94,97].

Influence on fertility. Despite the healthful phytochemicals in coffee, there are concerns that excessive consumption could impair fertility. In animal studies, high caffeine intake (~6 cups of coffee) has been found to relax fallopian tube muscles, thereby impairing embryo transport, development, and implantation [98,99]. However, a systematic review of human clinical studies found that caffeine, regardless of dose, does not appear to increase the risk of infertility [100]. Other studies have also found no association between coffee or caffeine consumption and fertility treatment outcomes [101,102]. However, a study in Denmark among ~1700 females undergoing fertility treatments found that daily consumption of 1 to 5 cups of coffee increased the likelihood of successful pregnancy and live birth after intrauterine insemination compared with females who did not consume coffee, adjusting for factors such as age, BMI, cigarette smoking, weekly alcohol consumption, chronic diseases, education, and treatment frequency [103]. Regarding coffee or caffeine consumption during pregnancy, several review studies have reported an increased risk of spontaneous abortion among females who consume ≥100 mg caffeine/d [98,104,105]. In summary, the effects of coffee or caffeine consumption on female fertility are inconclusive, warranting more research in this area.

Fruits, vegetables, and micronutrients

Influence on cancer survivorship

Fruits and vegetables contain several biologically active micronutrients that can potentially inhibit cancer progression [17]. Micronutrients are important vitamins and minerals required in small quantities as dietary components and are essential for catabolic and anabolic processes [106]. Many fruits and nonstarchy vegetables such as apples, carrots, broccoli, and cruciferous vegetables contain phytochemicals like glucosinolates, carotenoids, dietary fiber, vitamin C, and folate that prevent cancer and inhibit cancer progression [107,108]. Carotenoids, dietary fiber, and vitamin C have antioxidant properties that reduce free radical damage to DNA, preventing cancer initiation and progression [108,109]. Moreover, carotenoids reduce cell growth and stimulate programmed cell death [108,110]. Likewise, folate maintains cellular DNA by turning off oncogenes, whereas glucosinolates reduce inflammation and subsequent cellular damage [108,111,112].

A meta-analysis of 95 cohort studies investigating the association between fruit and vegetable intake and cardiovascular disease, total cancer, and all-cause mortality found significant reductions in the risk of developing cancer by ≤15% for intakes of 550 to 600 g/d (5 to 6 servings) of fruits and vegetables [113]. Pertaining to cancers in females , the Women's Healthy Eating and Living study, a randomized control trial including over 3000 females in the United States, tested the effects of dietary intake on the likelihood of survival in females treated for early-stage breast cancer and found that longitudinal exposure to carotenoids in fruits and vegetables was associated with longer duration of recurrence-free survival adjusting for factors including age, tumor characteristics, smoking status, and tamoxifen use [114]. Higher levels of blood concentrations of carotenoids have an even stronger association with reductions in breast cancer risk as reported in a systematic review and meta-analysis of 25 prospective studies [17].

Similarly, analysis involving a cohort of 609 Australian females with ovarian cancer found adherence to a diet high in vegetables, particularly cruciferous vegetables, resulted in a higher survival advantage, whereas females who consumed diets high in animal meat compared with vegetable intake had a lower likelihood of survival controlling for factors such as tumor stage, age, grade, total energy intake, and BMI [115]. This finding is supported by a recent meta-analysis of 28 articles that reported a reduction in ovarian cancer mortality by ≤40% in total for higher (≥5 servings in total) fruit and vegetable consumption [116]. Increased consumption of fruits and vegetables has also been found to reduce the risk of CVD, which is a significant problem for many cancer survivors [113]. Lastly, consuming a variety of fruits and vegetables is recommended because the synergistic effects of consuming these foods together are thought to exceed the benefits of consuming specific foods and nutrients in isolation [17].

Influence on female fertility

Fruits and vegetables are important sources of many micronutrients and antioxidants, which improve fertility by promoting embryo development [32]. Therefore, females intending to get pregnant should be encouraged to meet micronutrient recommended dietary allowances (RDAs) with dietary sources and supplement micronutrients with low bioavailability in foods they regularly consume. Micronutrients are essential during pregnancy to prevent adverse conditions such as pre-eclampsia, preterm delivery, low birth weight, neural tube defects, and congenital anomalies involving the cardiovascular and/or genitourinary system, among others [117]. However, much less emphasis has been placed on the importance of micronutrients on female fertility in general, despite the vital role micronutrients play at various stages of fertility. For example, folate is required in adequate levels for oocyte quality, maturation, fertilization, and implantation [118]. Preconception folic acid supplementation improves folate levels and reduces homocysteine levels in follicular fluid [119]. This is particularly important because elevated homocysteine in follicular fluid is inversely associated with IVF/ICSI outcomes, with regard to the number of preantral follicles, oocytes retrieved, and overall embryo quality [120]. Consequently, folic acid supplementation has been found to be beneficial in several fertility studies [27]. Findings from the EARTH study revealed females consuming >0.8 mg/d of folic acid during ART had a higher likelihood of live birth than those who consumed <0.4 mg/d [121]. Supplementing folic acid is also beneficial for sub-fertile couples with failed previous ARTs by providing 1 carbon cycle support, which is required for homocysteine metabolism [119]. Studies also show a synergistic beneficial effect of supplementing vitamin B12 with folic acid due to its role in the homocysteine pathway, and females with high levels of both serum folate and vitamin B12 have almost twice the probability of live births compared with females with low levels [28]. This assertion is supported by a randomized control trial in the United States among 93 sub-fertile females who took a daily micronutrient fertility blend containing folic acid, B12, and B6 and had an increased pregnancy rate than females in the placebo group [122].

Other micronutrients, including iron, vitamin D, and nutrients that function as antioxidants, have also been implicated in fertility outcomes. Consuming iron supplements and diets containing micronutrients decreased the risk of ovulatory infertility among females in the NHS II cohort [123]. Similarly, micronutrients with antioxidant properties, such as selenium, enhance progesterone secretion by the corpus luteum, thereby improving the receptiveness of the endometrium for implantation [118]. Low levels of vitamins with antioxidant activity, such as vitamins A and C and glutathione peroxidase, and high levels of lipid peroxidation in serum and follicular fluid, indicative of oxidative stress, were found among a sample of females receiving IVF in Turkey, which improved with multi-mineral supplementation [124]. Adequate levels of micronutrients could potentially improve fertility chances because oxidative stress has been linked to impaired fertility [118]. Silvestris et al. [119] also reported in their review that adequate intake of antioxidants and multi-mineral supplementation shortens the time to conception. However, not all studies assessing antioxidant effects on fertility have been positive, and very few have tested the same interventions, making it difficult to draw strong conclusions [28]. Likewise, for vitamin D, although animal studies have found uterine hypoplasia, impaired follicular development, and anovulation among female rodents fed a vitamin D deficient diet, and those with vitamin D receptor (VDR) knocked out, human studies have found little to no association between vitamin D, ovulatory infertility, and other fertility outcomes [28]. This indicates the need for future studies to investigate these micronutrients further and their role in female fertility.

Alcohol

Influence on cancer survivorship

Alcohol intake has a complex and multifaceted relationship with cancer risk and survivorship. Whereas some studies have found benefits of red wine consumption and reduced cancer risk, the overall effect of alcohol on cancer is negative [125,126]. Red wine might offer protective effects against certain cancers such as colon and breast cancer, due to its large array of polyphenols, which reduce oxidative damage, modulate colonic microbiota, and inhibit enzymes involved in cancer pathogenesis and progression [127,128]. However, there is currently no recommended serving size for red wine that offers a protective effect against cancer.

Contrary to the reported beneficial effects of red wine, alcohol consumption in general accounts for ~6% of all cancers and 4% or cancer-related mortality in the United States [129]. Gastrointestinal and breast cancers are among the most common cancers associated with alcohol consumption [129]. There are several identified mechanisms involved in cancer etiology related to alcohol intake. Acetaldehyde, a product of alcohol metabolism, is a carcinogenic and mutagenic substance that damages cellular DNA, resulting in cancer [130]. Chronic alcoholic consumption also promotes inflammation, alters hormone levels, and impairs immune function, and all these mechanisms have been linked to carcinogenesis [131–133]. Consuming alcohol during cancer treatment could worsen treatment-related symptoms and make treatment less effective [129,134]. Evidence also suggests that regular alcohol intake among cancer survivors may increase the chance of cancer recurrence [134]. However, despite these findings regarding alcohol consumption, a cross-sectional study involving over 15,000 adult cancer survivors in the United States reported ~80% as current drinkers, with almost 25% engaging in binge drinking and ~38% engaging in hazardous drinking [135]. These findings highlight the need for more research and interventions to address alcohol use among cancer survivors.

Influence on female fertility

Research suggests that consumption of alcohol could have deleterious effects on female fertility. Alcohol consumption can disrupt the balance between estrogen and progesterone, leading to irregular ovulation and anovulatory cycles. Additionally, alcohol intake is associated with reduced fallopian tube smooth muscle contraction, uterine implantation defects, and an increased risk of miscarriage [136,137]. Although much of the research regarding alcohol intake and female fertility has inconsistencies regarding cut-off values, units of measurement, and type of alcohol consumed, consuming any amount or type of alcohol has been found to reduce fecundity in females [137,138]. A dose–response meta-analysis involving over 90,000 reproductive-aged females found that compared with nondrinkers, drinking was significantly associated with 13% (any drinking), 11% (light drinking: $<$12.5 g/d), and 23% (for moderate-heavy drinking:$>$12.5 g/d) decrease in fecundability or likelihood of pregnancy in a given month [138]. Additionally, the dose–response analysis found that females who consume $>$1 alcoholic drink (12.5 g/d) will experience a 2% reduction in their fecundability [138].

Studies on ART also suggest alcohol can negatively impact outcomes, even at moderate levels. This includes reducing the number of retrieved eggs, lowering pregnancy rates, and decreasing embryo quality [139,140]. A multicenter comparative study in the United States involving 221 couples with female factor infertility undergoing IVF and Gamete Intrafallopian Transfer found that females who consumed $>$1 drink per d ($>$12 g/d) a month before the procedure had almost 3 times increased risk of not achieving a pregnancy [141]. When the same amount of alcohol was consumed a week before the procedure, the risk increased to 4 times; however, this finding was not statistically significant [141]. Other studies investigating alcohol intake and IVF outcomes have also reported similar findings [142,143]. Although most studies regarding the effect of alcohol intake on female fertility and ART success are observational, strong evidence suggests that alcohol has detrimental effects on female fertility.

Dietary patterns

Dietary patterns and cancer survivorship

Dietary pattern analysis has emerged as an alternative and complementary approach to determining the connection between diet and health outcomes. Dietary pattern analysis looks at the effects of the overall diet as opposed to individual nutrients or foods and provides a holistic picture of food and nutrient consumption, making it a better predictor of disease risk and outcomes [144]. It is recommended that cancer survivors follow a healthful dietary pattern rich in vegetables, fruits, whole grains, nuts, legumes, and seafood, with limited red meat, alcohol, and processed meat, such as the plant-forward dietary patterns recommended by the AICR including the AICR's New American Plate and the Mediterranean diet [145]. These dietary patterns also closely align with recommended dietary patterns in the DGA 2020–2025 [146]. Therefore, adhering to dietary patterns recommended by these expert bodies could improve overall health and cancer survivorship [145,147].

The plant-forward approach to cooking and eating emphasizes plant-based foods, though it may include other ingredients such as meat as long as they are not the primary focus of the meal [148]. Several studies show that plant-forward diets reduce cancer risk and improve cancer survivorship. For example, a study involving almost 1200 participants found that having a high Healthy Eating Index-2015 score, a measure of diet quality based on the DGAs, reduced mortality by 65% compared with survivors who did not adhere to these recommendations, adjusting for age, sex, income, education, BMI, and comorbidities [149]. Although this study has some limitations, including failure to adjust for cancer stage or treatment and the use of 24-h dietary recalls, which may not be representative of habitual dietary behavior, the findings are important because they show that when cancer survivors adhere to a healthful dietary pattern, they could improve their survival rates. Similarly, a Mediterranean-type dietary pattern could reduce the risk of weight gain, overweight, and obesity, which have been linked to several cancers, including breast, ovarian, and uterine cancers [82,147]. This is supported by a meta-analysis of 83 studies, which found higher adherence to a Mediterranean dietary pattern was inversely associated with cancer mortality and the risk of developing certain cancers such as colorectal, breast, gastric, liver, and head and neck cancers [150].

Dietary patterns and female fertility

Dietary patterns consisting of fruits and vegetables, unsaturated fats, and low glycemic carbohydrates, such as whole grains, benefit female fertility. In the NHS II cohort, females who had greater adherence to a "fertility diet" comprising high monounsaturated fat, vegetable protein, high-fat dairy, low glycemic carbohydrates, multi-vitamins, and nonheme iron from plants and supplements, had a lower possibility of ovulatory infertility [27]. Likewise, a study in the Netherlands involving 199 couples undergoing preconception nutrition counseling during IVF treatment found a one-point increase in preconception dietary risk (PDR) score to be associated with a 65% increased chance of ongoing pregnancy after adjusting for the age of female partner, smoking of female partner, PDR of the male partner, BMI of the couple and treatment indication [151]. PDR calculation was based on dietary recommendations by the Netherlands Nutrition Center consisting of 4 slices of whole wheat bread daily (or comparable servings of cereals), the use of monounsaturated or polyunsaturated oils, ≥200 g of vegetables daily, ≥2 pieces of fruit daily, ≥3 servings of meat or meat replacers weekly, and ≥1 serving of fish weekly. A score of 1 was assigned to each food group if a participant met the recommendation [151]. Another study by Karayiannis et al. [152] in Greece, among 244 normal-weight females undergoing IVF treatment, found that having a higher score for Mediterranean diet adherence was positively related to clinical pregnancy and live birth among younger females (<35 y), controlling for factors such as age, BMI, ovarian stimulation, and dietary supplement use. Similarly, the Preconception Dietary Supplements In Assisted Reproduction (PREPARE) trial in the United Kingdom which examined the importance of key components of the Mediterranean diet, including olive oil, Ω-3 fatty acids (both EPA and DHA) from seafood, and vitamin D, found increased EPA, DHA, vitamin D, and improved embryo quality among the intervention group [21]. Likewise, another study in China by Sun et al. [153], among a large sample of 590 females undergoing IVF, also found higher adherence to a Mediterranean dietary pattern increased the number of available embryos, adjusting for age, duration of infertility, and BMI. When Vujkovic et al. [120] in the Netherlands investigated the relationship between preconception dietary patterns and IVF/ICSI among 161 couples, they also found that adhering to a Mediterranean-type dietary pattern increased the chance of pregnancy after treatment by ≤40% as compared to a health conscious-low processed diet adjusting for age, BMI, use of vitamin supplements, and total protein in follicular fluid. This study additionally found that adhering to a Mediterranean dietary pattern increased vitamin B6 levels in blood and follicular fluid, which has been linked to enhanced reproductive performance by increasing the chance of conception and reducing the risk of miscarriage [120].

Although the definition of Mediterranean and other healthful dietary patterns vary across studies, there are overlaps in whole grains, fruits, vegetables, and fish rich in long-chain Ω-3 PUFAs and olive oil (rich in MUFA), most of which have been found to improve ART outcomes and the likelihood of pregnancy [119]. Moreover, these foods are consistent with the United States-style dietary pattern and other recommended dietary patterns in the DGAs [11]. Additionally, although the time assessed for adherence to dietary patterns in several studies was short, significant improvements in fertility outcomes were observed, indicating that healthful nutrition within a short period could positively influence female fertility. Longer-term studies are needed.

Body weight

Body weight and cancer survivorship

Cancer treatment often results in body weight changes such as unhealthy weight loss or obesity [17]. Treatment side effects may affect eating behaviors, which can subsequently lead to a loss of lean body mass and excessive weight loss [154]. Conversely, certain cancer treatments involving chemotherapy, steroid medications, and hormonal therapy could also predispose survivors to weight gain. These adverse treatment outcomes have prompted several organizations, such as the ACS and the AICR, to recommend weight management for cancer survivors [17, 155]. Currently, the prevalence of obesity among cancer survivors is estimated at 31.7%, and younger cancer survivors are twice as likely to experience obesity compared with their siblings who do not have a cancer diagnosis [155,156].

Accumulating evidence suggests that obesity increases the risk of cancer recurrence and reduces the likelihood of disease-free and overall survival among individuals diagnosed with cancer [17]. Excess body weight disrupts the balance of hormones such as insulin, growth hormones, leptin, and ghrelin. This imbalance can cause disruptions to metabolic and physiological processes, leading to further weight gain, metabolic disorders, and cancer [157]. Consequently, intentional weight loss following treatment recovery could improve survivorship, although data supporting this assertion is limited. Reducing the caloric density of a person's diet through increasing their intake of low-energy-dense foods like vegetables and fruits and limiting the intake of foods and beverages high in fat and added sugar could improve the hormonal milieu and promote healthy weight control among cancer survivors [17]. Even if an ideal body weight is not achieved, it is likely that weight losses of 5% to 10% could have significant health benefits for cancer survivors with overweight or obesity [17]. For example, a large multicenter randomized control trial involving over 2500 breast cancer survivors in the United States found that adhering to a low-fat diet that resulted in weight loss of ~4% of initial body weight minimized the risk of cancer recurrence among postmenopausal females, especially those with estrogen receptor-negative tumors [158].

After cancer treatment, weight loss or weight gain should be managed using a combination of dietary, physical activity, and behavioral strategies [17]. For cancer survivors who need to gain weight because of cancer diagnosis or treatment, energy intake from food should be increased to exceed energy expenditure as opposed to cancer survivors who are overweight or obese. Those at risk of malnutrition should be referred to a Registered Dietitian for personalized nutritional counseling. Additionally, an oral nutritional supplement may be necessary if oral intake does not provide energy expenditure needs. If further support is needed, enteral nutrition tube feeding or parenteral nutrition should be considered. Cancer survivors in stable health after treatment are, however, advised to follow cancer prevention recommendations by the WCRF, AICR, and ACS, such as maintaining a healthy weight, regular physical activity, and consuming a plant-forward diet low in red and processed meats, sugar-sweetened drinks, highly processed foods, and refined grains, as well as avoiding or limiting alcohol intake. Survivors should seek nutritional care and physical activity guidance from professionals [20]. Dietary interventions should be carefully tailored to meet the needs of cancer survivors to help them achieve and maintain a healthy body weight.

Body weight and female fertility

Body weight has been found to influence fertility outcomes in females, and weight assessment is customary during the ART treatment process, with ≤50% of United States-based infertility clinics having a BMI cut-off for performing procedures [11]. Upper limit BMI cut-off typically ranges from 30 to 55, with a mean of 40 kg/m^2, although physicians and practices are often reluctant to establish BMI restrictions in order not to seem discriminatory [159]. In general, having a body weight that is too low or too high can negatively impact fertility as well as the success of ART treatment [11]. For example, among the NHS II cohort, females classified as underweight (BMI <18.5) and females with obesity (BMI ≥30), had a higher risk of ovulatory infertility than females classified as normal weight (BMI: 18.5–24.9), after controlling for diet intake, age, smoking, and oral contraceptive use [123]. Among a representative sample of United States females undergoing ART, a BMI ≥ 25 was associated with greater odds of failing to achieve clinical pregnancy than among females with a BMI of 18.5 to 24.9, adjusting for factors such as age, race and ethnicity, height, nulligravidity, infertility diagnoses of male factor, endometriosis, and ovulation disorders [11]. A randomized controlled trial by Moran et al. [43], in Australia, among 46 females with overweight and obesity undergoing IVF involving a low-calorie, high-protein diet, found a reduction in waist circumference resulted in increased odds of achieving pregnancy. Moreover, in this study, females who were randomized into the control group had significant reductions in waist circumference in the absence of the individualized weight loss intervention, indicating that providing standard healthy lifestyle guidance without individualized care or follow-up is enough to attain healthy lifestyle changes [43]. This could be indicative that females undergoing fertility treatment may be more motivated to adopt healthy lifestyle practices. In contrast, being on a "weight loss diet" had a negative association with blastocyst formation in a cross-sectional study in Brazil among 269 females undergoing IVF/ICSI [32]. However, this finding should be taken with caution because there was no information gathered on the type of weight loss diet and whether it was approved by a registered nutritionist or dietetics professional.

Fertility Counseling, Assessment, and Treatment

Owing to the risk of infertility among female cancer survivors, the need for information, and advances in fertility preservation and treatment strategies, professional bodies such as the American Society for Reproductive Medicine (ASRM) and the American Society of Clinical Oncology (ASCO) have provided recommendations on fertility counseling, assessment, and preservation options for cancer survivors [10]. The rationale for fertility counseling before cancer treatment is to inform patients and their families about future fertility prospects and to facilitate fertility preservation. Fertility counseling during this period informs individuals about the risk of infertility due to cancer and its treatment, provides fertility preservation options before cancer treatment, and psychological support for cancer survivors [13]. Cancer survivors who undergo precancer treatment fertility counseling and assessment are reported to have improved decision-making on fertility preservation options and have significantly improved quality of life [10,13].

Initial fertility counseling and assessment are typically done at the time of diagnosis where a medical practitioner or reproductive specialist discusses threatened fertility with a patient. Subsequent follow-up counseling and assessment after oncological treatment may be scheduled when the patient has completed treatment and is considering pregnancy (Table 1) [13]. The early counseling process entails a detailed description of all available preservation techniques appropriate for the patient including procedures, timing, possible complications of fertility treatment, and results. Additionally, clinicians are mandated to differentiate well-known procedures from experimental ones [160].

The uptake of fertility preservation before oncological treatment is low and females may miss this opportunity probably because they are too young at the time of diagnosis [80]. Consequently, young female cancer survivors report moderate to high reproductive concerns even after pretreatment fertility counseling and this hinders many from seeking fertility care after cancer treatment [80]. Higher level of reproductive concerns despite pretreatment counseling suggests the need to improve the quality of fertility counseling for female cancer survivors and to place equal emphasis on counseling after cancer treatment to assist females who want to get pregnant [10]. Fertility counseling and assessment for cancer survivors should be an iterative process and must go beyond the provision of medical information only to incorporate therapeutic exploration of reproductive concerns and fertility treatment needs. Additionally, fertility counseling should be more holistic and multidisciplinary, incorporating evidence-based adjunctive treatment methods such as nutrition to support fertility during follow-up counseling and assessment [11,13,161]. Thus, the period of fertility counseling, particularly after cancer treatment, provides a unique opportunity for implementing nutritional guidance for female cancer survivors. Healthful nutrition could support fertility preservation and treatment efforts, especially during IVF [119]. However, there are currently no nutrition-related guidelines in the United States or several other countries to support fertility treatment for females, especially female cancer survivors [11]. It is important to tailor nutrition-related periconceptional advice and to determine the frequency and the best method of implementation for this guidance to female cancer survivors presenting for fertility treatment to support positive dietary changes that could improve the likelihood of pregnancy and live birth.

Bridging the Gap: a Strong Rationale for Future Studies

Understanding female cancer survivors' nutrition-related knowledge, attitudes, and beliefs about fertility

Having a child is an important milestone many cancer survivors want to attain. The potential loss of fertility can be as painful as the cancer diagnosis itself and for some young cancer survivors, the possibility of having a biological child is instrumental to coping with cancer [10]. Females with infertility may be highly

TABLE 1
Summary of specific foods influencing cancer survivorship and female fertility

Food/nutrient	Cancer survivorship	Female fertility
Red and processed meat	May increase the risk for certain cancers (colorectal, pancreatic, lung) through low-grade inflammation, free radicals and by producing carcinogenic compounds in the body.	Reduces fertility and pregnancy chances. Decreases the chances of embryo formation, negatively affects ovulation, and can cause endometriosis. Meat consumption in general negatively affects ovulation.
Fatty acids and Seafood	Improved quality of life, reduces cancer risk, reduces CVD risk, and decreases cancer-related mortality.	Fatty acids are required for oocyte maturation and early embryo development. Key for implantation and maintaining pregnancy.
Whole grains	Contain important hormonal and antioxidant effects, which reduce cancer risk and progression and reduce CVD risk.	Antioxidant, anti-inflammatory properties, pro-estrogenic and antiestrogenic properties that work together to improve fertility in females.
Soy	Contain important isoflavones that reduce breast cancer incidence, recurrence, and mortality.	Increases endometrial thickness and chances of ongoing pregnancy. Increases live births for females undergoing ART.
Legumes	Contain dietary fiber, resistant starch, and several phenolic compounds, which may prevent cancer risk and improve survivorship by promoting a healthy microbiome and healthy body weight.	Good source of plant-based protein that reduces risk of ovulatory infertility. Pulses improve insulin response and lipid profiles, both of which are associated with egg quality and development.
Dairy	Contain important micronutrients and bioactive compounds that may be protective against colorectal cancers but not cancers at other sites.	Mixed findings, no strong conclusions can be drawn regarding periconceptional dairy intake and female fertility.
Sugar	Increased risk of weight gain, overweight, and obesity. Artificial sweeteners – inconclusive evidence.	Reduces pregnancy chances. Artificial sweeteners – cause oxidative stress in ovaries, reduce ovarian follicles, and disrupt steroidogenesis in granulosa cells.
Caffeine	Contain antioxidants and phytochemicals that reduce risk for endometrial cancers. Inconclusive findings for cancers at other sites.	Excessive caffeine intake during pregnancy associated with increased risk of miscarriage. However, overall effects on female fertility are inconclusive.
Fruits, vegetables and micronutrients	Contain glucosinolates, micronutrients, and antioxidants that prevent cancer and inhibit cancer progression by reducing inflammation, stimulating cell death and preventing free radical damage respectively.	Micronutrients and antioxidants promote embryo development and endometrial receptiveness.
Alcohol	Acetaldehyde, a product of alcohol metabolism, is a carcinogenic and mutagenic substance. Chronic alcohol consumption promotes inflammation, alters hormone levels and impairs immune function. This increases cancer risk, progression and recurrence.	Alcohol disrupts estrogen and progesterone levels, leading to irregular ovulation and anovulatory cycles. It reduces fallopian tube smooth muscle contraction, uterine implantation defects and increases risk of miscarriage. In females undergoing ART, alcohol reduces the number of retrieved eggs, lowering pregnancy rates, and decreases embryo quality.

ART, assisted reproductive technology; CVD, cardiovascular disease.

committed to altering their lifestyle, especially diet- and exercise-related [162]. However, several misconceptions and misinformation exist related to these modifiable lifestyle factors, particularly nutrition misinformation. There is a need to assess female cancer survivors' perceptions and perspectives about fertility nutrition to address misconceptions and misinformation about foods and dietary patterns that support fertility. This will help develop nutrition-related guidance tailored for female cancer survivors undergoing fertility treatments.

Characterizing the barriers and challenges to improving nutrition-related behaviors among female cancer survivors

Cancer survivors struggle to meet dietary and physical activity recommendations [52]. Up to 94% of young cancer survivors do not meet national recommendations for the intake of several nutrients. Many consume unhealthy diets with high fat and low fruit and vegetable intakes [163]. Compared to the general population, they are also unlikely to meet physical activity guidelines and are generally more sedentary than their siblings with no history of cancer [52].

Barriers to improving lifestyle behaviors among cancer survivors exist at multiple levels [164]. A study involving breast cancer survivors identified individual, social, and organizational level barriers to healthy diet and lifestyle behaviors, with the majority of females reporting ≥1 barrier at each level. Additionally, females who reported individual-level barriers such as lack of time and/or motivation, and social-level barriers such as lack of support had lower fruit and vegetable intakes than those who did not perceive a barrier at these levels [165]. These multilevel barriers present several challenges that could influence dietary intake among female cancer survivors and possibly affect their fertility. Identifying these barriers and challenges is the first step to developing strategies and interventions to improve nutrition-related behaviors among this population.

Assessing interest in and preferences for nutrition-related lifestyle guidance during fertility counseling, assessment, and treatment among female cancer survivors

The period of cancer survivorship presents an opportunity to adopt a healthier lifestyle because it is during this time that survivors and their families are more open to engaging in education and adhering to an intervention. The ACS provides evidence-based guidelines on nutrition and physical activity for cancer survivors in 3 broad categories, which involve maintaining a healthy body weight, engaging in regular physical activity, and following a healthy dietary pattern of high fruit, vegetable, and whole grain intake [166]. Interestingly, similar evidence-based recommendations have been shown to increase the likelihood of pregnancy for females undergoing fertility treatment [11]. Therefore, female cancer survivors who adhere to healthy nutrition-related lifestyle recommendations will likely improve their reproductive and general health.

Despite demonstrated evidence of the importance of positive nutrition-related behaviors on cancer survivorship, a significant proportion of cancer survivors are unable to meet these recommendations [167]. Cancer survivors are consuming more than the recommended daily intake of sugar and fat, fewer servings of fruits and vegetables, and are also less likely to meet physical activity guidelines than the general population [52]. Consequently, there is a high demand for survivorship programs that focus on healthful nutrition and physical activity tailored toward the unique needs of young adult cancer survivors [52]. It is important to design interventions that consider the desires and preferences of this population, to enable young adult cancer survivors to meet lifestyle recommendations. Regarding fertility, future research should assess female cancer survivors' interest in and preferences for nutrition guidance during fertility counseling and treatment, to program appropriate interventions for this population.

Limitations of Current Study

This article presents evidence regarding the relationship between cancer survivorship nutrition and fertility nutrition. Some limitations of this review include the potential for subjectivity bias. Although the authors reviewed foods that align with the DGA 2020–2025, the selection of studies was according to the authors' expertise and judgment. Additionally, the authors acknowledge that this may not be an exhaustive search of the literature, therefore, other important studies published in less prominent journals or outside the authors' immediate field may have been missed. Furthermore, articles not published in English were excluded from the review. Also, because this narrative review synthesized information from different types of studies, only associations can be made and causality cannot be established. However, despite these limitations, this article is a valuable tool for summarizing and contextualizing existing knowledge regarding the topic. Moreover, we have identified gaps in the literature and areas for future research to improve our knowledge of the relationship between nutrition, cancer survivorship, and female fertility.

Summary

Infertility is a major quality-of-life challenge for many female cancer survivors. Although fertility preservation and treatment methods have improved in recent times, infertility remains high among this population, warranting the need to explore modifiable lifestyle factors that could improve pregnancy chances [8, 11]. Healthful dietary patterns support both cancer survivorship and fertility. High intakes of fruits, vegetables, whole grains, legumes, nuts, lean meat, soy, and seafood while limiting intake of red and processed meat and sugar-sweetened beverages, have been found in several studies to improve both fertility and cancer survivorship. Moreover, these dietary patterns are also in line with United States DGA 2020–2025. Fertility counseling and assessment, particularly after cancer treatment presents a unique opportunity to integrate evidence-based nutrition-related guidance into fertility treatment for female cancer survivors. Dietary interventions represent a promising strategy to improve pregnancy chances and overall quality of life. This assertion is buttressed by this review article, which has illustrated the parallels between cancer survivorship nutrition and fertility nutrition.

Implications for Practice

At present, there are no specific nutritional guidelines available for female cancer survivors who are undergoing fertility treatment. Although separate guidelines for cancer survivorship and female fertility exist, they have not been combined into a single set of recommendations for this specific population. This presents an opportunity to create such guidelines by utilizing the existing ones, which are already in line with the DGA 2020–2025. This is particularly important because it is recommended that the DGAs are adopted by health professionals to meet the specific needs of patients with chronic diseases as part of a comprehensive treatment plan [146]. Integrating these guidelines into regular fertility treatment procedures may potentially enhance fertility outcomes for female cancer survivors and improve their overall health. It would be useful to create practical meal-planning tools similar to MyPlate and the AICR's New American Plate to help female cancer survivors plan healthy meals. Additionally, there is a need to involve certified nutrition professionals such as registered dietitians in the fertility treatment process for female cancer survivors.

Author contributions

The authors' responsibilities were as follows: CK and BJM designed the review; CK conducted the literature search and produced the initial draft of the manuscript. CK wrote the initial draft and revised it multiple times with BJM. MV, JD, KF, JAN, and DS provided ongoing feedback. MM and LC provided expert opinions on fertility treatment and dietary guidance, respectively. CK, BJM, and MV were responsible for the final draft. All authors read, revised, and approved several versions of the manuscript.

Conflict of Interest

The authors have no conflicts to declare.

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Data availability

Data described in the manuscript will be provided upon request after contacting the authors.

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