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Nutrition and Cancer Research: Resources for the Dietetics Professional

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Abstract

This issue of the Journal focuses on issues in the intersection of nutritional science and cancer prevention research. In this commentary, we provide a high-level orientation for the reader to nutrition and cancer. We begin by reviewing the burden of cancer which has necessitated public policy recommending improvements to diet for the prevention of cancer in the U.S., although this is true of many other countries as well. These policy recommendations are based on the critical review of scientific evidence linking diet and cancer. We then discuss the inconsistencies in the nutrition-cancer scientific literature and the subsequent issues Registered Dietitian Nutritionists (RDNs) face when translating this literature in the clinic. We conclude with some resources for practitioners and general guidance.

Keywords

Cancer Prevention; Diet; Oncology Nutrition; Oncology Recommendations; Research

Cancer Burden and Cancer Prevention at the Population Level

The U.S. has a high burden of cancer and the U.S. public health policy uses nutrition recommendations as a tool to help combat this burden.¹ In 2017, the American Cancer Society projects over 1.68 million new cancer cases will be diagnosed in the United States.² The 2014 American Association for Cancer Research Report to Congress estimated more

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than half of all cancers are due to preventable causes; in particular, modifiable exogenous and environmental cancer risk factors, such as tobacco use, diet, and obesity.^{3, 4, 5}

For decades, U.S. public health messages have advocated changes in specific health behaviors to minimize disease risk.⁶ Specifically, the most recent 2015-2020 U.S. Dietary Guidelines for Americans, jointly issued by U.S. Department of Health and Human Services and U.S. Department of Agriculture, have served as a national target for public health policy to prevent cancer and other diseases.⁶ The U.S. Dietary Guidelines recommend Americans select an eating pattern reflecting not just individual dietary preferences, but also consider personal dietary requirements to promote health, prevent chronic disease, and achieve and maintain a healthy body weight.⁶ Some examples of evidence-based, cancer-relevant public health messages in the U.S. Dietary Guidelines include: avoid or limit exposure to known environmental carcinogens (e.g., tobacco and aflatoxins) and adopt health promoting behaviors and lifestyles (e.g., increase physical activity, consume a healthy diet, and prevent obesity) to reduce risks for developing cancer.^{7, 8, 9} These recommendations result from careful review of the scientific literature. Yet they face many unique challenges as a result of null and conflicting research findings as we will discuss below. These challenges limit the evidence base and thus the quality of dietary recommendations for the prevention of cancer.^{10, 11, 12, 13}

Milestones in the Review of the Nutrition and Cancer Scientific Literature

In 1997, the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) conducted the first global systematic literature review evaluating decades of epidemiologic and basic nutrition science evidence, culminating in the first expert authoritative diet and exercise recommendations for preventing cancer.¹⁴ In 2007, a second, more mechanistically-focused WCRF/AICR expert report rated the scientific evidence supporting the association between a dietary component and a cancer site as “Convincing”, “Probable”, “Limited-suggestive”, and “Substantial effect on risk unlikely”.¹⁰ This 2007 WCRF/AICR Report evaluated all epidemiological and nutritional science evidence globally, recommending policy and public health actions aimed at reducing cancer risk and occurrence worldwide as well as elucidating knowledge gaps in the diet and cancer scientific literature.¹⁰

Today, the WCRF/AICR Continuous Update Project (CUP) provides valuable, periodic updates for numerous site-specific cancers for use by researchers, clinicians and policymakers alike.¹¹ The CUP project is the most respected source for expert vetted information on diet and cancer; identifying current research gaps for future prevention research efforts. The preponderance of published nutritional science discoveries suggests whole foods and individual dietary constituents are associated with cancer incidence and mortality.^{15, 16, 17, 18, 19, 20, 21, 22} Yet, the CUP project has produced few diet-cancer relationships that are supported by a “convincing” level evidence due to a lack of large human trials, a reliance on small studies and general inconsistencies in the nutritional sciences literature.¹¹

Diet-Cancer Prevention Literature Inconsistencies

Despite the best efforts of nutritional science researchers, inconsistencies exist across the diet-cancer prevention scientific literature. Differences in study design (e.g., poor statistical power from a small sample or small effect size, variable exposure level and duration, imprecise measurement of diet), dietary interventions tested (e.g., whole foods, single dietary components, dietary supplements), baseline eating patterns (e.g., western, prudent), and populations sampled (e.g., age, health status, individual genetics) account for many of the inconsistencies observed across diet and cancer prevention studies.^{23, 24, 25} However, a researcher cannot possibly avoid all of these pitfalls while staying within their project budget. For example, mechanistic studies often inherently limit the researcher to using only a single food component at a single dose to elucidate a complex mechanism. This more “reductionist approach” can lead to study irreproducibility because of the complex nature of evaluating human dietary exposures when a hypothesis is moved from a basic study in cells or an animal to a human.^{13, 26}

Dietetic and other practitioners must sort through the nutritional science literature and hierarchically prioritize research findings by levels of evidence.²⁷ Diverse lines of preclinical evidence (e.g., cell culture, genetic animal models) provide important investigational links often describing scientific phenomenon, testing hypotheses, elucidating potential mechanisms of action influencing carcinogenic events, and evaluating dose efficacies. Adequate research hypotheses testing and validation are critical to generating robust preclinical research before proceeding towards larger, more costly studies. Large cohort observational epidemiological evidence, while associational in nature, can hypothesize cancer risk, making important research contributions and providing early human evidence. The National Institutes of Health reinforces stringent testing of mechanistically-based hypotheses when evaluating observational data to ensure study rigor and reproducibility.^{28, 29} Clinical trials are the gold standard of research, but are often not feasible, cost-prohibitive or not possible for some nutrition and cancer hypotheses. Study replication and validation efforts serve as important steps as well as preventive strategies against replication failures often attributed to confounding variables, including inter-individual responses to dietary interventions.^{11, 30} Still, null effects and unintended consequences occur even in large human clinical trials.^{31, 32}

While small Phase 0 clinical trials may provide initial evidence suggesting potential dietary efficacy in preventing cancer; larger studies, meeting necessary Federal research standards for scientific rigor and reproducibility are needed.^{28, 29} However, even in the absence of additional adequately powered trials, knowledge can be gained and scientific consensus built from expert opinion to inform clinical guidelines (e.g., essential fatty acids and heart disease).³³ In summary, all models have strengths and weakness imposed by physiological or mechanistic differences limiting predictive power and clinical utility and should be evaluated based on their strengths and weaknesses when estimating relationships between diet and cancer risk.^{30, 34}

Dietetics Practitioner Role and Resources

The 2012 Academy of Nutrition and Dietetics revised professional performance nutrition care Standard 3: Nutrition Intervention states “The registered dietitian (RD) identifies and implements, appropriate, purposefully planned interventions designed with the intent of changing a nutrition-related behavior, risk factor, environmental condition, or aspect of health status for an individual, target group, or community at large.”³⁵ The body of scientific data should be compelling before translating scientific findings to our at-risk, presumed healthy clients for disease prevention and patients with a good prognosis undergoing treatment. Nutrition recommendations should be client-tailored considering individual health history. For cancer patients, individual cancer type, stage, and prognosis, should also be discussed with the care team. This charge requires RDNs and Nutrition and dietetic technicians, registered provide clear nutrition recommendations that accurately describe the level of evidence supporting the recommendations. Below we provide a list of resources for dietetic practitioners which the Academy and physician oncologists have recognized as reputable.

Associations between nutrition and prevention of primary cancers—As mentioned above, the WCRF/AICR CUP project continues to be the premiere expert summary on the direction, magnitude and strength of evidence supporting relationships between nutrition and specific cancers. Carcinogenic initiation and promotion events produce profound differences within tissues and across organ sites exerting metabolic pathway perturbations.³⁶ Increasing individual adherence to WCRF/AICR recommendations is significantly associated with reductions in several cancer types, including breast, endometrial, esophageal, kidney, liver, lung, and upper aerodigestive tract cancers.³⁷ No association was found for preventing bladder, ovarian, pancreatic or prostate cancers.³⁷ The American Cancer Society also provides nutrition and physical activity guidelines for cancer prevention. Individuals whose behaviors are consistent with recommendations to maintain a healthy body weight, to be physically active, consume a mostly plant-based dietary pattern, and limit alcohol consumption are at lower risk of developing and dying from cancer.^{38, 39, 40}

Associations between nutrition and cancer survivorship—National Comprehensive Cancer Network Guidelines for cancer survivors stress the best formula for reducing cancer recurrence is a healthy lifestyle founded upon healthy dietary habits, weight management and exercise to reduce the risk of cancer recurrence and death.⁴¹ As nutrition experts, RDNs are ideally positioned to promote and implement healthy lifestyle interventions for those most at high-risk for developing cancer as well in cancer patients and survivors. Early adoption of healthy dietary behaviors may reduce the physiologic impact of past low quality dietary patterns, improve quality of life and reduce future cancer risks.⁴² The American Cancer Society also provides nutrition and physical activity guidelines for cancer survivors by cancer type, when evidence is sufficient.⁴³

Practice guides for Oncology Dietetics Practitioners—The Academy’s Oncology Dietetics Practice Group provides a tailor-made resource for Dietetics Practitioners in

Oncology that spans Prevention, Medical Nutrition Therapy for specific cancer types, exercise and survivorship.⁴⁴

General resources for evaluating diet-cancer research—The Academy Evidence Analysis Library provides specific practice recommendations and rates the evidence supporting those recommendations.⁴⁵ RDNs often must evaluate research study findings to determine potential study strengths and weaknesses; including seeking additional independent studies to answer patient/client queries. The Academy and many major scientific organizations (e.g., National Institutes of Health) offer a “refresher” for health professionals in evaluating cancer prevention research findings.^{46, 47, 48}

Nutrition and genetic testing related to cancer—The level of evidence supporting nutrigenetic testing to determine individual nutritional requirements for use in either reducing cancer risk or treating cancer is insufficient at present. Dietetics practitioners should understand direct-to-consumer nutrigenetic test limitations before advocating use in determining individual nutritional needs to reduce cancer risk or guide cancer patient nutritional care practices. We anticipate the use of these tests will only increase as the body of evidence expands, and RDNs will benefit by staying abreast of changes in this area. While the U.S. Food and Drug Administration (FDA) has legal authority in regulating genetic tests, at this time the agency does not evaluate whether direct-to-consumer genetic tests are clinically useful.⁴⁹

This is in stark contrast to, and should not be confused with, Clinical Laboratory Improvement Amendments genetic testing for disease screening, disease diagnosis and monitoring for which there is a significant amount of evidence for use and efficacy.⁴⁹ The American Medical Association notes genetic tests are traditionally available only through physicians and limited health care providers such as genetic counselors.⁵⁰ For example, the Clinical Laboratory Improvement Amendments approved cancer genetic testing help physicians determine cancer treatment regimens (e.g., Her2 neu breast cancer status)^{50, 51} or even practice guidelines for individuals at high risk of cancer (e.g., BRCA mutation carrier).⁵² U.S. Food and Drug Administration also provides a web-based list of all cleared or approved genetic tests to tailor treatment.⁵³ For more information on how genetic testing is regulated see this resource provided by the National Institutes of Health.⁵⁴ Patients who have cancer or are at high risk for cancer should receive medical nutrition therapy based on the magnitude of the risk and their entire medical history, regardless of whether they were identified via genetic testing or other tests.

Conclusions

RDNs are uniquely positioned to provide balanced evidence-based information from peer-reviewed literature to assist at-risk and cancer patients understand the strength of the evidence guiding individual health decisions. Long-term, federally supported large scale dietary intervention trials require substantial justification prior to initiation and so they are often unavailable to the practitioner faced with a question from a patient. Thus, thoughtful hierarchical review of the existing medical and research evidence,^{55, 56} and clear communication to the patient of the level of evidence is the best clinical practice in the face

of conflicting information. Dietetic practitioners are encouraged to refer to topical articles within this issue of the Journal for more detail on specific nutrition-cancer research questions.

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Biographies

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