



Published in final edited form as:

Leuk Lymphoma. 2010 June ; 51(6): 1047–1054. doi:10.3109/10428191003690364.

Vegetable and fruit intake and non-Hodgkin lymphoma survival in Connecticut women

XUESONG HAN¹, TONGZHANG ZHENG¹, FRANCINE FOSS², THEODORE R. HOLFORD¹, SHUANGGE MA¹, PING ZHAO³, MIN DAI³, CHRISTOPHER KIM¹, YAQUN ZHANG⁴, YANA BAI⁵, and Yawei ZHANG¹

¹ School of Public Health, Yale University, New Haven, CT, USA

² School of Medicine, Yale University, New Haven, CT, USA

³ Cancer Institute/Hospital, Chinese Academy of Medical Sciences, Beijing, P.R. China

⁴ Gansu Provincial Design and Research Institute of Environmental Science, Lanzhou, P.R. China

⁵ School of Public Health, Lanzhou University, Lanzhou, P.R. China

Abstract

We investigated whether an increased intake of vegetables and fruits favors NHL survival. A cohort of 568 female cases of incident NHL diagnosed during 1996–2000 in Connecticut was followed up for a median of 7.7 years. Adjusted hazard ratios (HRs) were estimated by Cox proportional hazard models. Our results show that a pre-diagnostic high intake of vegetables appeared to favor overall survival (HR = 0.74, 95% CI 0.57–0.98) among patients with NHL who survived longer than 6 months. In particular, pre-diagnostic high intakes of green leafy vegetables and citrus fruits were associated with 29% (95% CI 0.51–0.98) and 27% (95% CI 0.54–0.99) reduced risk of death, respectively. When different types of vegetables and fruits were investigated separately, their impacts were found to vary in NHL subtypes. Our study suggests that increasing vegetable and citrus fruit consumption could be a useful strategy to improve survival in NHL patients.

Keywords

Vegetables and fruits; non-Hodgkin lymphoma; prognosis; survival

Introduction

Non-Hodgkin lymphoma (NHL) represents a heterogeneous group of malignancies arising from lymphocytes throughout the body. Since the 1970s, the incidence rate of NHL has doubled in the United States [1,2]. Although the human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic during the 1980s explains part of the increasing trend, other reasons remain unclear [3]. It was estimated that a total of 65 980 people would be diagnosed with and 19 500 would die from NHL in 2009 in the USA [4].

Several clinical features were identified as NHL prognostic factors, including age at diagnosis, tumor stage, and presence of B-symptoms (fever, night sweats, generalized pruritus, or weight loss of greater than 10% of total body mass) [3,5]. Higher socioeconomic background was also associated with better survival in patients with NHL [6,7]. Other lifestyle factors have rarely been studied for NHL survival. Vegetables and fruits contain numerous antioxidants, folate, and fiber, which could be beneficial in multiple mechanisms of tumor development and progression. It was reported that a high vegetable and fruit intake was associated with a reduced risk of NHL [8–14], and studies showed that dietary patterns with high vegetables and fruits might improve prognosis in survivors of breast cancer [15–18], lung cancer [19], stomach cancer [20], oral cancer [21], and laryngeal cancer [22].

In order to investigate whether vegetable and fruit intake improves the prognosis of NHL, we conducted a survival analysis by NHL subtype. We used cases recruited from a population-based case–control study [11,23] with a median follow-up time of 7.7 years and a maximum follow-up time of 11.8 years. According to the Surveillance, Epidemiology and End Results (SEER) statistics for NHL cases aged 21–84 and diagnosed in Connecticut from 1996 to 2000, the 5-year survival rate is 59.0% and the 10-year survival rate is 46.4% [1].

Materials and methods

Study population

The study population has been described elsewhere [24,25]. In brief, a total of 1122 potential female NHL cases aged between 21 and 84 years were identified through the Yale Comprehensive Cancer Center's Rapid Case Ascertainment Shared Resource (RCA), a component of the Connecticut Tumor Registry (CTR), between 1996 and 2000. Among those cases, 167 women died before they could be interviewed, and 123 were excluded because of doctor refusal, previous diagnosis of cancer, or inability to speak English. Out of 832 eligible cases, 601 gave written consent and completed an in-person interview. Pathology slides or tissue blocks were obtained from the hospitals where the cases had been diagnosed. The specimens were reviewed by two independent study pathologists. All cases of NHL were classified according to the World Health Organization (WHO) classification system [26,27].

Vital status for these NHL cases was abstracted at the CTR in May–October 2008. Other follow-up information was also abstracted, including date of death, cause of death, most recent follow-up date, type and date of treatments, B-symptoms, and tumor stage. Of the 601 cases, 13 were not able to be identified in the CTR system, 13 were found to have a cancer history prior to diagnosis of NHL, and seven had diet information missing, yielding 568 patients with NHL in the final analyses. Of these, 180 had diffuse large B-cell lymphoma (DLBCL); 131 had follicular lymphoma (FL); 63 had chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL); 39 had marginal zone B-cell lymphoma (MZBL); and 42 had T/natural killer (NK)-cell lymphoma (T-cell).

The study was approved by the Human Investigation Committee at Yale University and the Connecticut Department of Public Health.

Exposure assessment

A standardized, structured questionnaire was used to obtain demographic information such as age, race, highest education level, height and weight, and major known or suspected risk factors for NHL through in-person interviews. A semi-quantitative food frequency questionnaire (FFQ) developed by the Fred Hutchinson Cancer Research Center (Seattle, Washington) was completed by each subject. With the understanding that this information is

highly correlated with diet in the more distant past [28], the subject was asked to characterize her usual diet 1 year before diagnosis.

The FFQ collects data on consumption frequency and portion size for approximately 120 foods, including 20 vegetables and 11 fruits (Table I). Besides overall vegetable intake, we individually analyzed bean vegetables, cruciferous vegetables, green leafy vegetables, red vegetables, and yellow vegetables. In addition to total fruit intake, we individually analyzed citrus fruits.

Statistical analysis

Intakes of vegetables and fruits were categorized as high or low levels according to the 2000 *Dietary guidelines for Americans* [29] (five servings of vegetables and fruits combined per day, three servings of vegetables per day, and two servings of fruit per day). Intakes of special vegetable or fruit types were categorized as high or low levels according to the 0.75 quantile of the study population. Survival analyses were done for both overall survival (OS) and lymphoma-specific survival. In OS analysis, deaths from any cause were events, and being alive was censoring; in lymphoma-specific survival analysis, deaths from NHL, Hodgkin lymphoma (HL), and lymphocytic leukemia were events, and otherwise were censorings.

Multivariate analysis was performed by Cox regression models, and the results are expressed as adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). Age (continuous), education (high school or less, some college, and college graduate or more), stage (I, II, III, IV, and unknown), B-symptom (yes, no/unknown), initial treatment (none, radiation only, chemotherapy-based regimen, and other), and total energy intake (continuous) were adjusted as *a priori* confounder variables. Adjustments of race, body mass index, smoking, and intake of protein, fat, carbohydrate, or meat did not result in material changes for the observed associations, and thus were not included in the final model. The assumption of proportionality of hazards (PH) for each covariate was assessed by plotting the log-cumulative hazards of the subgroups of the covariate under investigation versus log-time. The PH assumption was met for all covariates except age. We added a time-dependent variable for age; the time-dependent variable did not result in material changes for the observed associations and was not included in the final model. The goodness of fit for the whole model was assessed using the Cox–Snell residual test and proved to be adequate. Statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC).

Results

Overall, 13.2%, 43.8%, and 21.5% of the subjects with NHL followed the guidelines for vegetable, fruit, and combined fruit and vegetable intake, respectively. Demographic characteristics for 568 NHL cases are presented in Table II. A majority of these patients (60%) had stage I or II disease and 6% had B-symptoms. The most common initial therapy was a chemotherapy-based regimen (52%), followed by observation (35%), and radiation only (12%). During the follow-up period, 250 patients died (148 from lymphoma and 102 from other causes). Median follow-up time was 3.58 years for the deceased and 9.07 years for the survivors. Mean follow-up time was 4.06 years (SD = 2.73, range: 0.33–11.01) for the deceased and 8.98 years (SD = 1.56, range: 1.32–11.79) for the survivors.

Table III presents adjusted HRs for risk of death among patients with NHL according to NHL subtype. After adjustment for demographic and clinical prognostic factors, high intakes of vegetables and fruits, vegetables, green leafy vegetables, and citrus fruits gave 27–42% lower risks of death in patients with NHL overall compared to low-intake groups.

In subtype analyses, high intakes of vegetables and fruits combined and citrus fruits were associated with 45% and 60% reduced risk of death for patients with DLBCL, respectively. Patients with FL who had high intakes of vegetables and green leafy vegetables experienced a 73% reduced risk of death. Patients with CLL/SLL with a high intake of vegetables and fruits combined had a 3.13-fold increased risk of death. Despite the small number of cases, favorable effects of high intakes of cruciferous vegetables and green leafy vegetables were observed in patients with T-cell lymphoma. Comparable results were found in the analyses for risk of death from lymphoma (Table IV), except that we were not able to detect the associations for MZBL and T-cell lymphoma given the small number of deaths from lymphoma among these two subtypes.

Discussion

Our study offers the first analysis of the impact of pre-diagnostic diet on survival for NHL and NHL histological subtypes. In this follow-up study, we found that a pre-diagnostic high intake of vegetables and citrus fruits appeared to prolong the survival of patients with NHL. No beneficial impact was found for total fruit intake, and this could be because the same amount of fruit generally contains less fiber, minerals, and vitamins and more sugar and calories compared with vegetables. When different types of vegetables and fruits were investigated separately, their impacts were found to vary in NHL subtypes: a high intake of citrus fruits favored DLBCL survival; a high intake of green leafy vegetables favored FL survival; and a high intake of cruciferous vegetables and green leafy vegetables favored T-cell lymphoma survival. Our results suggest that dietary habits can be important in the mechanisms of tumor progression.

Vegetables and fruits contain proportionally fewer calories and ample nutrients, including vitamins and minerals, dietary fiber, and many other phytochemicals that have demonstrated anticarcinogenic activity in laboratory settings. Individually, or more likely in combination with one another, these nutrients may hinder tumor initiation and promotion through antioxidant activity, modulation of detoxification enzymes, and stimulation of the immune system [30]. Extensive epidemiological studies have shown a relationship between a high intake of vegetables and/ or fruits and reduced risk of cancer development, including NHL [8–14]. When different types of vegetables and fruits were investigated separately, cruciferous vegetables, green leafy vegetables, and red vegetables reduced NHL risks, especially among women [9,10,12].

It is hypothesized that a healthy diet is important not only in influencing the development of cancer, but also in cancer prognosis [31]. Previous studies have provided evidence supporting this hypothesis in different types of cancer survivors [15–22], especially breast cancer survivors [15–18]. Our study provides the first evidence for patients with NHL. Although the mechanisms underlying the relationship between vegetable and fruit intake and NHL survival are currently unclear, it is possible that vegetables' and fruits' biological effects of antioxidant activity, modulation of detoxification enzymes, and stimulation of the immune system may play a role not only in tumor initiation and promotion but also in hindering tumor progression. It is also possible that high vegetable and fruit intake could reduce the risk of co-morbidities such as cardiovascular disease (CVD) [32–34], to which cancer survivors are especially prone [31]. There was no information on co-morbidity available for our study population. However, efforts were made by looking at the cause of death. Of the deaths, 11.3% (14 out of 124) in the high vegetable and fruit intake group were due to CVD, compared with 11.9% of deaths (15 out of 126) in the low-intake group.

In order to investigate the generalizability of the study results, we compared the observed survival curve with that of 13 899 female patients with NHL aged 21–84 diagnosed during

1996–2000 at 17 SEER registries [35]. The two survival curves were parallel throughout the follow-up period except for the first half-year, during which 15.8% SEER patients died, while only 0.7% of patients in the Connecticut study died. Considering that 167 out of 1122 (14.9%) identified cases were not able to be enrolled in the Connecticut study because they died before interview [23], the survival of our case series is comparable to the survival observed by SEER, conditioned on surviving 6 months after diagnosis. Our results might not apply to the most aggressive NHL cases with short-term survival, since there were few cases in our study who died within a half-year. Whereas rituximab has become standard care for patients with DLBCL and is widely used for patients with FL, our cases were enrolled from 1996 to 2000 in the pre-rituximab era. Future studies with more recently enrolled NHL patients would be needed to investigate whether the associations we observed still hold in the contemporary environment.

Compared to most published clinical reports on NHL survival, our study has a larger sample size, which provided power to detect differences among NHL subtypes, especially for the two most common subtypes: DLBCL and FL. Another strength of our study is utilizing the CTR to abstract follow-up information. Through the CTR, we were able to obtain information on tumor stage, B-symptoms, and initial treatment; by adjusting them as *a priori* confounders in our analysis, we were able to detect the independent effect of vegetable and fruit intake on NHL prognosis and survival. However, the CTR does not have detailed treatment information on the specific regimen of chemotherapy, and follow-up treatment information might be incomplete, which may introduce residual confounding to the results.

Prior knowledge of the high correlation between food frequency questionnaires regarding diet 1 year before diagnosis and food intake in the distant past helped to minimize the possibility of information bias due to nutritional modification during the lead time. However, our patients were interviewed only at entrance to the study, and some subjects may have changed their dietary habits during follow-up. If some change did occur, it is more likely that it was toward increasing vegetable and fruit intake because of raised health awareness, leading to underestimation of exposure. We speculate that a person acquires dietary habits over long periods of his/her life span, and it is usually not easy to change at an older age. In fact, a 10-year follow-up study of a group of women in New York at midlife and older showed that most women had a consistent orientation to food and nutrition even in the face of expected and unexpected changes in health, social environment, and role [36]. Nevertheless, more evidence would be needed to confirm our speculation, and our observation reveals only the association between pre-diagnostic vegetable and fruit consumption and NHL survival. Further studies such as a well-designed randomized clinical trial would be needed to answer whether changing a patient's diet after diagnosis could actually improve prognosis.

Residual confounding by other nutritional and lifestyle factors may be present. With a limited sample size and multiple covariates, there is a possibility of false positives caused by multiple comparisons.

Only about a quarter of our study population reached the minimum vegetable and fruit intake level (five servings per day) recommended by the 2000 *Dietary guidelines for Americans* [29] and the *Healthy people 2010* target [37]. The new guidelines released in 2005 recommended twice the intake level [38]. Along with our findings that high intakes of vegetables and certain fruits might prolong the survival of patients with NHL, public health efforts should be made to promote the intake of vegetables and fruits in cancer patients.

In conclusion, this study shows that increased pre-diagnostic intake of vegetables may positively affect the prognosis and survival for patients with NHL surviving longer than 6

months. The analyses for different histological subtypes suggest that the effect of vegetable and fruit intake on prognosis and survival might be different among NHL subtypes. Our study raises the hypothesis that eating more vegetables and citrus fruits could be useful in improving prognosis and survival in patients with NHL.

Acknowledgments

Declaration of interest: This study is supported by Hull Argall & Anna Grant 22067A from the Yale Cancer Center, by grant CA62006 from the National Cancer Institute (NCI), and by Fogarty training grants 1D43TW008323-01 and 1D43TW007864-01 from the National Institutes of Health (NIH). This publication was made possible by CTSA Grant number UL1 RR024139 from the National Center for Research Resources (NCRR), a component of the NIH and NHL Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR. This research was approved by the DPH HIC. Certain data used in this study were obtained from the Connecticut Department of Public Health. The authors assume full responsibility for analyses and interpretation of these data.

References

1. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence -SEER 17 Regs Limited-Use + Hurricane Katrina Impacted Louisiana Cases, Nov 2007 Sub (1973–2005 varying) - Linked To County Attributes - Total U.S., 1969–2005 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008, based on November 2007 submission.
2. Muller AM, Ihorst G, Mertelsmann R, Engelhardt M. Epidemiology of non-Hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology. *Ann Hematol.* 2005; 84:1–12. [PubMed: 15480663]
3. Clarke, C.; O'Malley, C. Non-Hodgkin lymphoma. In: Ries, LAG.; Yong, JL.; Keel, GE.; Eisner, MP.; Lin, YD.; Horner, M-JD., editors. *Cancer survival among adults: US SEER Program, 1988–2001, patient and tumor characteristics.* Bethesda, MD: National Cancer Institutes, SEER Program, NIH; 2007. p. 235-242.
4. Horner, MJ.; Ries, LAG.; Krapcho, M., et al., editors. *SEER Cancer Statistics Review, 1975–2006.* National Cancer Institute; Bethesda, MD: http://seer.cancer.gov/csr/1975_2006/, based on November 2008 SEER data submission, posted to SEER website 2009
5. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. *N Engl J Med.* 1993; 329:987–994. [PubMed: 8141877]
6. Bray C, Morrison DS, McKay P. Socio-economic deprivation and survival of non-Hodgkin lymphoma in Scotland. *Leuk Lymphoma.* 2008; 49:917–923. [PubMed: 18464111]
7. Roswall N, Olsen A, Christensen J, Rugbjerg K, Mellekjaer L. Social inequality and incidence of and survival from Hodgkin lymphoma, non-Hodgkin lymphoma and leukaemia in a population-based study in Denmark, 1994–2003. *Eur J Cancer.* 2008; 44:2058–2073. [PubMed: 18657412]
8. Chiu BC, Cerhan JR, Folsom AR, et al. Diet and risk of non-Hodgkin lymphoma in older women. *JAMA.* 1996; 275:1315–1321. [PubMed: 8614116]
9. Kelemen LE, Cerhan JR, Lim U, et al. Vegetables, fruit, and antioxidant-related nutrients and risk of non-Hodgkin lymphoma: a National Cancer Institute-Surveillance, Epidemiology, and End Results population-based case-control study. *Am J Clin Nutr.* 2006; 83:1401–1410. [PubMed: 16762953]
10. Zhang SM, Hunter DJ, Rosner BA, et al. Intakes of fruits, vegetables, and related nutrients and the risk of non-Hodgkin's lymphoma among women. *Cancer Epidemiol Biomarkers Prev.* 2000; 9:477–485. [PubMed: 10815692]
11. Zheng T, Holford TR, Leaderer B, et al. Diet and nutrient intakes and risk of non-Hodgkin's lymphoma in Connecticut women. *Am J Epidemiol.* 2004; 159:454–466. [PubMed: 14977641]
12. Chang ET, Smedby KE, Zhang SM, et al. Dietary factors and risk of non-Hodgkin lymphoma in men and women. *Cancer Epidemiol Biomarkers Prev.* 2005; 14:512–520. [PubMed: 15734980]
13. Talamini R, Polesel J, Montella M, et al. Food groups and risk of non-Hodgkin lymphoma: a multicenter, case-control study in Italy. *Int J Cancer.* 2006; 118:2871–2876. [PubMed: 16385566]

14. Ward MH, Zahm SH, Weisenburger DD, et al. Dietary factors and non-Hodgkin's lymphoma in Nebraska (United States). *Cancer Causes Control*. 1994; 5:422–432. [PubMed: 7999964]
15. Kwan ML, Weltzien E, Kushi LH, Castillo A, Slattery ML, Caan BJ. Dietary patterns and breast cancer recurrence and survival among women with early-stage breast cancer. *J Clin Oncol*. 2009; 27:919–926. [PubMed: 19114692]
16. Kroenke CH, Fung TT, Hu FB, Holmes MD. Dietary patterns and survival after breast cancer diagnosis. *J Clin Oncol*. 2005; 23:9295–9303. [PubMed: 16361628]
17. Pierce JP, Stefanick ML, Flatt SW, et al. Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. *J Clin Oncol*. 2007; 25:2345–2351. [PubMed: 17557947]
18. Rock CL, Demark-Wahnefried W. Nutrition and survival after the diagnosis of breast cancer: a review of the evidence. *J Clin Oncol*. 2002; 20:3302–3316. [PubMed: 12149305]
19. Goodman MT, Kolonel LN, Wilkens LR, Yoshizawa CN, Le Marchand L, Hankin JH. Dietary factors in lung cancer prognosis. *Eur J Cancer*. 1992; 28:495–501. [PubMed: 1591072]
20. Palli D, Russo A, Saieva C, Salvini S, Amorosi A, Decarli A. Dietary and familial determinants of 10-year survival among patients with gastric carcinoma. *Cancer*. 2000; 89:1205–1213. [PubMed: 11002214]
21. Crosignani P, Russo A, Tagliabue G, Berrino F. Tobacco and diet as determinants of survival in male laryngeal cancer patients. *Int J Cancer*. 1996; 65:308–313. [PubMed: 8575849]
22. Sandoval M, Font R, Manos M, et al. The role of vegetable and fruit consumption and other habits on survival following the diagnosis of oral cancer: a prospective study in Spain. *Int J Oral Maxillofac Surg*. 2009; 38:31–39. [PubMed: 18951763]
23. Morton LM, Holford TR, Leaderer B, et al. Cigarette smoking and risk of non-Hodgkin lymphoma subtypes among women. *Br J Cancer*. 2003; 89:2087–2092. [PubMed: 14647142]
24. Zhang Y, Holford TR, Leaderer B, et al. Hair-coloring product use and risk of non-Hodgkin's lymphoma: a population-based case-control study in Connecticut. *Am J Epidemiol*. 2004; 159:148–154. [PubMed: 14718216]
25. Morton LM, Holford TR, Leaderer B, et al. Alcohol use and risk of non-Hodgkin's lymphoma among Connecticut women (United States). *Cancer Causes Control*. 2003; 14:687–694. [PubMed: 14575367]
26. A clinical evaluation of the International Lymphoma Study Group classification of non-Hodgkin's lymphoma. The Non-Hodgkin's Lymphoma Classification Project. *Blood*. 1997; 89:3909–3918. [PubMed: 9166827]
27. Harris NL, Jaffe ES, Diebold J, et al. World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting-Airlie House, Virginia, November 1997. *J Clin Oncol*. 1999; 17:3835–3849. [PubMed: 10577857]
28. Willett, WC. *Nutritional epidemiology*. New York, NY: Oxford University Press; 1998.
29. United States Department of Agriculture & United States Department of Health and Human Services. *Dietary guidelines for Americans, 2000*. 5. Washington, DC: US Government Printing Office; 2000.
30. Lampe JW. Health effects of vegetables and fruit: assessing mechanisms of action in human experimental studies. *Am J Clin Nutr*. 1999; 70:475S–490S. [PubMed: 10479220]
31. Demark-Wahnefried W, Rock CL, Patrick K, Byers T. Lifestyle interventions to reduce cancer risk and improve outcomes. *Am Fam Physician*. 2008; 77:1573–1578. [PubMed: 18581838]
32. Retelny VS, Neuendorf A, Roth JL. Nutrition protocols for the prevention of cardiovascular disease. *Nutr Clin Pract*. 2008; 23:468–476. [PubMed: 18849551]
33. Fuchs SC, Moreira LB, Camey SA, Moreira MB, Fuchs FD. Clustering of risk factors for cardiovascular disease among women in Southern Brazil: a population-based study. *Cad Saude Publica*. 2008; 24(Suppl 2):S285–S293. [PubMed: 18670708]
34. Nikolic M, Nikic D, Petrovic B. Fruit and vegetable intake and the risk for developing coronary heart disease. *Cent Eur J Public Health*. 2008; 16:17–20. [PubMed: 18459474]
35. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence -SEER 17 Regs Limited-Use, Nov 2006 Sub (1973–2004 varying) - Linked

To County Attributes - Total U.S., 1969–2004 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2007, based on November 2006 submission.

36. Edstrom KM, Devine CM. Consistency in women's orientations to food and nutrition in midlife and older age: a 10-year qualitative follow-up. *J Nutr Educ.* 2001; 33:215–223. [PubMed: 11953243]
37. US Department of Health and Human Services. *Healthy people 2010: understanding and improving health.* 2. Washington, DC: US Government Printing Office; 2010.
38. United States Department of Agriculture & United States Department of Health and Human Services. *Dietary guidelines for Americans, 2005.* 6. Washington, DC: US Government Printing Office; 2005.

Table I

Vegetables and fruits in food frequency questionnaire and cut-offs for low/high intake group.

Category of food	Composition of food category	Cut-off of low-/high-intake groups (servings per day)*
Vegetables and fruits	Vegetables; fruits	5
Vegetables	Bean vegetables; cruciferous vegetables; green leafy vegetables; red vegetables; yellow vegetables; avocado or guacamole; corn; summer squash such as zucchini; onions, leeks, including in cooking; mixed lettuce salad with vegetables, such as carrots, red vegetables, etc; other potatoes (boiled, baked, mashed)	3
Fruits	Apples, pears; bananas; peaches, nectarines or plums; cantaloupes; other melon, watermelon, honeydew, etc.; apricots; other dried fruit, raisins, prunes, etc.; strawberries; any other fruit (fruit cocktail, berries, apple-sauce, grapes, pineapple, etc.); citrus fruits	2
Bean vegetables	String beans, green beans; peas; beans, such as baked beans, pinto, kidney, lima beans, lentils	0.3
Cruciferous vegetables	Broccoli; coleslaw; cabbage, sauerkraut, brussels sprouts; cauliflower	0.2
Green leafy vegetables	Cooked greens (spinach, mustard greens, turnip greens, collards, etc.); lettuce, plain lettuce salad	0.3
Red vegetables	Tomatoes, fresh or juice; tomatoes cooked, tomato sauce, salsa	0.3
Yellow vegetables	Carrots, including in mixed dishes; winter squash, such as acorn, butternut; sweet potatoes, yams	0.3
Citrus fruits	Oranges, grapefruit or tangerines; orange juice, grapefruit juice, or vitamin C-enriched fruit drinks	1.1

* Cut-offs for vegetables and fruits combined, vegetables, and fruits are from *Dietary guidelines for Americans, 2000* [29]; cut-offs for other vegetable and fruit groups are the 0.75 quantiles of the study population.

Table II

Selected demographic characteristics of NHL cases, Connecticut, 1996–2000.

Characteristic	Number	Percentage
Age at diagnosis (years)		
≤45	68	12.0
46–55	110	19.4
56–65	119	20.9
66–75	164	28.9
≥76	107	18.8
Race		
White	538	94.7
Black	18	3.2
Other	12	2.1
Education		
High school or less	244	43.0
Some college	187	32.9
College graduate or more	137	24.1
Family history		
None	121	21.3
Any other cancer	439	77.3
NHL	8	1.4
BMI (kg/m ²)		
<25	281	49.5
25–29.99	179	31.5
≥30	108	19.0

NHL, non-Hodgkin lymphoma; BMI, body mass index.

Table III

Adjusted hazard ratios for risk of death from any cause associated with vegetable and fruit intake among NHL patients by subtype.

Intake	NHL overall	Number of deaths/total patients and hazard ratio* (95% CI)							T-cell			
		DLBCL	FL	CLL/SLL	MZBL							
Vegetables and fruits												
Low	204/446	1	36/99	1	25/51	1	14/35	1	15/31	1		
High	46/122	0.68 (0.49–0.95)	16/41	0.55 (0.31–0.99)	11/32	0.63 (0.30–1.31)	8/12	3.13 (1.22–8.06)	0/4	—	0/11	—
Vegetables												
Low	224/493	1	43/110	1	29/55	1	13/37	1	15/37	1		
High	26/75	0.58 (0.38–0.89)	10/23	0.74 (0.35–1.55)	4/21	0.27 (0.09–0.80)	4/8	1.98 (0.57–6.84)	1/2	2.77 (0.16–48.46)	0/5	—
Fruits												
Low	135/319	1	47/101	1	22/73	1	17/37	1	10/28	1	9/21	1
High	115/249	0.91 (0.70–1.18)	37/79	0.78 (0.49–1.24)	25/58	1.00 (0.52–1.89)	16/26	2.18 (0.99–4.82)	4/11	1.08 (0.28–4.16)	6/21	0.41 (0.05–3.43)
Bean vegetables												
Low	188/425	1	62/136	1	36/95	1	28/53	1	11/32	1	12/29	1
High	62/141	1.14 (0.85–1.54)	22/43	1.50 (0.88–2.56)	11/35	0.83 (0.38–1.79)	5/10	1.37 (0.47–4.01)	3/7	2.17 (0.36–12.96)	3/13	0.38 (0.04–3.84)
Cruciferous vegetables												
Low	186/416	1	63/131	1	32/95	1	23/45	1	13/36	1	14/31	1
High	59/138	0.91 (0.67–1.24)	20/46	0.83 (0.49–1.41)	13/30	1.27 (0.59–2.73)	10/17	1.58 (0.66–3.76)	1/3	0.80 (0.05–14.10)	1/10	50.01 (50.01–0.90)
Green leafy vegetables												
Low	176/388	1	57/118	1	38/92	1	25/48	1	11/27	1	12/31	1
High	49/129	0.71 (0.51–0.98)	19/42	0.78 (0.45–1.36)	5/28	0.27 (0.10–0.76)	5/12	1.64 (0.43–6.31)	1/8	0.15 (0.01–1.99)	2/9	0.12 (0.01–0.92)
Red vegetables												
Low	185/419	1	55/126	1	37/97	1	27/49	1	11/30	1	12/30	1
High	60/139	1.03 (0.76–1.38)	24/48	1.16 (0.68–1.95)	10/33	0.70 (0.34–1.45)	6/14	1.46 (0.44–4.85)	3/9	3.99 (0.62–25.84)	3/10	0.49 (0.07–3.69)
Yellow vegetables												
Low	181/416	1	57/129	1	36/97	1	28/49	1	11/33	1	12/31	1
High	63/138	0.93 (0.69–1.25)	26/49	0.98 (0.59–1.64)	10/31	0.76 (0.35–1.62)	5/12	0.67 (0.21–2.13)	2/4	7.07 (0.49–102.98)	2/10	0.17 (0.02–1.34)
Citrus fruits												
Low	182/402	1	66/126	1	31/90	1	23/49	1	9/30	1	11/29	1
High	55/134	0.73 (0.54–0.99)	15/47	0.40 (0.22–0.72)	15/31	1.30 (0.65–2.58)	9/13	2.02 (0.83–4.92)	3/6	2.20 (0.42–11.47)	1/8	0.09 (50.01–26.48)

* Models were adjusted for age (continuous), education (high school or less, some college, and college graduate or more), stage (I, II, III, IV, and unknown), B-symptom (yes, no/unknown), initial treatment (none, radiation only, chemotherapy-based regimen, other), and total energy intake (continuous).

NHL, non-Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma; MZBL, marginal zone B-cell lymphoma; T-cell, T/NK-cell lymphoma.

Table IV

Adjusted hazard ratios for risk of death from lymphoma associated with vegetable and fruit intake among patients with NHL by subtype.

Intake	Number of lymphoma-specific deaths/total patients and hazard ratio* (95% CI)							
	NHL overall	DLBCL	FL	CLL/SLL				
Vegetables and fruits								
Low	123/446	1	41/139	1	22/99	1	14/51	1
High	25/122	0.70 (0.45–1.10)	10/41	0.63 (0.30–1.33)	6/32	0.66 (0.25–1.71)	3/12	3.20 (0.66–15.45)
Vegetables								
Low	134/493	1	44/157	1	27/110	1	16/55	1
High	14/75	0.58 (0.33–1.03)	7/23	0.95 (0.39–2.33)	1/21	0.10 (0.01–0.78)	1/8	0.46 (0.04–5.45)
Fruits								
Low	79/319	1	26/101	1	13/73	1	8/37	1
High	69/249	1.04 (0.74–1.45)	25/79	0.94 (0.51–1.71)	15/58	1.10 (0.49–2.45)	9/26	4.28 (1.26–14.58)
Bean vegetables								
Low	113/425	1	38/136	1	23/95	1	14/53	1
High	35/141	1.05 (0.71–1.55)	13/43	1.52 (0.76–3.03)	5/35	0.42 (0.14–1.31)	3/10	1.97 (0.43–9.06)
Cruciferous vegetables								
Low	115/416	1	40/131	1	22/95	1	11/45	1
High	30/138	0.75 (0.49–1.14)	11/46	0.76 (0.37–1.54)	4/30	0.39 (0.12–1.24)	6/17	4.26 (0.83–21.82)
Green leafy vegetables								
Low	103/388	1	35/118	1	21/92	1	12/48	1
High	32/129	0.82 (0.54–1.23)	12/42	0.78 (0.39–1.57)	4/28	0.38 (0.11–1.26)	3/12	3.02 (0.50–18.15)
Red vegetables								
Low	107/419	1	32/126	1	22/97	1	13/49	1
High	38/139	1.11 (0.76–1.62)	16/48	1.38 (0.71–2.66)	6/33	0.65 (0.26–1.64)	4/14	1.08 (0.22–5.35)
Yellow vegetables								
Low	102/416	1	33/129	1	22/97	1	15/49	1
High	42/138	1.11 (0.77–1.61)	18/49	1.18 (0.63–2.22)	5/31	0.65 (0.23–1.84)	2/12	0.25 (0.03–2.43)
Citrus fruits								
Low	108/402	1	41/126	1	17/90	1	12/49	1
High	33/134	0.81 (0.54–1.20)	9/47	0.36 (0.16–0.80)	10/31	1.81 (0.76–4.31)	5/13	2.48 (0.70–8.82)

* Models were adjusted for age (continuous), education (high school or less, some college, and college graduate or more), stage (I, II, III, IV, and unknown), B-symptom (yes, no/unknown), initial treatment (none, radiation only, chemotherapy-based regimen, other), and total energy intake (continuous).

NHL, non-Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma.