HHS Public Access

Author manuscript

Cancer Epidemiol. Author manuscript; available in PMC 2018 August 10.

Published in final edited form as:

Cancer Epidemiol. 2012 February ; 36(1): 52–59. doi:10.1016/j.canep.2011.05.014.

Anthropometric factors, physical activity, and risk of Non-Hodgkin's lymphoma in the Women's Health Initiative

Geoffrey C. Kabat[a,*], **Mimi Y. Kim**[a], **Jean-Wactawski-Wende**[b], **Jennifer W. Bea**[c], **Kerstin L. Edlefsen**[d], **Lucile L. Adams-Campbell**[e], **Anneclaire J. De Roos**[f], and **Thomas E. Rohan**[a]

[a]Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA

[b]Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo, Buffalo, NY, USA

[c]Department of Medicine, Arizona Cancer Center, Tucson, AZ, USA

[d]Department of Laboratory Medicine, University of Washington, Seattle, WA, USA

[e]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA

[f]Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Abstract

Background—Incidence rates of non-Hodgkin's lymphoma (NHL) increased substantially in the United States and worldwide during the latter part of the 20th century, but little is known about its etiology. Obesity is associated with impaired immune function through which it may influence the risk of NHL; other factors reflecting energy homeostasis (height, abdominal adiposity, and physical activity) may also be involved.

Methods—We examined the association of anthropometric factors and physical activity with risk of NHL and its major subtypes in a large cohort of women aged 50–79 years old who were enrolled at 40 clinical centers in the United States between 1993 and 1998. Over a mean follow-up period of 11 years, 1123 cases of NHL were identified among 158,975 women. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI).

Results—Height at baseline was positively associated with risk of all NHL and with that of diffuse large B-cell lymphoma ($HRs_{q4vs.q1}$ 1.19, 95% CI 1.00–1.43 and 1.43, 95% CI 1.01–2.03, respectively). Measures of obesity and abdominal adiposity at baseline were not associated with risk. Hazard ratios for NHL were increased for women in the highest quartile of weight and body mass index at age 18 ($HRs_{q4vs.q1}$ 1.29, 95% CI 1.01–1.65 and 1.27, 95% CI 1.01–1.59, respectively). Some measures of recreational physical activity were modestly associated with increased risk of NHL overall, but there were no clear associations with specific subtypes.

[*]Corresponding author. Tel.: +1 718 430 3038; fax: +1 718 430 8653.

Conflict of interest

None of the authors has any conflict-of-interest.

Conclusion—Our findings regarding anthropometric measures are consistent with those of several previous reports, suggesting that early life influences on growth and immune function may influence the risk of NHL later in life.

Keywords

Non-Hodgkin's lymphoma; Body mass index; Weight; Height; Waist circumference; Hip circumference; Physical activity; Metabolic equivalent tasks; Postmenopausal women

1. Introduction

Non-Hodgkin's lymphoma (NHL) comprises a clinically heterogeneous group of cancers derived from lymphocytes and is estimated to account for 4.5% of total cancer incidence and 3.5% of total cancer mortality in the U.S. [1]. Incidence and mortality rates of NHL increased dramatically in both sexes in the U.S. and worldwide during the latter half of the 20th century [2,3], but started to level off or decline in the past decade in developed countries [4]. While some of the increase may be due to improved diagnostic procedures and changes in classification, it is unlikely that these advances can largely, or totally, account for the increased rates observed in the U.S. and European countries in earlier decades [2–4].

Known risk factors for NHL account for only a small proportion of NHL incidence, with the most important being a compromised immune system [2,5,6]. Other factors include a family history of NHL and exposure to specific infectious organisms, including human T-cell leukemia/lymphoma virus, human immunodeficiency virus, human herpes virus 8, and Epstein-Barr virus, which have been directly implicated in the development of some lymphoma subtypes [2,5,6]. During the past few decades the prevalence of obesity has increased in the developed world as result of a variety of factors, including increased physical inactivity and increased consumption of high-fat, calorie-dense foods. In this regard, it has been suggested that the obesity epidemic may be a contributing factor to the rising incidence of NHL [7]. Obesity and other anthropometric factors may influence the development of NHL through a variety of mechanisms, including hyperinsulinemia resulting from insulin resistance, and chronic inflammation [8–10]. However, findings of studies that have examined the association of body mass index with NHL are inconsistent [10–40], and few studies have addressed the roles of central adiposity, height, and physical activity in older women, or weight in early adulthood.

We therefore evaluated these associations in the Women's Health Initiative, a large cohort of postmenopausal women with information obtained at baseline on measured height, weight, waist circumference, and hip circumference, as well as self-reported information on recreational physical activity and weight earlier in life.

2. Methods

The Women's Health Initiative (WHI) is a large, multi-center, multi-faceted study designed to advance understanding of the determinants of major chronic diseases in women. It is composed of a Clinical Trial component (CT) and an Observational Study component (OS) [41]. Women between the ages of 50 and 79 and representing major racial/ethnic groups

were recruited from the general population at 40 clinical centers throughout the United States between 1993 and 1998. Details of the design and reliability of the baseline measures have been published [41,42].

2.1. Data collection and variable definition

At study entry, self-administered questionnaires were used to collect information on demographics, medical, reproductive and family history, and on dietary and lifestyle factors, including smoking history, alcohol consumption, and recreational physical activity. All participants had their weight, height, and waist and hip circumferences measured by trained staff at baseline. In addition, women in the OS were asked about their weight and height at ages 18, 35, and 50. Questions about physical activity at baseline referred to a woman's usual pattern of activity, including walking and sports. First, women were asked to report how often they walked outside the home for 10 min or more without stopping ("rarely or never," "1–3 times each month," "1 time each week," "2–3 times each week," "4–6 times each week," "7 or more times each week"), duration (<20 min, 20–39 min, 40–59 min, 1 h or more), and their usual speed (casual strolling, average or normal, fairly fast, very fast, do not know). Next women were asked how often they engaged in strenuous or very hard exercise (during which they worked up a sweat and increased their heart rate). Examples of strenuous exercise provided were: aerobics, aerobic dancing, jogging, tennis, and swimming laps. Women were also asked how often they engaged in moderate exercise (examples provided were: biking outdoors, using an exercise machine like a stationary bike or treadmill, calisthenics, easy swimming, and dancing) and mild exercise (examples provided were: slow dancing, bowling, and golf). For each of the 3 levels of exercise, respondents were instructed to report the frequency (none, 1, 2, 3, 4, or 5 or more days per week) and how long they usually exercised at this level at one time (less than 20 min, 20–39 min, 40–59 min, or 1 h or more). Finally, they were asked whether they engaged in strenuous exercise at least 3 times a week at ages 18, 35, and 50 years old.

Several composite variables were computed to summarize recreational physical activity [43]. The midpoint value for the intervals of frequency and duration were used to multiply frequency *X* min (and divided by 60) to obtain "hours of exercise per week," separately for strenuous, moderate, and mild exercise. In addition, metabolic equivalent (MET) values for strenuous, moderate, and light exercise were assigned: 7, 4, and 3 METs, respectively [43]. For mean walking speeds "average" [2–3 mph], "fast" [3–4 mph], and "very fast" [>4 mph] the corresponding MET values were 3, 4, and 4.5, respectively. A variable "current total leisure-time physical activity" (MET-hours/week) was computed by multiplying the number of hours per week of leisure-time physical activity by the MET level of the activity and summing the products of all types of activities [44].

We also extracted information on illnesses linked to immune suppression and/or inflammation (rheumatoid arthritis, ulcerative colitis, lupus, diabetes, and multiple sclerosis) and use of medications associated with immunosuppression/inflammation (corticosteroid, NSAIDs, aspirin, insulin, anti-inflammatory agents, and statins).

Clinical outcomes (including cancer diagnoses) were updated semi-annually in the CT and annually in the OS by mailed or telephone questionnaires. Self-reports of non-Hodgkin's

lymphoma were verified by centralized review of medical records and pathology reports [45]. As of August 14, 2009, a total of 1154 incident cases of NHL (including chronic lymphocytic leukemia and small lymphocytic lymphoma) had been diagnosed among the 160,654 participants in the OS and CT after a median of 11.0 years of follow-up. The proportion of the cohort that was lost to follow-up was less than 1%.

For the analyses reported here, we excluded women who reported a history of lymphoma or leukemia at recruitment ($N = 391$), women with missing or extreme values for baseline body mass index (<15 kg/m^2 and >50 kg/m^2, $N = 2261$), and women who were missing MET-h/wk ($N = 181$), leaving 1123 cases and 157,852 non-cases for analysis.

An earlier analysis of intentional weight loss and NHL in the WHI OS by De Roos et al. [40] reported on body mass index at earlier ages and at baseline (but not height) in relation to NHL. That analysis was based on 412 cases of NHL identified over 9.9 years of follow-up of the OS cohort. By including both the OS and the CT with an average follow-up of 11 years, the present analysis is based on 1123 cases, providing a substantial increase in power.

2.2. Statistical analysis

Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CI) for the associations of anthropometric variables and physical activity with risk of all NHL ($N = 1123$) and of the major subtypes; the latter included diffuse large B-cell lymphoma (DLBCL: ICD-O-3 codes 9678–9680 and 9684, $N = 302$); follicular lymphoma (ICD-O-3 codes 9690–9698 ($N = 214$); and chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL: ICD-O-3 codes 9823 and 9670, $N = 298$). The remaining 309 cases were a heterogeneous group and were not analyzed as a separate group. We created quartiles of the following variables based on their distribution in the entire cohort: height, weight, waist circumference, hip circumference, waist-to-hip ratio, body mass index, self-reported BMI at ages 18, 35, and 50, and MET-h/wk of total recreational physical activity. In order permit comparison with the results of other studies, we present the baseline BMI results according to the WHO classification: <25, 25–<30, 30–<35, ≥35. To assess confounding, age-adjusted and multivariable-adjusted results were compared. We selected variables for inclusion in the multivariable models based on whether their inclusion altered the parameter estimate for the exposure of interest by >10%. The following covariates were included in the final multivariable models: age (continuous), alcohol intake (servings per week –continuous), pack-years of smoking (0, >0–<20, 20–<40, ≥40), caloric intake (kcal/day–continuous), education (less than high school graduate, high school graduate/some college, college graduate, post-college), race/ethnicity (non-Hispanic white, black, other), and enrollment in the OS/treatment arm assignment in the each of the 3 clinical trials (hormone therapy, calcium plus vitamin D, and dietary modification). To assess the effects of individual anthropometric factors, we examined each one both with and without other pertinent anthropometric factors in the model. In most cases, the estimates from the two models did not differ. We present estimates for the effect of height, adjusted for weight and physical activity, for BMI adjusted for physical activity, and for other anthropometric measures (weight, waist circumference, hip circumference, waist-hip-ratio)

adjusted for height and physical activity. In alternative models, anthropometric variables and physical activity-related variables were entered as continuous variables.

We also carried out four sensitivity analyses: 1) excluding cases of NHL diagnosed within the first 3 years of follow-up; 2) excluding women who reported any cancer diagnosis prior to enrollment to rule out an effect of pre-existing disease on anthropometric factors and physical activity; 3) excluding women with a history of conditions linked to immune suppression and/or inflammation; and 4) excluding women who at baseline were taking medications associated with immune suppression and/or inflammation.

The association of each anthropometric factor and physical activity with all NHL was examined within strata of age (<65, ≥65), ethnicity (white, black, other), and caloric intake (<1626 kcal/day, ≥1626 kcal/day) in order to detect possible effect modification. Formal tests for interaction were performed by comparing models with and without the product terms representing the variables of interest with a likelihood ratio test.

For categorical variables, tests for trend were performed by assigning the median value to each category and modeling this variable as a continuous variable. All *P*-values are two-sided.

3. Results

Compared to controls, cases were older, had slightly greater levels of physical activity, parity, and caloric intake, an older age at menopause, and were less likely to have used oral contraceptives, and were more likely to be White (Table 1). Cases and controls were generally similar in terms of other variables, including anthropometric factors (based on mean values).

Height at baseline was positively associated with risk of all NHL and with DLBCL ($HRs_{q4vs.q1}$ 1.19, 95% CI 1.00–1.43 and 1.43, 95% CI 1.01–2.03, respectively), and showed a borderline positive association with CLL/SLL ($HR_{q4vs.q1}$ 1.37, 95% CI 0.96–1.94) (Table 2). When the second quartile of height was taken as the reference group, the associations were: $HRs_{q4vs.q2}$ 1.32, 95% CI 1.11–1.58; 1.39, 95% CI 0.99–1.94; and 1.31, 95% CI 0.94–1.84, respectively. Measures of obesity and abdominal adiposity at baseline, including baseline weight, body mass index, hip circumference, waist circumference, and waist-to-hip ratio were not associated with risk.

Height at age 18 was associated with increased risk of DLBCL ($HR_{q4vs.q1}$ 1.81, 95% CI 1.10–2.98) but not with risk of all NHL or of other subtypes (Table 3). Hazard ratios for NHL were increased for women in the highest quartile of weight and body mass index at age 18 ($HRs_{q4vs.q1}$ 1.29, 95% CI 1.01–1.65 and 1.27, 95% CI 1.01–1.59, respectively). However, none of these associations was statistically significant, when the second quartile was used as the reference group.

Total recreational physical activity (MET-h/wk) and hours of moderate or strenuous recreational physical activity per week were associated with a borderline positive risk of NHL overall (HR for >17.5 MET-h/wk vs. <1.6: 1.17, 95% CI 0.98–1.39), but no specific

subtype showed a clear positive association (Table 4). Hours of strenuous activity per week, minutes of walking, and total hours of recreational physical activity were not associated with risk. Use of continuous variables gave very similar results. Having engaged in intense physical activity at ages 35 and 50, but not at age 18, was positively associated with risk of NHL: HR 1.18, 95% CI 1.04–1.33 and 1.14, 95% CI 1.01–1.29, but, again, there were no clear associations with specific subtypes.

When cases diagnosed during the first 3 years of follow-up ($N = 221$) were excluded from the analysis, the results for all variables examined were similar, although due the reduced sample size some of the HR estimates were more imprecise and no longer statistically significant. When women who reported any cancer prior to baseline were excluded from the analysis (103 cases; 14,100 non-cases), the results were essentially unchanged. Exclusion of women with illnesses and medications associated with immune suppression and/or inflammation did not materially affect the results.

In stratified analyses, baseline height showed positive associations with NHL only in women aged ≥65 and in women with relatively high caloric intake (data not shown). Height at age 18 was associated with NHL only in older women (i.e., those ≥65 years of age). However, the tests for interaction between height and age and caloric intake were not statistically significant. The associations of the other anthropometric factors and physical activity with NHL did not differ by levels of age, ethnicity, or caloric intake.

4. Discussion

In this large cohort of postmenopausal women, height measured at baseline showed modest positive associations with risk of NHL overall and of the DLBCL subtype, whereas self-reported height at age 18 was associated only with risk of DLBCL. In addition, self-reported weight and body mass index at age 18 showed modest positive associations with risk of NHL overall and of DLBCL. Baseline weight, BMI and markers of abdominal adiposity were not associated with risk of NHL or its major subtypes. Some measures of physical activity showed slight positive associations with risk of NHL overall; however, other measures were null and there were no clear associations with any subtypes. The association of anthropometric factors and physical activity with risk of NHL did not vary by levels of age, ethnicity, or caloric intake.

Studies that have examined anthropometric factors in relation to the risk of NHL have focused mostly on obesity, with somewhat conflicting findings [10–40]. Two recent meta-analyses [36,37] reported a positive association between body mass index and risk of non-Hodgkin's lymphoma: a meta-analysis of 10 cohort and 6 case–control studies [36] found that, compared to individuals of normal weight (BMI <25 kg/m^2), those who were overweight (BMI ≥25 and <30) had a relative risk for NHL of 1.07 (95% CI 1.01–1.14), whereas those who were obese (BMI ≥30) had a relative risk of NHL of 1.20 (95% CI 1.07–1.34); a second meta-analysis [37], restricted to cohort studies, reported a risk ratio of 1.06 (95% CI 1.03–1.09) per 5 kg/m^2 increase in BMI in men and 1.07 (95% CI 1.00–1.14) in women. In contrast, a pooled analysis of 18 case–control studies [38] containing over 10,000 NHL cases and 16,000 controls showed no association between obesity and risk of all NHL.

Findings concerning the association between obesity and specific NHL subtypes have been inconsistent, although one meta-analysis [36] and the pooled analysis [38] both noted a positive association of BMI with DLBCL.

Several recent studies have reported a positive association of BMI or weight at an early age with risk of NHL, and in some cases this association was stronger than that with BMI measured at enrollment, reflecting BMI at a later age [10,32–35]; whereas one study found no association between body mass index at age 18 and NHL [13]. Our finding of an association of weight and BMI at age 18 with risk of NHL and DLBCL is consistent with the results of those studies which found either an association only with body weight in early life or a stronger association with body weight in early adulthood compared to that with body weight later in life [10,32,33,35]. Taken together, these more recent studies suggest that body weight earlier in life may be more relevant to the development of NHL.

Consistent with our results, several previous studies have examined abdominal adiposity [10,13,19,29,31], with uniformly null results. No studies, however, have included measures of abdominal adiposity earlier in life.

Height has been reported to be a risk factor for NHL in most [10,23,29–35] but not all studies [13,19,21]. In a pooled analysis of 18 case–control studies from 13 countries [38] found that the tallest men had a slightly increased risk compared to those of midrange height but no association was seen in women. Of six studies (4 cohort and 2 case–control) which examined the association of height with specific subtypes, three observed a significant positive association with DLBCL [29,33,34], one found an association [23] with follicular lymphoma, and one reported an association with CLL/SLL [10]. Our finding of a positive association with DLBCL is consistent with those of three earlier cohort studies [29,33,34].

Physical activity has received less attention in relation to risk of NHL, with two case–control studies reporting an inverse association [20,23] and three cohort studies finding no association [10,13,29]. We found a borderline positive association of baseline total recreational physical activity, current moderate or strenuous physical activity, and intense physical activity at ages 35 and 50 with risk of NHL. However, other measures of physical activity (hours/week of strenuous physical activity, minutes of walking, total hours of recreational physical activity, and intense physical activity at age 18) showed no association. Furthermore, there were no clear associations with specific subtypes. Thus, our findings regarding the association of physical activity with risk of NHL are equivocal. The proportion of women who reported engaging in strenuous physical activity ≥2 h/wk in the WHI was small (only 10.4%).

We found no evidence that the associations of anthropometric factors and physical activity with risk of NHL were modified by age, ethnicity, or caloric intake. Few previous studies have examined effect modification [10,29,34].

The associations of anthropometric factors and physical activity with the risk of NHL may reflect roles of energy homeostasis and of growth during childhood and adolescence [47]. Both under- and over-nutrition can result in compromised immunity [8], and obesity has been associatedwith impaired immune function in both humans and genetically obese

rodents [7]. Excess weight and adiposity are associated with insulin resistance, compensatory hyperinsulinemia, increased levels of free insulin-like growth factor-1 (IGF-1), and chronic inflammation [8–10]. In these states, increased serum levels of pro-inflammatory factors (tumor necrosis factor (TNF)-α, interleukin-6, and C-reactive protein) may stimulate signaling pathways that inhibit apoptosis and promote proliferation of B-cells [21]. Height, in addition to having a genetic component, is influenced by nutrition and exposure to infections during childhood and adolescence [31]. Lu et al. [10] have described possible pathways underlying a link between height and risk of NHL. Both height and increased caloric intake in childhood are associated with increased circulating levels of IGF-1 [46–50], which in turn has an important influence on childhood growth and modifies the action of growth hormone [51]. IGF-1 has also been shown to promote pro-B to pre-B cell maturation [52] and B-cell proliferation [53], and to inhibit apoptosis [54], thereby contributing to increased risk of NHL. Thus, height may reflect IGF-1 levels and growth patterns in childhood that are associated with lymphomagenesis. All of these mechanisms may play a role in the development of NHL.

Strengths of this study include its prospective nature, the high degree of completeness of follow-up, the central diagnostic review of NHL cases, the large number of cases (and hence the large number of cases of the major NHL subtypes), the fact that anthropometric factors were measured by trained technicians at baseline, and the availability of a variety of anthropometric factors, including weight at different ages and height at age 18. A number of limitations also need to be considered. Anthropometric variables were measured at baseline and may have changed over the follow-up period, leading to non-differential misclassification. In addition, self-reports of height and weight at age 18 may be biased. In addition, although we included total energy intake (estimated from the food-frequency questionnaire) as a covariate in our models, this variable was essentially unrelated to biomarker-based (doubly labeled water) total energy consumption in WHI [55], and, therefore, control for energy intake is unlikely to have accomplished its intended purpose. Finally, questions regarding physical activity focused only on recreational physical activity and did not cover patterns of physical activity earlier in life or activity related to occupation or household work. A validation study showed that the WHI measure of leisure-time physical activity does not correlate tightly with an objective measure of total energy expenditure [56].

In conclusion, in a large cohort study of postmenopausal women followed for 11 years, baseline height and body weight at age 18 were associated with modestly increased risk of NHL overall, and of diffuse large B-cell lymphoma, whereas baseline weight, BMI, and markers of abdominal adiposity were not associated with risk. Some measures of physical activity showed a modest positive association with risk. Our findings regarding anthropometric measures are consistent with those of several previous studies and suggest that early life influences on growth and immune function may influence the risk of NHL later in life.

Acknowledgments

This work was supported by institutional funds.

References

1. American Cancer Society. Cancer facts and figures 2009. Atlanta: American Cancer Society; 2009.
2. Hartge P, Wang SS, Bracci PM, Devesa SS, Holly EA. Non-Hodgkin's lymphoma. In: Schottenfeld D, Fraumeni JF, Jr, editorsCancer epidemiology and prevention. New York: Oxford University Press; 2006. 898–918.
3. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005; 55:74–108. [PubMed: 15761078]
4. Bosetti C, Levi F, Ferlay J, Lucchini F, Negri E, La Vecchia C. Incidence and mortality from non-Hodgkin's lymphoma in Europe: the end of an epidemic? Int J Cancer. 2008; 123:1917–23. [PubMed: 18688859]
5. Morton LM, Wang SS, Devesa SS, Hartge P, Weisenburger DD, Linet MS. Lymphoma incidence patterns by WHO subtype in the United States, 1992–2001. Blood. 2006; 107:265–76. [PubMed: 16150940]
6. Muller AM, Ihorst G, Mertlelsmann R, Englehardt M. Epidemiology of non-Hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology. Ann Hematol. 2005; 84:1–12. [PubMed: 15480663]
7. Skibola CF, Holly EA, Forrest MS, Hubbard A, Bracci PM, Skibola DR, et al. Body mass index, leptin and leptin receptor polymorphisms, and non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev. 2004; 13:779–86. [PubMed: 15159310]
8. Marti A, Marcos A, Martinez JA. Obesity and immune function relationships. Obesity Rev. 2001; 2:131–40.
9. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanism. Nat Rev. 2004; 4:579–91.
10. Lu Y, Prescott J, Sullivan-Halley J, Henderson KD, Ma H, Chang ET, et al. Body size, recreational physical activity, and B-cell non-Hodgkin's lymphoma risk among women in the California Teachers Study. Am J Epidemiol. 2009; 170:1231–40. [PubMed: 19822569]
11. Holly EA, Lele C, Bracci PM, McGrath MS. A case-control study of non-Hodgkin's lymphoma among women and heterosexual men in the San Francisco Bay Area, California. Am J Epidemiol. 1999; 150:375–89. [PubMed: 10453814]
12. Wolk A, Gridley G, Svensson M, Nyren O, McLaughlin JK. A prospective study of obesity and cancer risk (Sweden). Cancer Causes Control. 2001; 12:13–21. [PubMed: 11227921]
13. Cerhan JR, Janney CA, Vachon CM, Habermann TM, Kay NE, Potter JD, et al. Anthropometric characteristics, physical activity, and risk of non-Hodgkin's lymphoma subtypes and B-cell chronic lymphocytic leukemia: a prospective study. Am J Epidemiol. 2002; 156:527–35. [PubMed: 12226000]
14. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. New Engl J Med. 2003; 348:1625–38. [PubMed: 12711737]
15. Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, et al. Obesity and incidence of cancer in a large cohort study of over 145,000 adults in Austria. Br J Cancer. 2005; 93:1062–7. [PubMed: 16234822]
16. Chang ET, Hjalgrim H, Smedly KE, Akerman M, Tani E, Johnsen HE, et al. Body mass index and risk of malignant lymphoma in Scandinavian men and women. J Natl Cancer Inst. 2005; 97:210–8. [PubMed: 15687364]
17. Bosetti C, Dal Maso L, Negri E, Talamini R, Montella M, Franceschi S, et al. Re: Body mass index and risk of malignant lymphoma in Scandinavian men and women. J Natl Cancer Inst. 2005; 97:860–1. [PubMed: 15928310]
18. Oh SW, Yoon YS, Shin S-A. Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. J Clin Oncol. 2005; 23:4742–54. [PubMed: 16034050]
19. MacInnis RJ, English DR, Hopper JL, Giles GG. Body size and composition and the risk of lymphohematopoietic malignancies. J Natl Cancer Inst. 2005; 97:1154–7. [PubMed: 16077074]

20. Pan SY, Mao Y, Ugnat A-M. Physical activity, obesity, energy intake, and the risk of non-Hodgkin's lymphoma: a population-based case-control study. Am J Epidemiol. 2005; 162:1162–73. [PubMed: 16269580]
21. Willett EV, Skibola CF, Adamson P, Skibola DR, Morgan GJ, Smith MT, et al. Non-Hodgkin's lymphoma, obesity and energy homeostasis polymorphisms. Br J Cancer. 2005; 93:811–6. [PubMed: 16160698]
22. Batty GD, Shipley MJ, Jarrett RJ, Breeze E, Marmot MG, Davey Smith G. Obesity and overweight in relation to organ-specific cancer mortality in London (UK): findings from the original Whitehall study. Int J Obesity. 2005; 29:1267–74.
23. Cerhan JR, Bernstein L, Severson RK, Davis S, Colt JS, Blair A, et al. Anthropometrics, physical activity, related medical conditions, and the risk of non-Hodgkin's lymphoma. Cancer Causes Control. 2005; 16:1203–14. [PubMed: 16215871]
24. Fernberg P, Odenbro A, Bellocco R, Boffetta P, Pawitan Y, Adami J. Tobacco use, body mass index and the risk of malignant lymphomas – a nationwide cohort study in Sweden. Int J Cancer. 2006; 118:2298–302. [PubMed: 16331621]
25. Lukanova A, Björ O, Kaaks R, Lenner P, Lindahl B, Hallmans G, et al. Body mass index and cancer: results from the Northern Sweden Health and Disease Cohort. Int J Cancer. 2006; 118:458–66. [PubMed: 16049963]
26. Samanic C, Chow W-H, Gridley G, Jarvholm B, Fraumeni JR Jr. Relation of body mass index to cancer risk in 362,552 Swedish men. Cancer Causes Control. 2006; 17:901–9. [PubMed: 16841257]
27. Chiu BC, Soni L, Gapstur SM, Fought AJ, Evens AM, Weisenburger DD. Obesity and risk of non-Hodgkin's lymphoma (United States). Cancer Causes Control. 2007; 18:677–85. [PubMed: 17484069]
28. Reeves GK, Pirie K, Beral V, Green J, Spenser E, Bull D. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. BMJ. 2007; 335:7630.
29. Lim U, Morton LM, Subar AF, Baris D, Stolzenberg-Solomon R, Leitzmann M, et al. Alcohol, smoking, and body size in relation to incident Hodgkin's non-Hodgkin's lymphoma risk. Am J Epidemiol. 2007; 166:697–708. [PubMed: 17596266]
30. Engeland A, Tretli S, Hansen S, Bjørge T. Height and body mass index and risk of lymphohematopoietic malignancies in two million Norwegian men and women. Am J Epidemiol. 2007; 165:44–52. [PubMed: 17041129]
31. Britton JA, Khan AE, Rohrmann S, Becker N, Linseisen J, Nieters A, et al. Anthropometric characteristics and non-Hodgkin's lymphoma and multiple myeloma risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). Hematologica. 2008; 93:1666–77.
32. Maskarinec G, Erber E, Gill J, Cozen W, Kolonel LN. Overweight and obesity at different times in life as risk factors for non-Hodgkin's lymphoma: the Multiethnic Cohort. Cancer Epidemiol Biomarkers Prev. 2008; 17:196–203. [PubMed: 18187389]
33. Pylypchuk RD, Schouten LJ, Goldbohm RA, Schouten HC, van den Brandt PA. Body mass index, height, and risk of lymphatic malignancies: a prospective cohort study. Am J Epidemiol. 2009; 170:297–307. [PubMed: 19478235]
34. Troy JD, Hartge P, Weissfeld JL, Oken MM, Colditz, Mechanic LE, et al. Associations between anthropometry, cigarette smoking, alcohol consumption, and non-Hodgkin's lymphoma in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Am J Epidemiol. 2010; 171:1270–81. [PubMed: 20494998]
35. Kanda J, Matsuo K, Suzuki T, Ichinohe T, Seto M, Morishima Y, et al. Association between obesity and the risk of malignant lymphoma in Japanese: a case-control study. Int J Cancer. 2010; 126:2416–25. [PubMed: 19821488]
36. Larsson SC, Wolk A. Obesity and risk of non-Hodgkin's lymphoma: a meta-analysis. Int J Cancer. 2007; 121:1564–70. [PubMed: 17443495]
37. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008; 371:569–78. [PubMed: 18280327]

38. Willett EV, Morton LM, Hartge P, Becker N, Bernstein L, Boffetta P, et al. Non-Hodgkin's lymphoma and obesity: a pooled analysis from the InterLymph consortium. Int J Cancer. 2008; 122:2062–70. [PubMed: 18167059]
39. Skibola CF. Obesity, diet and risk of non-Hodgkin's lymphoma. Cancer Epidemiol Biomarkers Prev. 2007; 16:392–5. [PubMed: 17337642]
40. De Roos AJ, Ulrich CM, Ray RM, Mossavar-Rahmani Y, Rosenberg CA, Caan BJ, et al. Intentional weight loss and risk of lymphohematologic cancers. Cancer Causes Control. 2009; 21:223–36. [PubMed: 19851877]
41. The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. Control Clin Trials. 1998; 19:61–109. [PubMed: 9492970]
42. Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol. 2003; 13:S107–21. [PubMed: 14575943]
43. McTiernan A, Kooperberg C, White E, Wilcox S, Coates R, Adams-Campbell LL, et al. Recreational physical activity and the risk of breast cancer in postmenopausalwomen: the Women's Health Initiative cohort study. JAMA. 2003; 290:1331–6. [PubMed: 12966124]
44. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc. 1993; 25:71–80. [PubMed: 8292105]
45. Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol. 2003; (9 Suppl):S122–8. [PubMed: 14575944]
46. Rogers I, Emmett P, Gunnell D, Dunger D, Holly J. Milk as a food for growth? The insulin-like growth factors link. Public Health Nutr. 2006; 9:359–68. [PubMed: 16684388]
47. Rogers I, Metcalfe C, Gunnell D, Emmett P, Dunger D, Holly J. Insulin-like growth factor-I and growth in height, leg length, and trunk length between ages 5 and 10 years. J Clin Endocrinol Metab. 2006; 91:2514–9. [PubMed: 16670160]
48. Hoppe C, Udam TR, Lauritzen L, Mølgaard C, Juul A, Michaelsen KF. Animal protein intake, serum insulin-like growth factor I, and growth in healthy 2. 5-y-old Danish children. Am J Clin Nutr. 2004; 80:447–52. [PubMed: 15277169]
49. Rogers IS, Gunnell D, Emmett PM, Glynn LR, Dunger DB, Holly JM. Cross-sectional associations of diet and insulin-like growth factor levels in 7- to 8-year-old children. Cancer Epidemiol Biomarkers Prev. 2005; 14:204–12. [PubMed: 15668496]
50. Schernhammer ES, Tworoger SS, Eliassen AH, Eliassen AH. Body shape throughout life and correlations with IGFs and GH. Endrocr Relat Cancer. 2007; 14:721–32.
51. Butler AA, Le Roith D. Control of growth by the somatotropic axis: growth hormone and the insulin-like growth factors have related and independent roles. Annu Rev Physiol. 2001; 63:141–64. [PubMed: 11181952]
52. Landreth KS, Narayanan R, Dorshkind K. Insulin-like growth factor-I regulates pro-B cell differentiation. Blood. 1992; 80:1207–12. [PubMed: 1515639]
53. Gibson LF, Piktel D, Landreth KS. Insulin-like growth factor-1 potentiates expansion of interleukin-7-dependent pro-B cells. Blood. 1993; 82:3005–11. [PubMed: 7693033]
54. Buckbinder L, Talbott R, Velasco-Miguel S, Takenaka I, Faha B, Seizinger BR, et al. Induction of the growth inhibitor IGF-binding protein 3 by p53. Nature. 1995; 377:646–9. [PubMed: 7566179]
55. Schoeller DA. Recent advances from application of doubly-labeled water to measurement of human energy expenditure. J Nutr. 1999; 129:1765–8. [PubMed: 10498745]
56. Evenson KR, Wilcox S, Pettinger M, Brunner R, King AC, McTiernan A. Vigorous physical activity through women's adult life: the Women's Health Initiative Observational Cohort Study. Am J Epidemiol. 2002; 156:945–53. [PubMed: 12419767]

Appendix A. Short list of WHI investigators

Program Office: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Joan McGowan, Leslie Ford, and Nancy Geller.

Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA). Ross Prentice, Garnet Anderson, Andrea LaCroix, Charles Kooperberg; (Medical Research Labs, Highland Heights, KY) Evan Stein; (University of California at San Francisco, San Francisco, CA) Steven Cummings.

Clinical Centers: (Albert Einstein College of Medicine, Bronx, NY) Sylvia Wassertheil-Smoller; (Baylor College of Medicine, Houston, TX) Haleh Sangi-Haghpeykar; (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (Brown University, Providence, RI) Charles B. Eaton; (Emory University, Atlanta, GA) Lawrence S. Phillips; (Fred Hutchinson Cancer Research Center, Seattle, WA) Shirley Beresford; (George Washington University Medical Center, Washington, DC) Lisa Martin; (Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA) Rowan Chlebowski; (Kaiser Permanente Center for Health Research, Portland, OR) Erin LeBlanc; (Kaiser Permanente Division of Research, Oakland, CA) Bette Caan; (Medical College of Wisconsin, Milwaukee, WI) Jane Morley Kotchen; (MedStar Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Northwestern University, Chicago/ Evanston, IL) Linda Van Horn; (Rush Medical Center, Chicago, IL) Henry Black; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (State University of New York at Stony Brook, Stony Brook, NY) Dorothy Lane; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Alabama at Birmingham, Birmingham, AL) Cora E. Lewis; (University of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of California at Davis, Sacramento, CA) John Robbins; (University of California at Irvine, CA) F. Allan Hubbell; (University of California at Los Angeles, Los Angeles, CA) Lauren Nathan; (University of California at San Diego, LaJolla/Chula Vista, CA) Robert D. Langer; (University of Cincinnati, Cincinnati, OH) Margery Gass; (University of Florida, Gainesville/ Jacksonville, FL) Marian Limacher; (University of Hawaii, Honolulu, HI) J. David Curb; (University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Massachusetts/Fallon Clinic, Worcester, MA) Judith Ockene; (University of Medicine and Dentistry of New Jersey, Newark, NJ) Norman Lasser; (University of Miami, Miami, FL) Mary Jo O'Sullivan; (University of Minnesota, Minneapolis, MN) Karen Margolis; (University of Nevada, Reno, NV) Robert Brunner; (University of North Carolina, Chapel Hill, NC) Gerardo Heiss; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (University of Tennessee Health Science Center, Memphis, TN) Karen C. Johnson; (University of Texas Health Science Center, San Antonio, TX) Robert Brzyski; (University of Wisconsin, Madison, WI) Gloria E. Sarto; (Wake Forest University School of Medicine, Winston-Salem, NC) Mara Vitolins; (Wayne State University School of Medicine/Hutzel Hospital, Detroit, MI) Michael S. Simon.

Women's Health Initiative Memory Study: (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker.

Table 1

Distribution of selected characteristics among NHL cases and non-cases.

Characteristic	Cases (*N* = 1123)	Non-cases (*N* = 157,852)	*P*-value
Means (SD):			
Age, mean	65.2 (6.9)	63.2 (7.2)	<0.0001
Parity, mean	2.7 (1.7)	2.6 (1.7)	0.08
Age at menopause, mean	47.8 (6.4)	47.3 (6.7)	0.03
Body mass index[a] (kg/m^2), mean	27.8 (5.8)	28.0 (5.9)	0.25
Height (cm), mean	162.1 (6.3)	161.8 (6.7)	0.11
Waist circumference (cm), mean	86.5 (14.1)	86.5 (13.8)	0.96
Physical activity (MET-h[b]/wk), mean	12.7 (14.2)	11.9 (13.7)	0.07
Caloric intake (kcal/d), mean	1664 (750)	1626 (717)	0.11
Alcohol intake (servings/wk), mean	2.3 (4.6)	2.4 (4.9)	0.57
Smoking (pack-years), mean	9.4 (18.9)	9.7 (18.1)	0.61
Proportions:			
Age ≤11 years at menarche (%)	20.8	21.9	0.40
Age ≥30 years at first birth (%)	10.1	9.1	0.40
Oral contraceptive use ever (%)	37.2	41.4	0.01
Hormone therapy ever (%)	57.7	56.2	0.34
History of diabetes	5.3	5.9	0.37
Education (% post-college)	26.0	28.6	0.12
Ethnicity			
White	91.0	82.7	
Black	4.0	9.1	
Other	5.0	8.2	<0.0001
Study component			
OS	58.0	57.6	
CT	42.0	42.4	0.81
History of diseases associated with immunosuppression/inflammation (% yes)	12.2	11.7	0.63
Use of medications associated with immunosuppression/inflammation (% yes)	44.3	42.0	0.12

Abbreviations: MET, metabolic equivalent task.

[a] Weight (kg)/height $(m)^2$.

[b] Defined as caloric need per kilogram of body weight per hour of activity divided by the caloric need per kilogram of body weight per hour of rest, per hour per week.

Table 2

Association of baseline anthropometric factors with risk of non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukemia/small lymphocytic lymphoma in the Women's Health Initiative.

	All NHL cases (*N* = 1123)			DLBCL (*N* = 302)			Follicular	lymphoma (*N* = 214)		CLL/SLL (*N* = 298)		
	No.	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**
Height (cm)[a,b]												
<157.6	278	1.00	reference	71	1.00	reference	60	1.00	reference	65	1.00	reference
157.6–<161.9	246	0.90	0.75–1.08	68	1.03	0.73–1.46	41	0.64	0.42–0.96	69	1.04	0.74–1.47
161.9–<166.1	299	1.11	0.93–1.32	78	1.20	0.85–1.69	56	0.88	0.60–1.28	82	1.27	0.90–1.78
≥166.1	300	1.19	1.00–1.43	85	1.43	1.01–2.03	57	0.98	0.66–1.45	82	1.37	0.96–1.94
Ptrend		0.02			0.03			0.75			0.05	
Weight (kg)[a,c]												
<62.0	287	1.00	reference	73	1.00	reference	57	1.00	reference	81	1.00	reference
62.0–<70.4	283	0.97	0.82–1.15	79	1.09	0.78–1.51	54	0.84	0.57–1.24	78	0.92	0.67–1.27
70.4–<81.6	308	1.08	0.91–1.28	80	1.11	0.79–1.56	57	0.97	0.66–1.43	79	0.93	0.67–1.30
≥81.6	245	0.92	0.76–1.12	70	1.05	0.72–1.52	46	0.88	0.57–1.34	60	0.72	0.50–1.05
Ptrend		0.71			0.77			0.72			0.12	
Waist circumference (cm)[a,c]												
<76.1	288	1.00	reference	70	1.00	reference	62	1.00	reference	75	1.00	reference
76.1–<84.6	292	1.01	0.85–1.19	80	1.13	0.82–1.58	52	0.80	0.54–1.16	81	1.10	0.80–1.51
84.6–<95.0	274	1.00	0.84–1.19	68	1.02	0.72–1.44	50	0.87	0.60–1.27	81	1.13	0.81–1.57
>95.0	267	0.99	0.83–1.19	84	1.28	0.91–1.81	50	0.87	0.58–1.29	60	0.88	0.61–1.26
Ptrend		0.91			0.25			0.57			0.57	
Missing	2			0			0			1		
Hip circumference (cm)[a,c]												
<98.1	302	1.00	reference	77	1.00	reference	61	1.00	reference	77	1.00	reference
98.1–<104.5	271	0.96	0.81–1.13	72	0.98	0.71–1.37	55	0.91	0.63–1.32	80	1.13	0.82–1.55
104.5–<112.6	286	0.96	0.81–1.14	76	1.04	0.75–1.45	52	0.80	0.54–1.18	78	1.04	0.75–1.45
≥112.6	262	0.95	0.80–1.14	77	1.10	0.78–1.55	46	0.82	0.54–1.23	62	0.88	0.61–1.26
Ptrend		0.64			0.56			0.25			0.46	

	All NHL cases (*N* = 1123)			DLBCL (*N* = 302)			Follicular lymphoma (*N* = 214)			CLL/SLL (*N* = 298)		
	No.	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**
Missing	2			0			0			1		
Waist-to-hip ratio[a,c]												
<0.76	280	1.00	reference	69	1.00	reference	55	1.00	reference	73	1.00	reference
0.76–<0.80	292	1.06	0.89–1.25	73	1.09	0.78–1.53	61	1.15	0.79–1.67	82	1.17	0.85–1.61
0.80–<0.86	280	1.02	0.86–1.21	80	1.19	0.85–1.67	53	1.06	0.71–1.56	74	1.06	0.76–1.48
≥0.86	269	1.02	0.86–1.22	80	1.24	0.88–1.75	45	0.90	0.60–1.37	68	1.04	0.74–1.47
Ptrend		0.90			0.19			0.57			0.97	
Missing	2			0			0			1		
BMI												
<25	391	1.00	reference	99	1.00	reference	72	1.00	reference	111	1.00	reference
25–<30	419	1.11	0.89–1.25	115	1.23	0.93–1.62	80	1.11	0.80–1.54	120	1.11	0.85–1.45
30–<35	215	1.13	0.86–1.21	55	1.11	0.78–1.58	44	1.29	0.87–1.91	51	0.94	0.67–1.33
≥35	98	0.94	0.86–1.22	33	1.30	0.85–1.99	18	0.97	0.57–1.66	16	0.52	0.31–0.90
Ptrend		0.77			0.25			0.56			0.07	

Abbreviations: NHL – non-Hodgkin's lymphoma; DLBCL – diffuse large B-cell lymphoma; CLL/SLL – chronic lymphocytic leukemia, small lymphocytic lymphoma; HR –hazard ratio; 95% CI – 95% confidence interval.

[a]Adjusted for age (continuous), pack-years of smoking (0, >0–<20, 20–<40, ≥40), servings of alcohol per week (continuous), education (less than high school graduate, high school graduate/some college, college graduate, post-college), ethnicity (white, black, other), physical activity (METs/wk–continuous), caloric intake (kcal/d), enrollment in the OS, and treatment arm assignment in the clinical trials.

[b]Additionally, adjusted for weight.

[c]Additionally, adjusted for height.

Table 3

Association of height, weight, and BMI at ages 18, 35, and 50 with risk of Non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukemia/small lymphocytic lymphoma in the Women's Health Initiative Observational Study.

	All NHL cases (*N* = 651)			DLBCL (*N* = 186)			Follicular lymphoma (*N* = 122)			CLL/SLL (*N* = 171)		
	No.	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**
Height at age 18 (cm)[a]												
<158.8	125	1.00	reference	28	1.00	reference	29	1.00	reference	32	1.00	reference
158.8–<163.8	186	1.16	0.92–1.47	51	1.54	0.96–2.47	37	1.00	0.61–1.64	52	1.21	0.77–1.89
163.8–<168.9	202	1.32	1.05–1.65	63	1.99	1.26–3.17	31	0.84	0.50–1.41	50	1.19	0.76–1.87
≥168.9	132	1.10	0.85–1.42	44	1.81	1.10–2.98	22	0.79	0.44–1.39	35	1.09	0.67–1.77
Ptrend		0.27			0.01			0.31			0.79	
Missing	6			0			3			2		
Weight at age 18 (kg)[a,b]												
<50.1	144	1.00	reference	39	1.00	reference	29	1.00	reference	40	1.00	reference
50.1–<54.2	135	1.28	1.00–1.63	36	1.28	0.81–2.06	22	1.13	0.64–2.03	36	1.17	0.74–1.86
54.2–<58.8	174	1.15	0.91–1.45	50	1.17	0.75–1.85	30	1.13	0.66–1.96	45	1.02	0.65–1.59
≥58.8	191	1.29	1.01–1.65	60	1.39	0.88–2.20	38	1.53	0.88–2.63	48	1.09	0.68–1.73
Ptrend		0.09			0.23			0.15			0.88	
Missing	7			1			3			2		
Weight at age 35(kg)[a,b]												
<54.2	130	1.00	reference	41	1.00	reference	28	1.00	reference	34	1.00	reference
54.2–<58.8	178	1.13	0.89–1.43	45	0.88	0.57–1.37	30	0.92	0.54–1.58	56	1.35	0.87–2.10
58.8–<63.3	162	0.95	0.74–1.21	39	0.64	0.40–1.03	34	1.02	0.59–1.75	38	0.83	0.50–1.35
≥63.3	174	1.07	0.83–1.37	60	1.05	0.67–1.66	27	0.81	0.45–1.46	41	0.89	0.54–1.48
Ptrend		0.97			0.97			0.58			0.22	
Missing	7			1			3			2		
Weight at age 50(kg)[a,b]												
<57.4	170	1.00	reference	46	1.00	reference	37	1.00	reference	44	1.00	reference
57.4–<61.9	148	1.01	0.81–1.27	41	1.04	0.67–1.61	21	0.69	0.40–1.20	50	1.24	0.81–1.88
61.9–<70.1	171	0.89	0.71–1.12	45	0.84	0.54–1.31	36	0.85	0.52–1.41	37	0.72	0.45–1.14

	All NHL cases (*N* = 651)			DLBCL (*N* = 186)			Follicular lymphoma (*N* = 122)			CLL/SLL (*N* = 171)		
	No.	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**
≥70.1	156	0.98	0.77–1.25	54	1.24	0.79–1.95	25	0.69	0.39–1.23	38	0.83	0.51–1.35
Ptrend		0.61			0.55			0.31			0.15	
Missing	6			0				3			2	
BMI at age 18[a]												
<18.9	143	1.00	reference	43	1.00	reference	27	1.00	reference	42	1.00	reference
18.9–<20.2	165	1.17	0.93–1.48	39	0.95	0.61–1.47	30	1.16	0.68–1.98	42	1.02	0.66–1.57
20.2–<21.8	158	1.07	0.85–1.35	50	1.19	0.78–1.81	24	0.88	0.50–1.55	44	1.03	0.67–1.58
≥21.8	178	1.27	1.01–1.59	53	1.33	0.87–2.02	38	1.46	0.87–2.43	41	0.93	0.59–1.45
Ptrend		0.09			0.11			0.26			0.77	
Missing	7			1			3			2		
BMI at age 35[a]												
<20.4	153	1.00	reference	48	1.00	reference	29	1.00	reference	41	1.00	reference
20.4–<21.8	186	1.26	1.02–1.57	48	1.12	0.75–1.68	30	0.96	0.57–1.63	51	1.32	0.87–2.00
21.8–<23.5	151	0.94	0.74–1.18	44	0.88	0.57–1.36	33	1.07	0.64–1.77	33	0.76	0.47–1.22
≥23.5	154	1.16	0.92–1.46	45	1.20	0.79–1.85	27	0.94	0.55–1.62	44	1.17	0.75–1.83
Ptrend		0.75			0.67			0.94			0.90	
Missing	7			1			3			2		
BMI at age 50[a]												
<21.5	165	1.00	reference	49	1.00	reference	29	1.00	reference	47	1.00	reference
21.5–<23.5	192	1.17	0.95–1.45	57	1.18	0.80–1.75	33	1.05	0.63–1.74	49	1.01	0.68–1.53
23.5–<26.4	148	0.95	0.75–1.19	34	0.78	0.50–1.23	30	0.99	0.58–1.66	44	0.94	0.62–1.43
≥26.4	140	1.05	0.82–1.33	46	1.32	0.86–2.04	27	1.04	0.60–1.80	29	0.68	0.42–1.12
Ptrend		0.82			0.60			0.95			0.14	
Missing	6			0			3			2		

Abbreviations: NHL – non-Hodgkin's lymphoma; DLBCL – diffuse large B-cell lymphoma; CLL/SLL – chronic lymphocytic leukemia, small lymphocytic lymphoma; HR–hazard ratio; 95% CI – 95% confidence interval.

[a]Adjusted for age (continuous), pack-years of smoking (0, >0–<20, 20–<40, ≥40), servings of alcohol per week (continuous), education (less than high school graduate, high school graduate/some college, college graduate, post-college), ethnicity (white, black, other), physical activity (METs/wk–continuous), caloric intake (kcal/d), enrollment in the OS, and treatment arm assignment in the clinical trials.

[b]Additionally, adjusted for height.

Table 4

Association of baseline recreational physical activity with risk of non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, and chronic lymphocytic leukemia/small lymphocytic lymphoma in the Women's Health Initiative.

	All NHL cases (*N* = 1123)			DLBCL (*N* = 302)			Follicular lymphoma (*N* = 214)			CLL/SLL (*N* = 298)		
	No.	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**	**No.**	**HR**	**95% CI**
Baseline recreational physical activity (MET-h/wk)												
MET-h/wk[a]												
<1.6	259	1.00	reference	68	1.00	reference	52	1.00	reference	67	1.00	reference
1.6–<7.5	266	1.05	0.88–1.25	76	1.10	0.78–1.53	40	0.80	0.53–1.22	74	1.13	0.81–1.58
7.5–<17.5	289	1.11	0.93–1.32	82	1.12	0.80–1.56	61	1.21	0.83–1.78	75	1.11	0.79–1.55
≥17.5	309	1.17	0.98–1.39	76	1.03	0.73–1.45	61	1.22	0.83–1.80	82	1.18	0.84–1.66
Ptrend		0.06			0.87			0.11			0.38	
Baseline moderate or strenuous recreational physical activity (h/wk)												
h/wk[a]												
None	384	1.00	reference	97	1.00	reference	79	1.00	reference	99	1.00	reference
0–<1	142	1.12	0.92–1.36	38	1.26	0.86–1.84	28	1.05	0.68–1.63	38	1.17	0.80–1.70
1–<2	164	1.11	0.92–1.34	52	1.39	0.97–1.97	24	0.80	0.50–1.28	40	1.03	0.71–1.51
2–<3	104	0.97	0.77–1.21	37	1.35	0.91–2.01	21	0.91	0.55–1.52	30	1.08	0.71–1.63
≥3	277	1.22	1.04–1.44	62	1.14	0.81–1.58	53	1.17	0.82–1.69	78	1.24	0.91–1.69
Ptrend		0.05			0.31			0.57			0.25	
Missing	52			16			9			13		
Baseline strenuous recreational physical activity (h/wk)												
h/wk[a]												
None	807	1.00	reference	214	1.00	reference	147	1.00	reference	211	1.00	reference
0–<1	60	1.01	0.78–1.32	17	1.15	0.70–1.88	14	1.23	0.70–2.17	16	0.99	0.59–1.64
1–<2	97	1.06	0.86–1.32	29	1.24	0.83–1.85	20	1.22	0.75–1.98	27	1.07	0.71–1.61
≥2	107	0.97	0.79–1.20	26	0.89	0.59–1.36	24	1.25	0.81–1.94	31	1.03	0.70–1.51
Ptrend		0.97			0.93			0.21			0.79	
Missing	52			16			9			13		

Abbreviations: NHL – non-Hodgkin's lymphoma; DLBCL – diffuse large B-cell lymphoma; CLL/SLL – chronic lymphocytic leukemia, small lymphocytic lymphoma; HR –hazard ratio; 95% CI – 95% confidence interval.

[a] Adjusted for age (continuous), pack-years of smoking (0, >0–<20, 20–<40, >40), servings of alcohol per week (continuous), education (less than high school graduate, high school graduate/some college, college graduate, post-college), ethnicity (white, black, other), body mass index (continuous), enrollment in the OS, and treatment arm assignment in the clinical trials.