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Diet and Incident Venous Thromboembolism: The Iowa Women's Health Study

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Abstract

Background—Little is known about the role of diet in the development of venous thromboembolism (VTE). We explored the prospective relation of dietary patterns, food groups, and nutrients to incident VTE in older women.

Methods—In 1986, Iowa women aged 55–69 completed a mailed survey, including a 127-item food frequency questionnaire. These data were linked to Medicare data from 1986–2004, and International Classification of Disease discharge codes were used to identify hospitalized VTE cases. Cox regression analyses evaluated relations of 2 principal components-derived dietary patterns, 11 food groups, and 6 nutrients to VTE, adjusted for age, education, smoking status, physical activity, and energy intake.

Results—Over 19 years of follow-up 1,950 of the 37,393 women developed VTE. Women consuming alcohol daily were at 26% (95% CI: 11%–38%) lower risk of VTE, as compared to nonconsumers. All alcoholic beverages types were in the direction of lower risk, however only beer and liquor were statistically significant. After basic adjustments coffee was inversely related to VTE, and diet soda and fish positively related. However, these associations were confounded, and became nonsignificant after adjustment for body mass index and diabetes. No associations were observed with consumption of 'Western' or 'Prudent' dietary patterns, fruit, vegetables, dairy, meat, refined grains, whole grains, regular soda, vitamins E, B6, B12, folate, omega-3 fatty acids, or saturated fat.

Conclusions—In this cohort of older women, greater intake of alcohol was associated with a lower risk of incident VTE. No other independent associations were seen between diet and VTE.

Keywords

Venous thromboembolism; Diet; Alcohol; Iowa Women's Health Study; Medicare

Background

VTE, comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major source of morbidity and mortality in the elderly^{1–3}. Diet is hypothesized to affect VTE risk

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by altering levels of homocysteine⁴ and coagulation factors^{5–7}, which have been extensively linked to the development of VTE⁸.

However, at present little is known about the role of dietary intake in the development of VTE. In the observational Longitudinal Investigation of Thromboembolism Etiology (LITE) study greater consumption of a ‘Western’ dietary pattern, and red and processed meat, were associated with an increased risk of validated VTE, while greater consumption of fruit and vegetables was associated with a decreased risk⁹. Consumption of whole grains, refined grains, and dairy were not associated with VTE risk. Alcohol’s relation to VTE has been explored in five studies, which have conflicting results. Two studies reported an inverse association^{10, 11}, whereas three others found no relation^{12–14}.

The relation of nutrients to VTE risk has been evaluated more broadly. In recent results from the Women’s Health Study, a significant 21% hazard reduction in risk of total VTE was observed in the group randomized to vitamin E supplementation, compared to the group randomized to placebo¹⁵. In LITE, VTE risk was inversely related to consumption of folate and vitamin B6⁹. However, analogous to results from recent trials which attempted to reduce cardiovascular disease (CVD) incidence by lowering homocysteine with B vitamins^{16–18}, trials similarly attempting to reduce VTE incidence¹⁹ and recurrence²⁰ yielded null results. LITE observed no associations between VTE risk and intakes of saturated fatty acids and vitamin B12⁹.

The current literature does not provide clear evidence regarding whether dietary intake influences VTE risk. Given the paucity of data, additional research is warranted. Thus, using data from the Iowa Women’s Health Study (IWHS)-Medicare linkage, we conducted a comprehensive exploration of the diet-VTE relation among elderly women, utilizing dietary patterns, multiple food groups, and selected nutrients. Based on theorized effects of diet on hemostatic factors levels, we hypothesized that consumption of a ‘Prudent’ dietary pattern, dairy, whole grains, fruit, vegetables, fish, coffee, alcohol, vitamin B6, vitamin B12, folate, vitamin E, and omega-3 fatty acids would be inversely associated with incident VTE, while a positive association would be observed with consumption of a ‘Western’ dietary pattern, meat, refined grains, regular (sugar-sweetened) soda, diet soda, and saturated fat.

Methods

IWHS Study Design and Medicare Linkage

The IWHS cohort commenced in January 1986 when a questionnaire was mailed to 99,826 Iowa women aged 55–69, who were randomly sampled from the State driver’s list. The 41,836 women who responded to this initial questionnaire constitute the IWHS cohort. Nonresponse bias appeared to be small, as assessed by the cancer rates and mortality of nonrespondents²¹. The University of Minnesota Institutional Review Board approved this study, and all participants gave informed consent.

Using a method employed previously²², the IWHS data were linked to U.S. Centers for Medicare Services (CMS) enrollment and health care utilization data from 1986 through 2004. Medicare is a U.S. government program which provides payment for all or part of health care for most U.S. residents aged 65 and older^{23, 24}, and data stemming from the payment of Medicare bills is now used widely as a population-based data source for clinical occurrences²⁵. Information about inpatient services, including discharge diagnosis codes, has been available since 1986. Of IWHS cohort members surviving to age 65, 99% (40,668 of 40,997) were successfully linked to CMS data.

Medicare beneficiary enrollment information from the denominator file was used to determine eligibility for inclusion in our analytic sample. We included only participants who, since 1986, were enrolled in at least one month of Fee-For-Service (FFS) Part A and Part B Medicare coverage after reaching age 65. People enrolling in Medicare at younger ages due to disability or end-stage renal disease only contributed to our analyses after age 65. Person-years for two groups unlikely to have complete claims histories were also excluded: 1) person-years when participants enrolled in managed care and 2) person-years when women had only Part A coverage. After these restrictions, our analytic dataset included 40,377 IWHs participants.

Dietary Assessment

The participants' usual diet was assessed at baseline with a Willett 127-item semi-quantitative food frequency questionnaire (FFQ)²⁶. For each food, a commonly used serving size was specified and participants were asked to report their frequency of consumption from among nine categories, ranging from never or <1 serving/month to ≥ 6 servings/day. As has been done in previous IWHs dietary analyses, participants were excluded if they left blank ≥ 30 FFQ-items ($n = 3,096$), or if they reported implausible energy intakes (i.e. <600 kcal/d, >5000 kcal/d) ($n = 569$).

To derive dietary patterns via principal components analysis, foods were categorized into 39 food groups according to similar nutrient content. For the analyses of major food groups, they were further aggregated into the following six groups: meat, dairy, fruit, vegetables, whole grains, and refined grains. The whole- and refined-grain groups were classified according to previously developed procedures²⁷. Five food subgroups of particular interest were also formed: fish, coffee, alcohol, regular soda, and diet soda.

The section of the FFQ on intake of vitamin supplements included questions on the name, frequency, and doses of multivitamins and of supplements. Nutrient intakes from food and supplements were calculated using the Harvard database.

Covariate Assessment

Information about the women's age, educational attainment, physical activity, smoking habits, height, weight, and diabetes status were queried in the baseline questionnaire. For physical activity, a 3-level index was created based on self-reported frequency of moderate (e.g. golf, long walks) and vigorous (e.g. swimming, aerobics) activities. Body mass index (BMI) was calculated as weight over height squared (kg/m^2).

VTE Ascertainment

Previous work comparing VTE International Classification of Disease (ICD) codes to medical records has found ICD codes to be reasonably valid indicators of VTE hospitalization^{2, 28–30}. IWHs participants were considered to have had a VTE if any of the following VTE ICD-9 codes occurred in any position on their Medicare MedPAR (hospitalization) discharge diagnosis records: 415.1x, 451.1x, 451.2, 451.81, 451.9, 453.0, 453.1, 453.2, 453.3, 453.4x, 453.8, 453.9. Information from the Medicare outpatient and carrier files were not used to identify VTE cases. VTE cases were classified as idiopathic ('unprovoked') or secondary (subsequent to provoking clinical conditions) according to an algorithm previously employed in this cohort³.

VTE incidence was computed with the number of persons with VTE as the numerator and person-years as the denominator. Person-years accumulated from meeting the enrollment criteria until VTE, death, FFS Part A and/or B disenrollment, or the end of December 2004. VTE history at baseline was unknown, thus we were unable to exclude from our analyses women with prior VTE.

Statistical Analysis

All analyses were performed with SAS (version 9.1; Cary, NC: SAS Institute Inc.). Principal components analysis was used to derive dietary patterns and determine factor loadings for each of the 39 food sub-groups. Varimax rotation was used to maintain uncorrelated factors and enhance interpretability. Eigenvalues greater than 2.0 were retained, resulting in a 2-factor solution. Dietary patterns were named according to the nature of the food groups loading highest for each factor.

The dietary patterns, major food groups, and nutrients were categorized into quintiles. Given their non-normal distribution of consumption, intake of fish, coffee, alcohol, regular soda, and diet soda were categorized on the basis of their observed distributions. For food groups of particular interest, associations of individual food items to VTE risk were also explored. The individual food items were also categorized based on their observed distributions.

Baseline characteristics of participants are described using means and proportions. Cox proportional hazards regression was used to assess the relation between diet and incident VTE. Hazard ratios (HRs) were obtained by entering the quintiles (or categories) into the models as indicator variables, using the lowest intake category as the referent. To test the trend across levels of consumption, quintiles were entered into the models as continuous terms. For categories, we created ordinal variables to designate the categories, and entered the ordinal variables into the models as continuous terms. HRs were also estimated for incident idiopathic and secondary VTE.

Model 1 adjusted for age, energy intake, educational attainment (3-levels), smoking status (current, former, never), and physical activity level (low, moderate, high). Model 2 attempted to determine whether associations were independent of obesity and diabetes status, by adjusting for baseline BMI (continuous) and diabetes (yes, no). In instances where Model 1 and Model 2 results were similar, only Model 1 estimates are shown. We also explored models in which, to account for dietary intercorrelation, multiple food groups and/or nutrients were included. Once again, results from these models were similar to Model 2, thus only Model 2 is reported. Tests of interaction by BMI and age with dietary factors were conducted using cross-product terms in the models.

Results

Following dietary and CMS enrollment exclusions, the cohort consisted of 37,393 IWHs participants, who were almost exclusively Caucasian (99%) and had a mean baseline age of 62 years (range: 55–69). Women were, on average 65.9 years old when they met our Medicare inclusion enrollment criteria, and began contributing person-years. Over 19 years of follow-up (median: 13 years), 489,000 person-years accrued, and there were 1,950 incident VTE events. Of the incident events, 22% (n = 424) were classified as idiopathic, and 78% (n = 1,526) as secondary. Distributions of baseline characteristics are presented in Table 1.

Factor analysis revealed two main dietary patterns. Factor 1, identified as a ‘Prudent’ dietary pattern, was characterized by high intake of vegetables, fruit, and poultry. Factor 2, the ‘Western’ dietary pattern, was typified by greater consumption of processed meat, non-cereal whole grains, and added fats and oils.

There was no relation between incident VTE and consumption of a ‘Prudent’ dietary pattern, a ‘Western’ dietary pattern, fruit, vegetables, dairy, meat, refined grains, or whole grains (Table 2). Associations remained largely null when VTE events were stratified by type (idiopathic and secondary). Though not statistically significant, there was evidence that whole grain intake was marginally inversely associated with incident secondary VTE. Hazard ratios (95% CIs) of

secondary VTE incidence across quintiles of whole grain intake following model 1 adjustments were 1.00 (reference), 1.02 (0.87–1.20), 0.95 (0.81–1.11), 0.92 (0.78–1.08), and 0.87 (0.72–1.04); (Model 1 $p_{\text{trend}}=0.06$). Hazards were attenuated slightly with BMI and diabetes adjustments (Model 2 $p_{\text{trend}}=0.09$) (data not shown).

Associations of intake of fish, coffee, alcohol, regular soda, and diet soda to incident VTE are presented in Table 3. Intake of fish was positively associated with risk of VTE following Model 1 adjustments ($p_{\text{trend}}=0.02$), but was not related to VTE risk after additional adjustment for BMI and diabetes (Model 2 $p_{\text{trend}}=0.12$). Likewise, coffee consumption was inversely related to VTE risk following Model 1 adjustments ($p_{\text{trend}}=0.04$), but the association was attenuated with Model 2 adjustments ($p_{\text{trend}}=0.11$).

Alcohol intake was inversely related to VTE risk ($p_{\text{trend}} \leq 0.001$). As compared to nonconsumers, the hazard for daily alcohol consumption was 0.74 (0.62–0.89). This association was attenuated, but retained statistical significance, following adjustment for BMI and diabetes ($p_{\text{trend}}=0.04$). Table 4 presents hazards of incident VTE according to alcoholic beverage type. While all types of alcoholic beverages were in the direction of lower risk, only beer and liquor were statistically significant. Following adjustment for BMI and diabetes (Model 2) beer remained statistically significant, while the association between VTE and liquor was attenuated.

Regular soda intake was not related to VTE risk (Table 3). Diet soda consumption was associated with elevated risk following Model 1 adjustments ($p_{\text{trend}} = 0.001$), but was attenuated after adjustment for BMI and diabetes status ($p_{\text{trend}} = 0.22$).

No associations were observed between risk of VTE and intake of any of the selected nutrients: vitamin B6, vitamin B12, folate, vitamin E, omega-3 fatty acids, and saturated fat (data not shown).

Sensitivity analyses in which we included only the first five years of follow-up yielded similar results. Neither age nor BMI appeared to modify relations between diet and incident VTE.

Discussion

Main Findings

In this prospective study of white women over 65, there was little evidence of a relation between diet and incident VTE, though greater alcohol consumption was associated with lower VTE risk. Prior to BMI and diabetes adjustment, intake of coffee was inversely related to VTE risk, and greater fish and diet soda consumption were positively related, however these associations were not independent of BMI and diabetes status. No relationships were observed between VTE and consumption of either dietary pattern, food groups other than alcohol, or selected nutrients.

Consistent with our *a priori* hypothesis, alcohol consumption was associated with a lower risk of VTE. Compared to women who did not consume alcohol, the 10% of the cohort with daily consumption were at 26% lower risk of VTE. While all types of alcoholic beverages had associations in the direction of lower VTE risk, the most robust associations were observed with consumption of beer. Previous studies assessing the relation between alcohol intake and VTE report inconsistent results; some studies demonstrated an inverse association^{10, 11}, whereas others found no relation^{12–14}. While the precise mechanisms by which alcohol may affect coagulation are uncertain, both experimental and observational data have suggested that moderate alcohol consumption may exert antithrombotic effects^{5–7}, which are most pronounced for consumption of 1–3 drinks/day⁶. It is presently unclear whether it is ethanol

that favorably affects coagulation, or if the beneficial effects are due to other compounds found in alcoholic beverages³¹. Resveratrol, which is present in red wine, has been associated with an antithrombotic profile³², as have numerous substances found in hops, a beer flavoring and stability agent³³. Conversely, heavy alcohol consumption or bingeing has been associated with a more thrombogenic profile^{5, 7}, and with elevated mortality and CVD risk^{5, 31}. Very few IWHS women were heavy drinkers; consequently we were unable to evaluate the relation of heavy alcohol consumption with VTE risk in our sample.

Possible Explanations

Contrary to our hypotheses, no relation was observed between incident VTE and consumption of dietary patterns, major food groups, or selected nutrients. There are several possible explanations for our findings. First, of course, it is possible that diet is truly not related to VTE risk. Second, while diet is known to alter levels of coagulation factors⁴⁻⁷, which are linked to VTE risk⁸, both the effect of diet on coagulation factor levels and of coagulation factor levels on VTE risk are relatively small in magnitude. It is possible that if diet influences VTE risk, its effect may be small and difficult to detect statistically. Nonetheless, significant associations were reported in the vitamin E supplementation arm of the Women's Health Study¹⁵, and for some exposures in LITE⁹.

Comparison with LITE

Given that IWHS and LITE are the only two observational studies of diet and VTE, their contrary findings warrant further investigation. LITE and IWHS both had key strengths and limitations. The most obvious source of difference between IWHS and LITE is the age of the participants – a mean of 72 at the midpoint of follow-up in IWHS as compared to 60 in LITE. Physiologic effects of diet are known to differ in middle-aged and older adults, and may explain the differing findings. For instance, metabolism changes with aging, and declines are generally seen in nutrient absorption, kidney function, and caloric needs³⁴. Thus, it is possible that, due to age-related physiologic differences, diet may play a bigger etiologic role for VTE in younger than older people.

Over the longer follow-up in IWHS than LITE age- and time-related changes in dietary intake may have led to comparatively greater dietary misclassification in the older IWHS population. For instance, dietary misclassification may have occurred since as people reach advanced ages appetite, the ability to prepare food, and even the ability to eat, are frequently hindered due to poor oral health, decreased mobility, economic hardship, medication use, and feelings of isolation and loneliness³⁴. Changes to the food supply³⁵ may also have led to comparatively greater dietary change, and therefore misclassification of diet, in IWHS due to its longer follow-up.

To assess whether increasing misclassification of dietary intake over follow-up may have influenced our results, we conducted sensitivity analyses in which we restricted our analyses to the first five years after the baseline survey. Results of these sensitivity analyses were, however, similar to those inclusive of the entire follow-up.

There are also important differences in IWHS and LITE dietary data collection methods. Though both studies used validated Willett FFQs, the IWHS FFQ had 127 items, while the LITE FFQ contained only 66 items. Thus, the food list was more comprehensive in IWHS. IWHS also collected information on dietary supplement use, which is relevant to the nutrient analyses, while LITE did not. LITE's dietary assessment may, however, be more precise as the FFQ was interviewer-administered as opposed to self-administered, and as food models were used⁹. Further, diet was also collected twice during LITE, thus permitting use of cumulative average diet³⁶, which may also have improved dietary precision.

In both cohorts, some food group misclassification likely occurred. For example, in differentiating whole grain from refined grain food items²⁷. Also, given the FFQs utilized, both studies sometimes could not determine the specific types of food consumed, or the preparation methods used.

VTE assessment also differed between the studies. In LITE VTEs were validated via medical record review⁹, while in IWHS VTEs were identified using ICD-9 discharge diagnosis codes from Medicare hospitalization data. Nonetheless, numerous studies have suggested that ICD-9 diagnosis codes from administrative data are reasonably valid indicators of VTE hospitalization^{2, 28–30}. In other analyses of the IWHS cohort³, age-specific VTE incidence rates were similar to those published previously^{1, 2}, suggesting that our VTE definition is legitimate.

Important strengths of IWHS are that given the large number of events which accrued, IWHS was unlikely to make a type II error, and had power to explore whether dietary risk factors varied according to VTE type (idiopathic or secondary). Generalizability of the IWHS data, however, is limited, as the study was conducted among mature women living in Iowa who were almost exclusively Caucasian.

Conclusions

At present, the associations of dietary patterns and food groups to VTE have only been observationally explored in the IWHS data, here, and in LITE⁹, and their findings differ. In addition to these observational studies, three clinical trials have also evaluated the relation of specific nutrients to VTE^{15, 19, 20}; once again their conclusions are inconsistent. Given these conflicts, further research examining the potential relation of diet to VTE is warranted.

In conclusion, in this large prospective cohort alcohol intake was inversely associated with risk of VTE. Otherwise, there was little association of diet to incident VTE.

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Table 1

Baseline characteristics of 37,393 Iowa Women's Health Study participants, 1986.

Demographic, Lifestyle & Anthropometric Characteristics	
Age *, mean years (SD)	65.9 (1.6)
Education, n (%)	
< High school	6,714 (18.0)
High school	15,726 (42.1)
> High school	14,883 (39.9)
Smoking status, n (%)	
Never	24,131 (65.4)
Current	5,435 (14.7)
Former	7,334 (19.9)
Physical activity, n (%)	
Low	17,409 (47.3)
Moderate	10,198 (27.7)
High	9,214 (25.0)
BMI, mean kg/m ² (SD)	27.0 (5.1)
Diabetic, n (%)	2,262 (6.1)
Energy, kcal per day	1802 (607)

VTE, venous thromboembolism; BMI, body mass index

* Age at which participants met Medicare enrollment criteria and began contributing person-years to this analysis.

Table 2

Hazard ratios (95% CIs)^{*} of incident VTE according to quintile (Q) of dietary pattern score and food group intake in 37,393 participants of the Iowa Women's Health Study, 1986–2004.

	Q1	Q2	Q3	Q4	Q5	P [†]
Dietary Pattern Scores [‡]						
'Prudent' Diet	-1.02 [§]	-0.57	-0.17	0.29	1.18	
HR	1.00	1.20(1.04–1.39)	1.16(1.00–1.35)	1.06(0.91–1.24)	1.17(0.99–1.38)	0.78
'Western' Diet	-1.12 [§]	-0.58	-0.14	0.37	1.29	
HR	1.00	0.93(0.80–1.08)	1.01(0.87–1.18)	0.95(0.81–1.13)	1.01(0.82–1.23)	0.29
Individual Food Groups(servings per week)						
Fruit	4.0	8.5	12.0	16.0	23.5	
HR	1.00	1.00(0.87–1.16)	1.01(0.87–1.17)	1.06(0.92–1.24)	1.02(0.88–1.20)	0.73
Vegetables	8.0	13.0	18.0	24.0	36.5	
HR	1.00	1.04(0.90–1.20)	1.02(0.88–1.17)	0.92(0.80–1.07)	1.02(0.87–1.19)	0.21
Dairy	5.0	9.5	13.5	20.5	28.5	
HR	1.00	1.19(1.03–1.38)	1.12(0.97–1.30)	1.08(0.93–1.26)	1.07(0.91–1.25)	0.54
Meat	4.0	6.5	8.5	11.0	16.5	
HR	1.00	1.01(0.87–1.17)	1.02(0.88–1.20)	1.05(0.90–1.23)	1.03(0.86–1.23)	0.27
Refined grains	2.5	4.5	7.0	10.5	19.0	
HR	1.00	0.95(0.82–1.11)	0.92(0.79–1.06)	0.96(0.83–1.11)	0.98(0.84–1.15)	0.66
Whole grains	7.0	12.0	17.5	23.5	36.0	
HR	1.00	1.05(0.91–1.21)	0.98(0.84–1.13)	0.97(0.84–1.12)	0.92(0.79–1.08)	0.10

VTE, venous thromboembolism; HR, hazard ratio

^{*} Adjusted for age, kcal, education, smoking status, and physical activity.

[†] Trend in HRs across median quintile of intake.

[‡] Assuming a 2-factor solution which identified 'Western' and 'Prudent' patterns.

[§] Median scores for quintiles.

Table 3

Hazard ratios (95% CIs) of incident VTE according to intake of alcohol, coffee, regular soda, diet soda, and fish in 37,393 participants of the Iowa Women's Health Study, 1986–2004.

Fish	< 0.5	0.5 to < 1	1.0 to 1.5	> 1.5 to 2.5	≥ 2.5	P*
Servings/wk						
Cases	218	380	484	482	386	
Person-years	60,590	94,070	119,192	128,125	87,023	
Model 1	1.00	1.14 (0.96–1.35)	1.17 (1.00–1.38)	1.10 (0.93–1.29)	1.30 (1.09–1.54)	0.02
Model 2	1.00	1.13 (0.95–1.34)	1.16 (0.98–1.36)	1.07 (0.91–1.26)	1.22 (1.03–1.46)	0.12
Coffee						
Servings/wk	0	< 7	7 - < 28	28 to < 42	≥ 42	
Cases	216	229	1,006	334	165	
Person-years	50,100	57,647	246,876	89,975	44,401	
Model 1	1.00	0.92 (0.76–1.12)	0.94 (0.81–1.10)	0.85 (0.71–1.01)	0.83 (0.67–1.03)	0.04
Model 2	1.00	0.94 (0.77–1.13)	0.97 (0.83–1.13)	0.88 (0.74–1.05)	0.86 (0.69–1.06)	0.11
Alcohol						
Servings/wk	0	0.5 to 3.0	3.5 to 6.5	≥ 7.0	--	
Cases	1,144	549	116	141	--	
Person-years	270,377	138,080	35,084	45,458	--	
Model 1	1.00	0.97 (0.87–1.07)	0.78 (0.64–0.96)	0.74 (0.62–0.89)	--	0.0003
Model 2	1.00	1.02 (0.92–1.13)	0.87 (0.71–1.06)	0.83 (0.69–1.00)	--	0.04
Regular Soda						
Servings/wk	0	0.5 to 3.0	3.5 to 6.5	≥ 7.0	--	
Cases	888	827	143	92	--	
Person-years	214,841	218,129	33,213	22,816	--	
Model 1	1.00	0.91 (0.82–1.00)	1.01 (0.84–1.22)	0.95 (0.76–1.19)	--	0.40
Model 2	1.00	0.93 (0.85–1.03)	1.05 (0.87–1.26)	0.96 (0.76–1.20)	--	0.63
Diet Soda						
Servings/wk	0	0.5 to 3.0	3.5 to 6.5	≥ 7.0	--	
Cases	1,013	621	150	166	--	
Person-years	266,899	150,499	37,127	34,474	--	
Model 1	1.00	1.12 (1.01–1.24)	1.09 (0.91–1.30)	1.31 (1.10–1.55)	--	0.001
Model 2	1.00	1.05 (0.95–1.16)	0.98 (0.82–1.18)	1.14 (0.96–1.35)	--	0.22

VTE, venous thromboembolism

* Trend in HRs across categories of intake.

Model 1: Adjusted for age, kcal. education (3-levels), smoking status (current, former, never), and physical activity (low, moderate, high).

Model 2: Adjusted for Model 1 + BMI (continuous), diabetes (yes/no).

Table 4
Hazard ratios (95% CIs) of incident VTE according to alcoholic beverage type in 37,393 participants of the Iowa Women's Health Study, 1986–2004.

	< 1 time/week	≥ 1 time/week
Beer (1 glass, bottle, or can)		
Cases, n	1,822	128
Person-years	444,138	44,862
Model 1	1	0.69(0.58–0.83)
Model 2	1	0.74(0.61–0.89)
Red wine (4 oz. glass)		
Cases, n	1,840	110
Person-years	457,115	31,885
Model 1	1	0.88(0.73–1.07)
Model 2	1	0.96(0.79–1.17)
White wine (4 oz. glass)		
Cases, n	1,804	146
Person-years	448,560	40,440
Model 1	1	0.94(0.79–1.12)
Model 2	1	1.04(0.88–1.24)
Liquor (1 shot or 1 drink)		
Cases, n	1,697	253
Person-years	416,560	72,440
Model 1	1	0.87(0.75–0.99)
Model 2	1	0.92(0.80–1.06)

VTE, venous thromboembolism; HR, hazard ratio

Model 1: Adjusted for age, kcal, education, smoking status, and physical activity.

Model 2: Adjusted for Model 1 + BMI and diabetes