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## FRUIT AND VEGETABLE CONSUMPTION AND THE INCIDENCE OF HYPERTENSION IN THREE PROSPECTIVE COHORT STUDIES

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### Abstract

Increased fruit and vegetable intake lowers blood pressure in short-term interventional studies. However, data on the association of long-term intake of fruits and vegetables with hypertension risk are scarce.

We prospectively examined the independent association of whole fruit (excluding juices) and vegetable intake, as well as the change in consumption of whole fruits and vegetables, with incident hypertension in three large longitudinal cohort studies: Nurses' Health Study (n=62,175), Nurses' Health Study II (n=88,475), and Health Professionals Follow-up Study (n=36,803). We calculated hazard ratios and 95% confidence intervals for fruit and vegetable consumption while controlling for hypertension risk factors. Compared with participants whose consumption was  $\leq 4$  servings/week, the pooled hazard ratios among those whose intake was  $\geq 4$  servings/day were 0.92(0.87–0.97) for total whole fruit intake and 0.95(0.86–1.04) for total vegetable intake.

Similarly, compared with participants who did not increase their fruit or vegetable consumption, the pooled hazard ratios for those whose intake increased by  $\geq 7$  servings/week were 0.94(0.90–0.97) for total whole fruit intake and 0.98(0.94–1.01) for total vegetable. Analyses of individual fruits and vegetables yielded different results. Consumption levels of  $\geq 4$  servings/per week (as opposed to  $< 1$  serving/month) of broccoli, carrots, tofu or soybeans, raisins and apples was associated with lower hypertension risk.

In conclusion, our results suggest that greater long-term intake and increased consumption of whole fruits may reduce the risk of developing hypertension.

### Keywords

hypertension; incidence; epidemiology; prospective studies; fruit; vegetables

## Introduction

Hypertension, a major risk factor for cardiovascular and renal diseases, continues to represent a growing public health concern nationwide and worldwide. It is estimated that 41% of adult Americans will have a diagnosis of hypertension by the year 2030<sup>1,2</sup>. The Dietary Approach to Stopping Hypertension (DASH) diet emphasizes the importance of increasing fruit and vegetable consumption while decreasing the intake of red meat<sup>3</sup>. Also, in a 6-month interventional trial, participants who were educated to increase their fruit and vegetable consumption had a 4mmHg average drop in their systolic blood pressure (BP) when compared with the control group<sup>4</sup>.

Several prospective studies assessed the long-term intake of fruits and vegetables with hypertension risk<sup>5–10</sup>. However, these studies differ in their design, dietary assessment, and length of follow-up. Only one study analyzed individual fruits<sup>9</sup>, but to our knowledge, individual vegetables have not been studied prospectively. We therefore examined the associations of individual fruit and vegetable intake with the risk of developing hypertension in three large prospective cohort studies consisting of 187,453 participants with more than 20 years of follow-up.

## Methods

### Study Population

Participants consisted of the Nurses' Health Study (NHS, N=121,700 women, aged 30–55 in 1976), the Nurses' Health Study II (NHS II, N=116,430 women, aged 25–42 in 1989), and the Health Professionals Follow-up Study (HPFS, N=51,529 men, aged 40–75 in 1986). Participants returned a questionnaire every two years reporting a diagnosis of hypertension by a health-care provider. Participants also answered semi-quantitative food frequency questionnaires (FFQs) every four years, reporting intake of more than 130 foods and beverages. Reproducibility and validity of these FFQs were described in previous work<sup>11,12</sup>. Participants who reported a diagnosis of hypertension at the baseline questionnaire were excluded from the analysis (1984 in NHS, 1991 in NHS II, and 1986 in HPFS). The resulting study population consisted of 62,175 women from NHS, 88,475 women from NHS II, and 36,803 men from HPFS. To analyze the change in fruit and vegetable consumption, we set two 8-year hypothetical intervention periods with subsequent 8-year follow-up periods in 1986 and 1994 for NHS and HPFS and in 1991 and 1999 for NHSII. Participants with a diagnosis of hypertension at or before 1994 for NHS and HPFS and 1999 for NHS II were excluded from our analysis. The resulting study population for this analysis of long-term change in intake was 123,059 participants (39,164 in NHS, 63,885 in NHS II and 20,010 in HPFS). The Institutional Review Board of Brigham and Women's Hospital approved the study. By virtue of voluntarily returning their questionnaires, participants provided implied consent. All procedures followed were in accordance with institutional guidelines.

## Assessment of Hypertension

Hypertension was self-reported on the baseline and biennial questionnaires. This method of reporting a diagnosis of hypertension was shown to be valid in the three cohorts<sup>13–15</sup>. In NHS, for example, 77% of 51 cases of self-reported hypertension had a blood pressure >160/95mmHg<sup>13</sup>.

A participant was considered to have prevalent hypertension if she or he reported this diagnosis on any questionnaire up to and including the 1984 (NHS), 1991 (NHS II), or 1986 (HPFS) questionnaire. Participants were determined to be cases if they reported a diagnosis of hypertension on subsequent questionnaires, with a date of diagnosis that was after the date of the baseline questionnaire.

## Assessment of Fruits and Vegetables Intake

A detailed dietary questionnaire was sent in 1984, 1986, and every four years thereafter. Similar FFQs were mailed every four years beginning in 1991 and 1986 for NHS II and HPFS, respectively. Participants answered how often, on average, they consumed a specific food; nine different response categories could be selected, ranging from “never or <1serving/month” to “≥6/day”. Multiple questions on the FFQ ascertained whole fruits: raisins (1oz.)/grapes (½cup), fresh apples/pears (1), bananas (1), strawberries (½cup), blueberries (½cup), prunes (½cup), avocado (½fruit), cantaloupe (¼melon), oranges (1) and peaches/apricots/plums (1 or ½cup canned). As for juices, we analyzed apple juice, orange juice, and other fruit juices (small glass). Vegetables consisted of raw and cooked spinach (½cup), kale (½cup), lettuce (per serving), broccoli (½cup), cauliflower (½cup), brussel sprouts (½cup), cabbage/cole slaw (½ cup), raw carrot (½carrot or 2–4 sticks) and/or cooked carrot (½cup), string beans (½cup), beans or lentils (½cup), peas/lima beans (½cup), corn (1 ear or ½cup), yams/sweet potatoes (½cup), eggplant/zucchini (½cup), celery (4” stick), green peppers (3 slices), tomatoes (1), and onions (1). The reproducibility and validity of the FFQ were evaluated in the three cohorts. As examples, the deattenuated correlation coefficients between FFQs and a seven-day dietary records in 173 women from NHS were 0.74 for apples and bananas and 0.53 for cabbage<sup>16</sup>. In the HPFS, a similar validation study was conducted; deattenuated Pearson correlation coefficients were 0.38 for tomatoes and 0.67 for all fruits<sup>17</sup>.

## Assessment of Covariates

On biennial questionnaires, participants reported updated information about weight, smoking status, body mass index (BMI) and physical activity (estimated as metabolic equivalent tasks [METs]). The FFQs were also used to ascertain participants’ consumption of alcohol, whole grains, animal flesh (red and processed meat, poultry, and fish), and others. These covariates have been validated with questionnaire-derived information (correlation coefficients of 0.97 for weight and 0.79 for physical activity)<sup>18,19</sup>.

## Statistical Methods

To decrease within-person variation, we used a cumulative average of an individual’s fruit and vegetable intake beginning with the baseline FFQ and including subsequent FFQs through the censoring event. Person-time of follow-up was calculated from the date of return

of the baseline questionnaire to the date of hypertension diagnosis, the date of death, or the end of follow-up, whichever came first.

Total whole fruits and total vegetables were grouped into 5 categories from “≤4 servings/month” (reference group) to “≥4 servings/day”. Individual fruits and vegetables were grouped into 4 categories, from “≤1 serving/month” (reference group) to “4–6 servings/week”. Participants’ fruit and vegetable intake was summed to create a new, combined variable of total whole fruits plus total vegetables; this variable was categorized into 4 categories, from “≤1 serving/day” (reference group) to “≥6 servings/day”.

For the change in consumption of total whole fruits and total vegetables, we calculated 8-year change in dietary intake by subtracting median value of initial intake level assessed 8 years prior to baseline survey from the median value of intake at baseline (for these analyses, “baseline” refers to 1994 in NHS and HPFS, and 1999 in NHS II). The 8-year change in consumption was divided into 7 categories ranging from a ≥7 servings/week decrease in intake to a ≥7 servings/week increase in intake (with “no change (±0.9 serving/week)” as the reference group).

We used Cox proportional hazards regression to calculate the hazard ratios (HRs) and 95% confidence intervals for incident hypertension. HRs were adjusted for potential confounders: age; BMI; change in weight; race/ethnicity; family history of hypertension; smoking status; physical activity (METs per week); post-menopausal; oral contraceptive use (in NHS II); non-narcotic analgesic; total energy intake; and intakes of alcohol, animal flesh (in 5 categories), whole grains, and sugar-sweetened and artificially-sweetened beverage. Adjusted multivariable HRs for the three cohorts were pooled using fixed effects meta-analysis.

We then created continuous variables to analyze the multivariable HRs per additional serving per day of total whole fruit, total vegetable and total fruit and vegetable consumption.

A variety of secondary analyses were also performed. First, we added intake of micronutrients (potassium, calcium, magnesium, sodium, and fiber) to our multivariable models. Second, we removed weight change from our models since this could be a causal intermediate. Third, we investigated whether the associations varied significantly according to age and BMI by creating stratified models and introducing multiplicative interaction terms to our unstratified multivariable models. Finally, we repeated our analyses using simple updating instead of cumulative averaging. All analyses were performed with SAS software (version 9.4; SAS Institute Inc, Cary, NC). All *P* values are two-sided.

## Results

### Association of fruits and vegetables with incident hypertension

Among 187,453 participants free from hypertension at the baseline questionnaire, 77,373 participants were diagnosed with hypertension in 2,939,124 person-years of follow-up

(35,375 cases/1,034,421 person-years in NHS, 25,246/1,344,475 in NHS II, and 16,752 / 560,228 in HPFS).

Supplementary Table S1 reports the baseline characteristics of participants in the three cohorts for different intake categories of total whole fruits and total vegetables. In all three cohorts, those with higher intakes of fruits and vegetables were older, more physically activity, had a higher daily caloric intake and were less likely to be current smokers.

Participants who consumed  $\geq 4$  servings/day of total whole fruits and total vegetables, as compared with  $\leq 4$  servings/week, had multivariable pooled HRs for incident hypertension of 0.92(95% CI: 0.87–0.97) and 0.95(0.86–1.04), respectively (Table 1). When fruits and vegetables were combined into one intake category, higher consumption ( $\geq 6$  servings/day) was associated with a lower risk of developing hypertension (HR=0.89[0.86–0.93]) when compared to  $\leq 1$  serving/day.

Table 2 reports the pooled HRs for most individual fruits and vegetables and the risk of incident hypertension (complete tables in Supplementary Table S2 and S3). Higher intakes of raisins/grapes and apples/pears, when consumed  $\geq 4$  servings/week, were associated with a decreased risk of hypertension; multivariable pooled HRs were 0.92(0.89–0.96) and 0.91(0.88–0.95), respectively. Blueberries and avocados were also associated with a significant trend towards a lower risk of hypertension; HRs were 0.92(0.83–1.03; p-trend=0.01) and 0.94(0.77–1.14; p-trend<0.001), respectively. In contrast to these fruits, higher cantaloupe intake was associated with an increased risk of hypertension (HR = 1.07[1.01–1.13]).

Broccoli, carrots, and tofu/soybeans were associated with a decreased risk of incident hypertension when consumed  $\geq 4$  servings/week as compared with  $< 1$  serving/month, with multivariable pooled HRs of 0.94(0.90–0.99), 0.95(0.91–0.99) and 0.88(0.79–0.99), respectively (Table 2). In contrast, eating more string beans and brussel sprouts was associated with an increased risk of hypertension with pooled HRs of 1.11(1.05–1.17) and 1.23(1.04–1.46), respectively. In addition, higher consumption of both corn and cauliflower were associated with an increased trend towards a higher risk of hypertension with multivariable pooled HRs of 1.05(0.98–1.12; p-trend<0.004) and 1.06(0.99–1.14; p-trend<0.001), respectively.

Furthermore, in a separate analysis, there was no association between fruit juices and hypertension (data not shown).

When continuous variables were used, every one additional serving per day of total whole fruit was associated with a lower risk of hypertension, (HR= 0.97[0.96–0.98]).

### **Association of 8-year change of fruits and vegetables consumption with subsequent hypertension risk**

In our analyses of 8-year change in intake with the subsequent development of hypertension, we defined a new “baseline” year of 1994 (for NHS and HPFS) and 1999 (for NHS II) to permit the calculation of change in consumption before baseline. After excluding participants who reported a diagnosis of hypertension at baseline, 44,032 participants were

diagnosed with hypertension in 1,517,157 person-years of follow-up (20,147 cases in 566,278 person-years in NHS, 15,972/683,702 in NHS II and 8,183/267,177 in HPFS). Increasing total whole fruit consumption by  $\geq 7$  servings/week in the preceding 8 years was associated with a lower risk of hypertension with a pooled HR 0.94(0.90–0.97; Supplementary Table S4, please see <http://hyper.ahajournals.org>) during the subsequent 5 years, whereas there was no association with incident hypertension when participants increased their total vegetable consumption (HR=0.98[0.94–1.01]). Associations between change in the consumption level of individual fruits and vegetables with incident hypertension were generally similar to those associations observed with long-term intake (Supplementary Tables S5, please see <http://hyper.ahajournals.org>)).

Overall, our secondary analyses had no substantial impact on the findings. Adjusting for potassium and other micronutrients (including calcium, magnesium, sodium and fiber) did not materially change the results. We also examined more extreme categories of total fruit and vegetable consumption and the results were mostly unchanged. There were no consistent interactions between fruit and vegetable intake and either age or BMI with hypertension risk. Removing weight change from our models did not change our findings. We also found similar results when the analyses were repeated with simple updating of dietary intake (rather than cumulative averaging).

## Discussion

In three prospective cohort studies of US women and men, long-term intake of total whole fruit was associated with a decreased risk of developing hypertension, whereas total vegetable intake was not. The association of whole fruit intake with hypertension incidence was independent of other known and potential risk factors for hypertension. Some vegetables (ie, broccoli, carrots, tofu) and some fruits (ie, raisins or grapes and apples or pears) were associated with a lower risk of hypertension, whereas some vegetables (ie, string beans, Brussels sprouts) and cantaloupe were associated with an increased risk of developing hypertension. To our knowledge, our study is the first to prospectively analyze individual vegetables, and has the longest follow-up period of any study of diet and hypertension.

Our finding that total whole fruit but not total vegetable intake is associated with a lower risk of developing hypertension is consistent with some earlier studies. The largest prior experience comes from the Women's Health Study, a prospective cohort of 28,082 female US health professionals with baseline semi-quantitative FFQ and 12.9 years of follow-up<sup>5</sup>. Those participants who consumed more dark-yellow vegetables had a lower adjusted risk of incident hypertension (HR = 0.88; 95 CI 0.82–0.95), while similar comparisons for cruciferous vegetables (such as brussel sprouts) yielded an increased risk of hypertension (HR = 1.14; 1.06–1.23)<sup>5</sup>. Also similar to our study, greater intake of apples and raisins were associated with lower risks of developing hypertension, with HRs of 0.91(0.85–0.99) and 0.90(0.85–0.96), respectively<sup>5</sup>.

Other studies are considerably smaller or are cross-sectional. In the OHASAMA study, for example, 745 non-hypertensive women and men aged  $\geq 35$  years were followed for 4 years

[8]. Participants in the highest compared with lowest quintile of fruit intake had a lower adjusted hypertension risk (odds ratio=0.40; 0.21–0.74, p-trend=0.03)<sup>6</sup>. The mechanisms by which fruits and vegetables may be associated with hypertension are probably multiple. One hypothesis pertains to the high flavonoid content of several fruits and vegetables, such as berries, apples, broccoli and others<sup>20</sup>. In a prospective study of the NHS I, NHS II and the HPFS, participants in the highest quintile intake of anthocyanins (mostly from blueberries and strawberries) had an 8% lower risk of hypertension<sup>21</sup>. Also, in a randomized controlled trial of men at risk for cardiovascular disease, a diet rich with high-flavonoid fruits and vegetables increased endothelium-dependent microvascular reactivity and plasma nitric oxide (NO), as well as decreased C-reactive protein and E-selectin<sup>22</sup>. Furthermore, grape polyphenols were found to potentiate vasorelaxation and decrease BP as well as endothelial dysfunction markers in a small, placebo-controlled, double-blind study of 24 men with metabolic syndrome<sup>23</sup>. Endothelial dysfunction, inflammation and oxidative stress are potential important factors in the development of hypertension<sup>24–26</sup>. Also, quercetin, a flavonoid found in apples, was found to decrease systolic BP by 3 mmHg ( $P<0.01$ ) when compared with placebo in a double-blind cross-over trial<sup>27</sup>. Similarly, soy isoflavones were found to decrease BP in a meta-analysis of randomized controlled trials<sup>28</sup>.

As with the Women's Health Initiative study<sup>5</sup>, we found a variable association of cruciferous vegetables with hypertension. Although broccoli was associated with a lower risk of hypertension, brussel sprouts seemed to increase hypertension risk when consumed  $\geq 4$  servings/week. In a recent meta-analysis of fruit and vegetable intake and the incidence of pancreatic cancer in 14 cohort studies, brussel sprouts were associated with an increased risk of pancreatic cancer; this association could be related to the use of pesticides or its carcinogenic abilities<sup>29</sup>. However, this association was not seen with broccoli, cauliflower or cabbage.

Another possible explanation for these differences is the cooking methods utilized when eating vegetables. While broccoli is commonly eaten steamed or raw, brussel sprouts (and string beans) are usually roasted, fried, or baked, and mixed with seasonings. However, additionally adjusting for total fats and micronutrients (including sodium) in our analyses did not materially alter our findings (data not shown). The effect of different cooking methods on flavonoids, other phenolic compounds, and the total antioxidant capacity of vegetables in the *Brassica* corps group is controversial<sup>30</sup>. In one study, for example, microwave cooking decreased broccoli's flavonoid content by 97%<sup>31</sup>. In another study, however, precooking and/or cooking methods did not alter the antioxidant capacities of broccoli<sup>32</sup>.

There are several limitations to our study. First, the diagnosis of hypertension was self-reported and participants' BPs were not directly measured. However, all participants are health professionals and this method of hypertension diagnosis in these cohorts has been validated in multiple studies<sup>14–16</sup>. Second, our participants were mostly non-hispanic white men and women and this analysis should be replicated in other populations. Third, the FFQ is an imperfect tool for assessing food intake, and therefore random misclassification of fruit and vegetable consumption may have occurred; this random error was likely to have been amplified in our analyses of change in intake over time. Yet this type of error would have the

effect of moving our hazard ratios toward the null (ie, toward finding no associations). Thus, it is possible that the associations we report are underestimates of the true relationships. Fourth, the associations that we found were modest; however, even these modest associations, if considered at the population level, could have important public health ramifications. Finally, as in any observational study, we cannot exclude the possibility that our findings are the result of residual confounding. Food preferences could also result in residual confounding.

However, we controlled for multiple known and potential risk factors for the development of hypertension in a prospective fashion.

In conclusion, we found a prospective, independent association between higher whole fruit intake, as well as a longitudinal increase in fruit intake, and a decreased risk of incident hypertension. No such association was noted with higher vegetable intake. While our study supports the hypothesis that specific fruits and vegetables may have important effects on blood pressure, these findings should be confirmed by randomized trials. Several unexpected results in this study, including disparate relations with different vegetables, merit further investigation.

## Perspectives

In summary, our observed findings continue to stress on the importance of dietary intake on diseases, especially cardiovascular diseases. Given the increasing prevalence of hypertension in the United States and around the world, these data have important public health implications. Future studies are needed to assess the potential mechanisms underlying these associations.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Contributors: Borgi, Muraki, Rimm and Forman contributed to the conception and design of the study. All authors were involved in the analysis and interpretation of the data. Borgi and Muraki designed and conducted the statistical analysis. Borgi and Muraki worked on the drafting of the manuscript, which was thoroughly reviewed and approved by all authors.

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## Novelty and Significance

### 1) What Is New?

- First study with more than 20 years of follow-up.
- New findings about individual fruits and vegetables consumption and incidence of hypertension.

### 2) What Is Relevant?

- Not all fruits and vegetables prevent hypertension.

### 3) Summary

- Not all vegetables are associated with a lower risk of hypertension. We found an increased risk of hypertension with an increased consumption of string beans, brussel sprouts and cantaloupe.

Table 1

Pooled hazard ratios (95% confidence intervals) of incident hypertension for total whole fruits and total vegetables consumption in Nurses' Health Study, Nurses' Health Study II and Health Professional Follow-up Study

| Fruits and Vegetables               | Consumption Levels |                 |                 |                 |                 |                |
|-------------------------------------|--------------------|-----------------|-----------------|-----------------|-----------------|----------------|
|                                     | ≤4 per week        | 5–6 per week    | 1 per day       | 2–3 per day     | ≥4 per day      | Linear P Trend |
| <b>Total Fruits//</b>               |                    |                 |                 |                 |                 |                |
| NHS *                               | 4,943/154,025      | 4,283/128,106   | 12,732/366,100  | 12,548/359,298  | 869/26,892      |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00(reference)    | 0.97(0.93–1.01) | 0.95(0.92–0.99) | 0.94(0.91–0.98) | 0.96(0.88–1.03) | 0.06           |
| NHS II <sup>†</sup>                 | 5,228/272,299      | 4,125/200,643   | 9,372/488,469   | 6,193/360,225   | 328/22,839      |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00               | 1.03(0.99–1.07) | 0.97(0.94–1.01) | 0.91(0.87–0.95) | 0.91(0.81–1.02) | <0.001         |
| HPFS <sup>‡</sup>                   | 2,827/91,348       | 1,914/63,222    | 5,330/177,585   | 5,941/200,187   | 740/27,887      |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00               | 0.95(0.89–1.00) | 0.92(0.88–0.97) | 0.92(0.87–0.97) | 0.88(0.81–0.97) | 0.01           |
| Pooled Results <sup>¶</sup>         | 1.00               | 0.99(0.96–1.01) | 0.95(0.93–0.97) | 0.93(0.90–0.95) | 0.92(0.87–0.97) | <0.001         |
| <b>Total Vegetables//</b>           |                    |                 |                 |                 |                 |                |
| NHS *                               | 137/4,225          | 341/10,250      | 3,250/99,574    | 20,298/589,705  | 11,349/330,667  |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00               | 0.95(0.77–1.16) | 0.90(0.76–1.07) | 0.89(0.75–1.05) | 0.87(0.73–1.03) | 0.02           |
| NHS II <sup>†</sup>                 | 237/14,685         | 446/25,753      | 3,290/187,949   | 14,198/750,828  | 7,075/365,261   |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00               | 1.01(0.86–1.18) | 0.96(0.84–1.09) | 0.97(0.85–1.11) | 1.01(0.88–1.15) | 0.04           |
| HPFS <sup>‡</sup>                   | 126/4,325          | 234/8,182       | 1,944/68,410    | 9,490/312,925   | 4,958/166,386   |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00               | 0.96(0.77–1.19) | 0.92(0.77–1.11) | 0.94(0.79–1.13) | 0.93(0.78–1.12) | 0.68           |
| Pooled results <sup>¶</sup>         | 1.00               | 0.98(0.88–1.09) | 0.93(0.85–1.02) | 0.94(0.86–1.03) | 0.95(0.86–1.04) | 0.59           |
| <b>Consumption Levels</b>           |                    |                 |                 |                 |                 |                |
| <b>Total Fruits and Vegetables</b>  |                    |                 |                 |                 |                 |                |
| NHS *                               | 1,052/31,868       | 11,318/339,541  |                 | 13,914/396,152  | 9,091/266,861   |                |
| Adjusted hazard ratio <sup>\$</sup> | 1.00(reference)    | 0.90(0.84–0.95) |                 | 0.88(0.83–0.94) | 0.85(0.80–0.91) | <0.001         |
| NHS II <sup>†</sup>                 | 1,427/79,840       | 10,019/528,610  |                 | 8,785/462,410   | 5,015/273,616   |                |

| Fruits and Vegetables              | Consumption Levels |                 |           |                 |                 | Linear P Trend |
|------------------------------------|--------------------|-----------------|-----------|-----------------|-----------------|----------------|
|                                    | ≤4 per week        | 5–6 per week    | 1 per day | 2–3 per day     | ≥ 4 per day     |                |
| Adjusted hazard ratio <sup>§</sup> | 1.00               | 0.97(0.92–1.03) |           | 0.95(0.89–1.00) | 0.94(0.88–0.99) | 0.02           |
| HPFS <sup>‡</sup>                  | 666/22,176         | 5,711/190,017   |           | 6,085/201,161   | 4,290/146,874   |                |
| Adjusted hazard ratio <sup>§</sup> | 1.00               | 0.93(0.85–1.01) |           | 0.91(0.83–0.98) | 0.89(0.81–0.97) | 0.02           |
| Pooled results <sup>¶</sup>        | 1.00               | 0.94(0.90–0.97) |           | 0.91(0.88–0.95) | 0.89(0.86–0.93) | <0.001         |

<sup>\*</sup> Follow-up in Nurses' Health Study was from 1984 to 2010 (cases/persons-years).

<sup>†</sup> Follow-up in Nurses' Health Study II was from 1991–2011

<sup>‡</sup> Follow-up in Health Professionals Follow-up study was from 1986 to 2010.

<sup>§</sup> Adjusted for age, race/ethnicity (white, African-American, Asian, Hispanic, other), body mass index, current smoking status, physical activity, weight change per food frequency questionnaire cycle, menopausal status (NHS and NHS II), alcohol intake, current oral contraceptive use (NHS II), analgesic use (nonsteroidal antiinflammatory drugs, acetaminophen, aspirin), family history of hypertension, total energy intake, animal flesh intake (combination of processed and unprocessed red meat, poultry and seafood), whole grains, sugar-sweetened beverage intake, artificially-sweetened diet beverage intake.

<sup>||</sup> Multivariable model including total vegetables was adjusted for total fruits intake (quintiles), and vice versa

<sup>¶</sup> Pooled hazard ratios of the three cohorts using a fixed effects model.

**Table 2**

Pooled hazard ratios (95% confidence intervals) of incident hypertension for several individual fruit and individual vegetable consumption in Nurses' Health Study, Nurses' Health Study II and Health Professional Follow-up Study

| Individual Fruits and Vegetables | Consumption Levels |                 |                 |                 |         |
|----------------------------------|--------------------|-----------------|-----------------|-----------------|---------|
|                                  | <1 per month       | 1–3 per month   | 1–3 per week    | ≥4 per week     | P Trend |
| Raisins or grapes *              | 1.00(reference)    | 0.98(0.96–1.00) | 0.94(0.92–0.97) | 0.92(0.89–0.96) | <0.001  |
| Apples or pears *                | 1.00               | 0.94(0.90–0.97) | 0.95(0.91–0.98) | 0.91(0.88–0.95) | <0.001  |
| Strawberries *                   | 1.00               | 0.98(0.96–1.00) | 0.99(0.97–1.02) | 1.01(0.95–1.07) | 0.79    |
| Blueberries *                    | 1.00               | 0.97(0.95–0.98) | 0.95(0.92–0.98) | 0.92(0.83–1.03) | 0.01    |
| Avocado *                        | 1.00               | 0.97(0.95–0.99) | 0.92(0.87–0.96) | 0.94(0.77–1.14) | <0.001  |
| Spinach *                        | 1.00               | 0.99(0.97–1.01) | 0.99(0.97–1.01) | 0.98(0.93–1.02) | 0.32    |
| String beans *                   | 1.00               | 1.02(0.99–1.05) | 1.05(1.02–1.09) | 1.11(1.05–1.17) | <0.001  |
| Corn *                           | 1.00               | 1.02(0.99–1.05) | 1.03(1.00–1.07) | 1.05(0.98–1.12) | 0.004   |
| Broccoli *                       | 1.00               | 0.99(0.96–1.03) | 0.97(0.93–1.00) | 0.94(0.90–0.99) | <0.001  |
| Cauliflower                      | 1.00               | 1.00(0.98–1.02) | 1.04(1.01–1.07) | 1.06(0.99–1.14) | <0.001  |
| Brussel Sprouts *                | 1.00               | 1.02(1.00–1.04) | 1.04(1.00–1.08) | 1.23(1.04–1.46) | 0.03    |
| Carrots *                        | 1.00               | 0.99(0.95–1.03) | 0.97(0.93–1.01) | 0.95(0.91–0.99) | 0.003   |
| Tofu or soybeans *               | 1.00               | 0.95(0.93–0.98) | 1.01(0.97–1.07) | 0.88(0.79–0.99) | 0.001   |
| Cantaloupe *                     | 1.00               | 1.03(1.01–1.05) | 1.06(1.03–1.08) | 1.07(1.01–1.13) | 0.002   |

\* Pooled hazard ratios of the three cohorts using a fixed effects model. Adjusted for age, race/ethnicity (white, African-American, Asian, Hispanic, other), body mass index, current smoking status, physical activity, weight change per food frequency questionnaire cycle, menopausal status (in NHS I and NHS II), alcohol intake, current oral contraceptive use (in NHS II), analgesic use (nonsteroidal antiinflammatory drugs, acetaminophen, aspirin), family history of hypertension, total energy intake, animal flesh intake (combination of processed and unprocessed red meat, poultry and seafood), whole grains (quintiles), sugar-sweetened beverage intake, artificially-sweetened diet beverage intake. All vegetables were adjusted for each other, with a reference group of < 1serving/month.