Original Article

Long-term yogurt consumption and risk of incident hypertension in adults

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Objective: To evaluate the relation between yogurt consumption as well as cheese, milk, and total dairy, and high blood pressure (HBP) in two Nurses' Health Study cohorts (NHS, $n = 69\,298$), NHS II ($n = 84\,368$) and the Health Professionals Follow-Up Study (HPFS, $n = 30\,512$).

Methods: NHS, NHS II, and HPFS participants were followed for incident HBP for up to 30, 20, and 24 years, respectively. Hazard ratios were calculated using time-dependent multivariate-adjusted Cox proportional hazards models. Pooled risk estimates were derived from fixed effects meta-analyses.

Results: Participants consuming at least five servings per week (vs. <1 serving per month) of yogurt in NHS, NHS II, and HPFS had 19% (95% CI 0.75–0.87), 17% (95% CI 0.77–0.90), and 6% (95% CI 0.83–1.07) lower HBP risks, respectively. In pooled analyses of these cohorts, higher yogurt consumption was linked with 16% (95% CI 0.80–0.88) lower HBP risk; higher total dairy (3 to <6 vs. <0.5 servings/day), milk (2 to <6/day vs. <4/week) and cheese (1 to 4/day vs. <1/week) were associated with 16% (95% CI 0.81–0.87), 12% (95% CI 0.86–0.90), and 6% (95% CI 0.90–0.97) lower HBP risks, respectively. After controlling for BMI as a possible causal intermediate, total dairy, yogurt, milk, and cheese were associated with 13, 10, 8, and 8% lower HBP risks, respectively. The combination of higher yogurt intake and higher DASH ('Dietary Approaches to Stop Hypertension') diet scores was associated with 30% (95% CI 0.66–0.75) lower HBP risk compared with lower levels of both factors.

Conclusion: Higher total dairy intake, especially in the form of yogurt, was associated with lower risk of incident HBP in middle-aged and older adult men and women.

Keywords: dairy, Dietary Approaches to Stop Hypertension, epidemiology, fermented foods, long-term diet, nutrition, yogurt

Abbreviations: ACE, angiotensin-converting enzyme; ARIC, Atherosclerosis Risk in Communities; BP, blood pressure; CI, confidence intervals; DASH, Dietary Approaches to Stop Hypertension; FFQ, Food Frequency Questionnaire; HBP, high blood pressure; HPFS, Health Professionals Follow-Up Study; IPP, isoleucine–proline–proline; MET, metabolic equivalents; MI, myocardial infarction; NHS, Nurses' Health Study; S/month, serving per month; S/week, servings per week; SHR, spontaneously hypertensive rats; T2DM, type II diabetes mellitus; VPP, valine–proline–proline

INTRODUCTION

About 80 million American adults have high blood pressure (HBP) [1], resulting in more than 65 000 deaths annually [2]. The beneficial effects of dairy consumption on BP was demonstrated in the 'Dietary Approaches to Stop Hypertension' (DASH) randomized clinical trial wherein the greatest BP-lowering effects were found in the combined dietary intervention arm focusing on increasing intakes of low-fat dairy and fruits and vegetables [3]. Subsequent longitudinal studies found dairy intake to be inversely associated with mean BP and HBP risk in normal-weight and overweight adults [4–6]. Reviews and meta-analyses have generally confirmed these earlier results [7,8]. The 2010 *Dietary Guidelines for Americans* [9] cited moderate evidence for a beneficial effect of dairy consumption on BP, as well as cardiovascular disease and type 2 diabetes mellitus (T2DM) risk.

Yogurt is a form of dairy with high concentrations of casein and whey proteins, as well as calcium, magnesium, and potassium [10], all of which have been linked with BP-lowering effects in animal studies and some observational and experimental human studies [11]. Findings from the few available longitudinal studies examining the direct effects of yogurt intake on BP have been inconclusive [12–14]. Relatively low levels of yogurt intake in most studies may limit the statistical power to capture the true effect of clinically meaningful amounts of yogurt consumption.

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The current study aims to estimate the associations of long-term yogurt intake and other forms of dairy on risk of incident HBP among over 180 000 middle-aged women and men followed for 20–30 years in three prospective cohorts: The Nurses' Health Study (NHS), Nurses' Health Study II (NHS II), and the Health Professionals Follow-Up Study (HPFS).

METHODS

Study sample

The NHS enrolled 121 741 female registered nurses, initially 30–55 years of age in 1976. The NHS II was initiated in 1989 with enrollment of 116 430 female registered nurses ages 25–42 years. The HPFS began in 1986 with 51 529 men ages 40–75 years enrolled from various medical fields. Follow-up in all cohorts was conducted via questionnaire. Medical and lifestyle data were collected at baseline and biennially thereafter.

For the current analyses, men and women with baseline diagnoses of prevalent HBP, angina, stroke, myocardial infarction (MI), revascularization procedures, diabetes (type 1, type 2, gestational), or cancer were excluded. Additional exclusions included: participants who left more than 70 of 131 items blank on the baseline food frequency questionnaire (FFQ), unusual total energy intakes (<500 or >3500 kcal/day for women and <800 or >4200 kcal/day for men), missing follow-up HBP information, missing total dairy, or unusually high intakes of total dairy (≥6 s/day), cheese (>4 s/day), or milk (≥6 s/day). After exclusions, data from 69 298 NHS, 84 368 NHS II, and 30 512 HPFS participants were included in the current analyses, which were approved by the Institutional Review Board of Boston University School of Medicine.

Assessment of dairy and yogurt consumption

At baseline and follow-up exams, participants were asked to report usual intake in the past year of various foods including all dairy products, using validated, semi-quantitative FFQs [15]. Response categories ranged from 'never to <1/month' to '6+ per day.' Reported intakes were converted to continuous values by assigning the midpoint value of the chosen response category for each item. For these analyses, FFQ serving sizes were converted to standard United States Department of Agriculture MyPyramid serving sizes [16]. Using the MyPyramid definition of a dairy product, cream cheese, butter, and cream were excluded from the total dairy variable [16]. Thus, total dairy intake included: milk (skim, low-fat, whole), ice cream, sherbet/frozen yogurt, cheese (cottage, ricotta, hard, sliced), and yogurt (all types).

High blood pressure outcome ascertainment

At every biennial questionnaire, participants were asked to self-report incident physician diagnoses of HBP, a method of self-report has been previously validated in the NHS and HPFS cohorts [17–19].

Covariate assessment

Data on chronic disease risk factors including weight, age, physical activity, smoking, and family history of HBP were gathered biennially. Height (in meters) and weight (kilograms) were used to calculate BMI (weight/height^2). Total metabolic equivalent (MET) hours of activity per week (MET-hours/week) were calculated based on participants' self-reported average weekly time (frequency and duration) spent in activities of variable intensity [20–22].

As yogurt has been associated with an overall higher diet quality [23], a previously-described DASH diet score was explored as a potential modifier of the association between yogurt intake and HBP [24]. Also, as dairy intake is a component of the DASH score, the relevant dairy foods were dropped from the calculation of the score for each analysis. For example, models examining the combination of yogurt intake and a DASH score included the following variables in the calculation of the DASH score: fruits; vegetables; nuts and legumes; whole grains; red and processed meats; sugar-sweetened beverages; sodium; and total dairy minus yogurt [24]. Yogurt was also examined in combination with other individual dietary factors linked with blood pressure such as fruits and vegetables, fiber, whole grains, sodium, potassium, magnesium, and the sodium to potassium ratio. The DASH score was used in the final stratified models as it was associated with the most consistent effect estimates and had the least associated variability.

Statistical analysis

The dietary exposure period began at the time of first dietary assessment. Follow-up for incident HBP started at the end of that exam and continued until the first of the following censoring events: incident HBP, death, lost to follow-up, or end of follow-up for these analyses (30 June 2010 for NHS, 30 June 2009 for NHS II, and 31 January 2010 for HPFS).

To estimate long-term dairy consumption and to minimize the possibility of reverse causation, average intake for each dairy food was calculated as a cumulative average of all reported dietary intakes from the baseline FFQ to the exam before the first censoring event. Dietary intakes were weighted equally in calculating cumulative average intakes [25]. Updating of intake was stopped in the event of an interim MI, revascularization, stroke, diabetes, or cancer, as these events may lead to changes in usual dairy intake [25,26]. For missing dietary data, intakes were carried forward from the last nonmissing exam to the next reported intake. To compare the effects of short-term dairy intake with those associated with cumulative average intakes, we also estimated the association between the most recently updated dairy intakes and incident HBP (supplemental Table 1, http://links.lww.com/HJH/A921).

Each dairy food was categorized using cutoff values chosen to optimize analytical power while also reflecting intakes that were easily interpretable and applicable to daily recommendations and existing FFQ categories. For example, yogurt intake was categorized as: less than one serving per month (s/mo), one serving per month to less than one serving per week, one to less than two servings per week, two to less than five servings per week, and at least five servings per week. Using sensitivity analyses, yogurt intake was then collapsed into three categories: less than one serving per month (low), one serving per month to less than five servings per week (moderate), at least five servings per week (high); these intake groups were then cross-classified with tertiles of the DASH diet score to explore possible combined associations between high-yogurt consumption and the DASH score.

Rates of HBP occurrence were calculated in each category of dairy intake. Time-dependent Cox proportional hazards models were used to estimate the hazard ratios and the 95% confidence intervals (CI) for risk of incident HBP according to intake. Factors retained in the final multivariable models were those that confounded the estimated effect of dairy and HBP in at least some of the models by at least 10%. These included age, race, smoking, family history of HBP, physical activity, intakes of total energy, total protein, fruits and vegetables, and other dairy foods (e.g., yogurt models controlled for cheese and milk). Finally, updated BMI was added in separate models as it may function as either a potential confounder or a causal intermediate between dairy and HBP risk. Other potential confounders that were explored included family history of diabetes, MI, or hypercholesterolemia, pack-years of cigarettes smoked, alcohol intake, postmenopausal hormone use, oral contraceptive use (in NHS), aspirin and multivitamin use, and cumulative average intakes of the following dietary factors: carbohydrates, total fat, and fat subtypes (saturated, monounsaturated, polyunsaturated, omega-3, *trans* fatty acids), protein (animal, and plant), whole grains, total fiber, cereal fiber, nuts, sugar-sweetened beverages, potatoes, beans, red and processed meats, vitamin D, sodium, potassium, calcium, and magnesium. These variables were dropped from the final model as they had no effect on the hazard ratios.

All analyses were initially conducted for each cohort separately and then pooled using fixed-effects meta-analyses. To test for linear trend, a regression model was used to examine the shape of the relation across categories of dairy intake and HBP. The proportional hazards assumption was tested using a likelihood ratio test comparing the model with and without an interaction term between time period and each dairy exposure category. All statistical analyses were carried out using Statistical Analysis Software (SAS) version 9.4 (SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

There were 82 382 total incident HBP cases in the three cohorts: 41 934 during 30 years of follow-up in NHS; 26 282 during 20 years in NHS II, and 14 166 during 24 years in the HPFS. Mean baseline ages in the three cohorts were 44.6, 35.8, and 50.7 years, respectively.

Age-adjusted baseline demographic characteristics according to yogurt intake categories (frequency of consuming one cup) in all three cohorts are shown in Table 1. Those with the highest yogurt intakes were more active, had lower BMIs, were less likely to smoke, and had higher diet quality as reflected in higher DASH diet scores.

Table 2 shows the association between total dairy intake and HBP risk in the three cohorts. After adjusting for age, race, physical activity, smoking, HBP family history, and intakes of fruits and vegetables, total protein and energy, those in the NHS, NHS II, and HPFS cohorts who consumed at least three servings per day (vs. <0.5 servings per day) of total dairy had 13% (95% CI 0.83–0.91), 25% (95% CI 0.70–0.79), and 7% (95% CI 0.86–1.00) lower risks of HBP, respectively. There were statistically significant inverse linear trends in all three cohorts. Addition of BMI to the models did not significantly change the beneficial associations for all three cohorts: NHS – 11%, NHS II – 19%, HPFS – 9%. The rates of HBP show that the younger women consuming at least three servings per day of dairy in NHS II had 637 fewer cases of incident HBP (per 100 000 person-years) than those consuming <0.5 s/day. In contrast, HPFS men (who were ≥50 years older) had only 166 fewer cases per 100 000 person-years associated with higher dairy intakes.

Table 3 shows the impact of long-term yogurt consumption on HBP risk. Those who regularly consumed at least five servings per week (vs. <1 s/mo) of yogurt in the NHS, NHS II, and HPFS cohorts, respectively, had 19% (95% CI 0.75–0.87), 17% (95% CI 0.77–0.90), and 6% (95% CI 0.83–1.07) lower risks of HBP. Addition of BMI to the models did not significantly change the hazard ratios for all three cohorts: NHS – 0.87, NHS II – 0.89, HPFS – 1.01. The HBP rate differences between the highest and lowest categories of yogurt intake were similar across the three cohorts (453, 374, and 446/100 000 person-years, respectively).

Table 4 shows fixed effects pooled analyses results examining HBP risk associated with intakes of total dairy, yogurt, cheese, and milk in the combined cohorts. Although the hazard ratios were not markedly different in the three cohorts, the I^2 values indicate that there was heterogeneity across the cohorts for milk and cheese intakes but not for yogurt. Overall, consuming at least three servings per day of dairy (vs. <0.5 servings/day) was associated with a 16% (95% CI 0.81–0.87) lower HBP risk. Regular yogurt intake (≥5 servings per week vs. <1 serving per month) was linked with a 16% lower HBP risk. Adding BMI to the multivariable models led to little attenuation of the pooled hazard ratios. HBP incidence rates among those with the lowest intakes of cheese, milk, and yogurt were 2507, 2593, and 2594 cases per 100 000 person-years, respectively. Increasing intakes (to the highest intake categories) was associated with reductions in these incidence rates by 325, 251, and 601 cases per 100 000 person-years, for cheese, milk, and yogurt, respectively. Finally, the linear model results found an 18% (95% CI 0.78–0.85) lower HBP risk associated with each additional serving of yogurt per day compared with lower risk reductions for other forms of dairy. Results using the most recent dairy exposures (not shown) yielded similar results compared with using cumulative average intakes.

Figure 1 and supplemental Table 2 (http://links.lww.com/HJH/A921) illustrates the combined associations of yogurt intake and the DASH diet score on HBP risk from a pooled analysis, adjusting for age, race, physical activity, total protein, energy, smoking, and HBP family history. Compared with those who had low yogurt intakes and a low DASH diet score (the referent group), those who had both a higher DASH diet score (highest tertile) and consumed at least five servings per week of yogurt had a 30% lower HBP risk (95% CI 0.66–0.75). In contrast, the highest DASH score alone led to only a 19% (95% CI 0.79–0.83) lower HBP risk among those who consumed yogurt less than once per week.

TABLE 1. Baseline characteristics of The Nurses' Health Study, Nurses' Health Study II, and the Health Professionals Follow-Up Study participants in each yogurt intake category

	Yogurt intake categories (1 cup)				
NHS (*N* = 69 298)	Less than one per month (*N* = 22 433)	One per month to less than one per week (*N* = 14 683)	One to less than two per week (*N* = 20 127)	Two to less than five per week (*N* = 10 718)	At least five per week (*N* = 1337)
Mean (SD)[a]					
Age (years)	46.7 (7.1)	45.1 (7.1)	44.5 (6.9)	44.4 (6.9)	45.1 (7.0)
Activity (MET-hours/week)	11.6 (15.5)	12.8 (19.2)	14.4 (18.9)	16.3 (21.4)	19.0 (27.1)
BMI (kg/m^2)	24.0 (4.1)	24.0 (4.1)	23.9 (3.9)	23.7 (3.9)	23.5 (3.9)
Current smoker, %	37.9	27.4	23.9	22.5	22.7
Energy (kcal/day)	1539 (504)	1538 (490)	1566 (490)	1639 (500)	1737 (540)
Total dairy (s/day)	1.4 (1.1)	1.6 (1.1)	1.7 (1.1)	2.0 (1.2)	2.4 (1.4)
Yogurt (s/day)	0.01 (0.02)	0.05 (0.08)	0.11 (0.19)	0.27 (0.37)	0.60 (0.83)
Milk (s/day)	0.80 (0.98)	0.87 (0.98)	0.90 (0.96)	0.96 (1.00)	1.05 (1.10)
Cheese (s/day)	0.48 (0.51)	0.52 (0.49)	0.56 (0.50)	0.61 (0.54)	0.65 (0.59)
DASH diet score	22.0 (4.5)	23.5 (4.4)	24.5 (4.4)	25.7 (4.4)	26.5 (4.4)
Fruits and vegetables (s/day)	3.5 (1.9)	3.9 (2.0)	4.1 (2.0)	4.6 (2.2)	5.0 (2.3)
Fiber (g/day)	15.4 (4.1)	16.2 (4.2)	16.8 (4.4)	17.5 (4.6)	17.6 (4.6)
Red and processed meats (s/day)	1.8 (0.99)	1.7 (0.96)	1.6 (0.94)	1.5 (0.91)	1.4 (0.95)
Total protein (g/day)	72.8 (14.7)	75.3 (14.7)	76.9 (14.8)	78.5 (15.2)	79.4 (15.7)
NHS II (*N* = 84 368)	(*N* = 23 616)	(*N* = 18 250)	(*N* = 23 339)	(*N* = 16 546)	(*N* = 2617)
Age (years)	36.0 (4.7)	35.9 (4.7)	35.9 (4.7)	36.0 (4.7)	36.1 (4.6)
Activity (MET-hours/week)	18.0 (24.8)	19.3 (25.5)	21.5 (27.0)	25.1 (31.3)	30.3 (36.1)
BMI (kg/m^2)	24.7 (5.4)	24.4 (5.0)	23.9 (4.5)	23.9 (4.6)	24.1 (5.0)
Current smoker, %	16.5	11.8	10.2	9.3	9.6
Energy (kcal/day)	1705 (547)	1752 (538)	1811 (534)	1893 (540)	1993 (571)
Total dairy (s/day)	1.5 (1.2)	1.7 (1.2)	1.9 (1.2)	2.1 (1.2)	2.5 (1.3)
Yogurt (s/day)	0.01 (0.03)	0.06 (0.07)	0.14 (0.18)	0.29 (0.30)	0.63 (0.63)
Milk (s/day)	1.0 (1.0)	1.1 (1.0)	1.1 (1.0)	1.2 (1.0)	1.2 (1.1)
Cheese (s/day)	0.41 (0.42)	0.44 (0.43)	0.46 (0.42)	0.48 (0.44)	0.49 (0.49)
DASH diet score	22.0 (4.7)	23.8 (4.7)	25.0 (4.8)	26.5 (4.8)	27.8 (4.9)
Fruits and vegetables (s/day)	4.3 (2.6)	4.8 (2.6)	5.3 (2.8)	6.0 (3.1)	6.7 (3.6)
Fiber (g/day)	17.0 (5.3)	18.1 (5.3)	18.7 (5.3)	19.5 (5.6)	20.1 (7.0)
Red and processed meats (s/day)	1.2 (0.7)	1.2 (0.7)	1.1 (0.7)	1.1 (0.7)	1.0 (0.7)
Total protein (g/day)	84.6 (16.0)	86.2 (15.0)	86.8 (14.7)	87.9 (14.7)	89.3 (15.9)
HPFS (*N* = 30 512)	(*N* = 15 860)	(*N* = 6205)	(*N* = 4921)	(*N* = 2883)	(*N* = 643)
Age (years)	52.6 (9.3)	50.7 (8.9)	50.0 (8.7)	51.2 (9.2)	51.4 (9.6)
Activity (MET-hours/week)	19.8 (27.1)	22.9 (33.0)	25.7 (33.7)	26.0 (29.2)	32.5 (41.3)
BMI (kg/m^2)	25.3 (3.0)	25.2 (3.0)	25.0 (3.0)	25.0 (3.1)	24.4 (2.8)
Current smoker, %	13.0	7.3	5.3	4.2	4.2
Energy (kcal/day)	1969 (617)	1984 (614)	2058 (614)	2123 (629)	2297 (673)
Total dairy (s/day)	1.4 (1.1)	1.4 (1.1)	1.6 (1.1)	1.8 (1.2)	2.4 (1.4)
Yogurt (s/day)	0.01 (0.02)	0.06 (0.08)	0.16 (0.20)	0.30 (0.29)	0.78 (0.76)
Milk (s/day)	0.9 (1.0)	0.9 (1.0)	0.9 (1.0)	1.0 (1.0)	1.1 (1.1)
Cheese (s/day)	0.41 (0.44)	0.41 (0.42)	0.44 (0.43)	0.44 (0.43)	0.52 (0.55)
DASH diet score	22.3 (5.0)	24.4 (5.0)	25.6 (4.9)	26.8 (4.9)	28.1 (4.9)
Fruits and vegetables (s/day)	4.8 (2.5)	5.5 (2.7)	6.0 (2.9)	6.5 (3.0)	7.0 (3.5)
Fiber (s/day)	19.6 (6.7)	21.5 (6.8)	22.3 (7.2)	23.2 (7.4)	23.2 (7.8)
Red and processed meats (s/day)	1.3 (0.9)	1.1 (0.8)	1.0 (0.8)	0.9 (0.8)	0.9 (0.8)
Total protein (s/day)	90.5 (16.4)	92.8 (16.1)	93.0 (15.6)	94.0 (16.1)	94.0 (16.7)

NHS, Nurses' Health Study; SD, standard deviation; s/day, servings per day; HPFS, Health Professionals Follow-Up Study.
[a]Values are means (SD) or percentages and are standardized to the age distribution of the study population.

DISCUSSION

Across all three cohorts, higher intakes of total dairy, and particularly yogurt, were associated with lower risks of incident HBP. Data from each cohort separately showed that total dairy consumption was more strongly associated with a lower HBP risk in the cohort of younger women (NHS II) than in the cohort of older men (HPFS). The associations between yogurt consumption and HBP risk were also weaker in the HPFS cohort, which could be because of inherent differences between the cohorts such as age or other diet and lifestyle factors. In addition, there were proportionately fewer men in the highest yogurt intake category, in which yogurt intakes were lower in men than in women.

Participants who consumed the most yogurt tended to have healthier diets overall as measured by a DASH diet score. These results suggest a combined positive association of yogurt consumption with a DASH diet in that participants in the highest category on both factors had

TABLE 2. Total dairy intakes and risk of high blood pressure in three cohorts

NHS					
Dairy intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard Ratio (95% CI)[b]
<0.5/day	3570	2903	1.00	1.00	1.00
0.5 to <1.5/day	19 027	3157	0.99 (0.95-1.02)	0.95 (0.92-0.99)	0.95 (0.92-0.98)
1.5 to <3/day	15 255	3195	0.96 (0.92-0.99)	0.90 (0.87-0.94)	0.90 (0.87-0.94)
3 to <6/day	4082	2864	0.96 (0.91-1.00)	0.87 (0.83-0.91)	0.89 (0.85-0.94)
		P for linear trend[c]	*0.003*	*<0.0001*	*<0.0001*
		Per one serving/day	0.98 (0.97-0.99)	0.96 (0.94-0.97)	0.97 (0.95-0.98)

NHS II					
Dairy intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<0.5/day	2379	2072	1.00	1.00	1.00
0.5 to <1.5/day	11 830	2056	0.99 (0.95-1.03)	0.96 (0.92-1.01)	0.96 (0.92-1.01)
1.5 to <3/day	9395	1917	0.94 (0.90-0.99)	0.88 (0.84-0.93)	0.91 (0.87-0.96)
3 to <6/day	2678	1435	0.84 (0.80-0.89)	0.75 (0.70-0.79)	0.81 (0.76-0.86)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		Per one serving/day	0.95 (0.93-0.96)	0.91 (0.90-0.93)	0.94 (0.92-0.95)

HPFS					
Dairy intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<0.5/day	1966	2961	1.00	1.00	1.00
0.5 to <1.5/day	7102	2996	0.98 (0.93-1.03)	0.98 (0.93-1.04)	0.97 (0.92-1.02)
1.5 to <3/day	3742	2847	0.90 (0.85-0.95)	0.90 (0.85-0.96)	0.89 (0.84-0.95)
3 to <6/day	1356	2795	0.94 (0.88-1.01)	0.93 (0.86-1.00)	0.91 (0.85-0.99)
		P for linear trend[c]	*0.001*	*0.0007*	*0.0005*
		Per one serving/day	0.97 (0.95-0.99)	0.96 (0.94-0.98)	0.96 (0.94-0.98)

NHS, Nurses' Health Study; HPFS, Health Professionals Follow-Up Study; I/100K PY, incidence per 100 000 person-years; CI, confidence interval.
[a]Adjusted for age, race, physical activity, smoking, HBP family history, and intakes of total energy, fruits and vegetables, and total protein.
[b]Multivariable model with BMI.
[c]Linear trend across total dairy intake categories was quantified with a Wald test for linear trend by assigning the median value from each category and modeling it as a continuous variable.

TABLE 3. Yogurt consumption and risk of incident high blood pressure in three cohorts

NHS					
Yogurt intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<1/month	18 062	2948	1.00	1.00	1.00
1/month to <1/week	9026	3115	1.01 (0.99-1.04)	1.00 (0.98-1.03)	1.00 (0.97-1.02)
1 to <2/week	9481	3507	1.00 (0.96-1.01)	0.98 (0.95-1.00)	0.99 (0.96-1.01)
2 to <5/week	4642	3227	0.92 (0.89-0.95)	0.92 (0.89-0.95)	0.95 (0.92-0.98)
≥5/week	723	2495	0.80 (0.75-0.87)	0.81 (0.75-0.87)	0.87 (0.81-0.94)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		Per one serving/day	0.81 (0.76-0.85)	0.80 (0.76-0.85)	0.87 (0.82-0.93)

NHS II					
Yogurt intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<1/month	9474	1936	1.00	1.00	1.00
1/month to <1/week	5709	1865	0.94 (0.91-0.97)	0.95 (0.92-0.98)	0.96 (0.93-1.00)
1 to <2/week	6016	2024	0.90 (0.87-0.93)	0.91 (0.88-0.94)	0.95 (0.92-0.98)
2 to <5/week	4352	1916	0.87 (0.84-0.91)	0.89 (0.86-0.93)	0.93 (0.90-0.97)
≥5/week	731	1562	0.80 (0.75-0.87)	0.83 (0.77-0.90)	0.89 (0.82-0.96)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		Per one serving/day	0.76 (0.72-0.82)	0.80 (0.75-0.85)	0.87 (0.82-0.93)

HPFS					
Yogurt intake	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<1/month	7832	3000	1.00	1.00	1.00
1/month to <1/week	3019	2852	0.96 (0.92-1.00)	0.98 (0.94-1.02)	0.98 (0.93-1.02)
1 to <2/week	1943	2902	0.90 (0.86-0.95)	0.93 (0.89-0.98)	0.94 (0.89-0.99)
2 to <5/week	1117	2823	0.90 (0.85-0.96)	0.94 (0.88-1.00)	0.95 (0.89-1.01)
≥5/week	255	2554	0.90 (0.80-1.02)	0.94 (0.83-1.07)	1.01 (0.89-1.15)
		P for linear trend[c]	*0.0003*	*0.03*	*0.26*
		Per one serving/day	0.83 (0.74-0.92)	0.89 (0.80-0.99)	0.94 (0.84-1.05)

NHS, Nurses' Health Study; HPFS, Health Professionals Follow-Up Study; I/100K PY, incidence per 100 000 person-years; CI, confidence interval.
[a]Adjusted for age, race, physical activity, smoking, HBP family history, and intakes of total energy, fruits and vegetables, total protein, milk, and cheese.
[b]Multivariable model with BMI.
[c]Linear trend across yogurt intake categories was quantified with a Wald test for linear trend by assigning the median value from each category and modeling this variable as a continuous variable.

TABLE 4. Pooled analyses of total dairy and individual forms of dairy and risk of incident high blood pressure

Total dairy	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[a]	Multivariable + BMI hazard ratio (95% CI)[b]
<0.5/day	7976	2610	1.00	1.00	1.00
0.5 to <1.5/day	37 974	2682	0.98 (0.96–1.01)	0.96 (0.94–0.99)	0.96 (0.93–0.98)
1.5 to <3/day	28 270	2580	0.94 (0.92–0.96)	0.90 (0.87–0.92)	0.90 (0.88–0.93)
to <6/day	8163	2156	0.92 (0.89–0.94)	0.84 (0.81–0.87)	0.87 (0.84–0.90)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		I^2	*87.4*	*91.6*	*74.3*
		Per one serving/day	0.97 (0.96–0.98)	0.94 (0.93–0.95)	0.96 (0.95–0.96)

Yogurt	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[d]	Multivariable + BMI hazard ratio (95% CI)[b]
<1/month	35 368	2594	1.00	1.00	1.00
1/month to <1/week	17 754	2530	0.98 (0.96–1.00)	0.98 (0.96–1.00)	0.98 (0.97–1.00)
1 to <2/week	17 441	2749	0.94 (0.93–0.96)	0.95 (0.93–0.97)	0.97 (0.95–0.99)
2 to <5/week	10 111	2463	0.90 (0.88–0.92)	0.91 (0.89–0.93)	0.94 (0.92–0.97)
≥5/week	1709	1993	0.82 (0.78–0.86)	0.84 (0.80–0.88)	0.90 (0.86–0.95)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		I^2	*4.3*	*34.8*	*0.0*
		Per one serving/day	0.79 (0.76–0.82)	0.82 (0.78–0.85)	0.88 (0.85–0.92)

Cheese	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[e]	Multivariable + BMI hazard ratio (95% CI)[b]
<1/week	13 789	2507	1.00	1.00	1.00
1–4/week	48 922	2655	1.00 (0.98–1.02)	0.99 (0.97–1.01)	0.97 (0.95–0.99)
5/week to <1/day	14 521	2563	0.98 (0.96–1.01)	0.97 (0.94–0.99)	0.94 (0.92–0.96)
1–4/day	5151	2182	0.97 (0.94–1.00)	0.94 (0.90–0.97)	0.92 (0.89–0.95)
		P for linear trend[c]	*0.008*	*<0.0001*	*<0.0001*
		I^2	*77.0*	*81.8*	*48.0*
		Per one serving/day	0.97 (0.94–0.99)	0.94 (0.91–0.96)	0.92 (0.89–0.94)

Milk	Cases	I /100K py	Age-adjusted hazard ratio (95% CI)	Multivariable hazard ratio (95% CI)[e]	Multivariable + BMI hazard ratio (95% CI)[b]
<4/week	30 843	2593	1.00	1.00	1.00
4/week to <1/day	15 429	2817	0.99 (0.97–1.01)	0.98 (0.96–1.00)	0.98 (0.96–1.00)
1 to <2/day	21 038	2573	0.97 (0.96–0.99)	0.95 (0.93–0.97)	0.96 (0.94–0.98)
2 to <6/day	15 013	2342	0.93 (0.91–0.95)	0.88 (0.86–0.90)	0.92 (0.90–0.94)
		P for linear trend[c]	*<0.0001*	*<0.0001*	*<0.0001*
		I^2	*92.0*	*93.1*	*80.6*
		Per one serving/day	0.97 (0.96–0.98)	0.95 (0.94–0.96)	0.96 (0.95–0.97)

[a]Baseline model is adjusted for age, race, physical activity, smoking, family history of HBP, intakes of fruits and vegetables, total protein, and total energy.
[b]Second model for each dairy food category adds BMI to each corresponding multivariable model.
[c]Linear trend across intake categories was quantified with a Wald test for linear trend by assigning the median value from each category and modeling this variable as a continuous variable.
[c]Baseline model with intakes of milk and cheese.
[d]Baseline model with intakes of yogurt and milk.
[e]Baseline model with intakes of yogurt and cheese.

lower risks of HBP. Previous analyses in the Framingham Offspring and Third Generation cohorts found that yogurt consumers (vs. nonconsumers) tended to have lower cardiometabolic risks including HBP, elevated triglycerides and glucose, and insulin resistance even after adjusting for diet quality [23]. Another Framingham analysis found that consuming at least one serving per week of yogurt was associated with lower SBP levels and HBP risk over 10 years of follow-up [12]. Some but not all other studies have also found yogurt consumption to be associated with reductions in cardiometabolic risk (including BP) [27–31], although most studies have had too few participants who consumed yogurt regularly to evaluate long-term effects.

Consistent with other studies [7,13,32], our results provide further support for current Dietary Guidelines promoting dairy intake [33] and also support the beneficial effects seen in earlier DASH diet trials [3,34]. Participants in this study consuming three to six servings per day of dairy had a 16% lower risk of developing HBP. These results are consistent with longitudinal data from the Framingham Offspring Study [12], Atherosclerosis Risk in Communities Study [13], and middle-aged adults in a French cohort [35]. A study of the general Dutch population found no consistent effect of total dairy but a trend toward lower risks of incident hypertension associated with low-fat dairy [36]. In the general British population, total dairy was associated with a weak, but nonstatistically significant trend toward lower hypertension risk [37].

We observed a small inverse association between cheese intake and HBP risk in our analyses. In a recent review of full-fat dairy products, Astrup *et al.* [38] concluded that

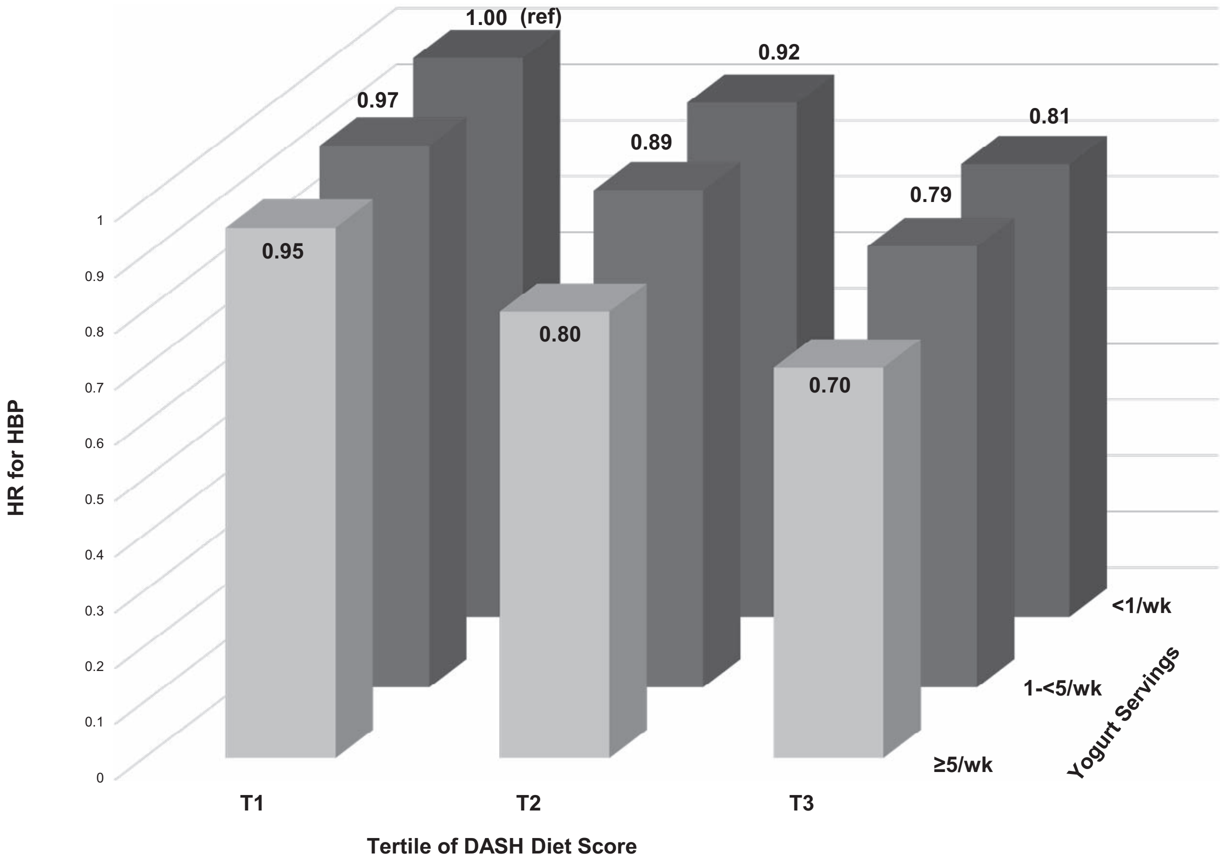

FIGURE 1 Pooled analysis of yogurt servings per week cross-classified with tertiles of a Dietary Approaches to Stop Hypertension diet score and risk of incident hypertension. Yogurt intake servings were classified into three categories of intake reflecting low, medium, and high intakes. DASH diet score were classified using tertiles of the score across the three cohorts. Analyses were adjusted for age, race, physical activity, energy intake, smoking, and family history of HBP. DASH, Dietary Approaches to Stop Hypertension; HBP, high blood pressure.

cheese consumption was not associated with adverse effects on metabolic health, including BP. A meta-analysis of four studies also found no association between cheese consumption and elevated BP [7].

The nutrient composition of dairy is one of several possible mechanisms that may benefit BP. Dairy is a source of potassium, for example, which has been shown to lower BP [39] in a dose–response manner among both normotensive and hypertensive individuals through its effects on smooth muscle relaxation and vasodilation.

Yogurt is made through fermentation, in which biologically active peptides, such as isoleucine–proline–proline (IPP) and valine–proline–proline (VPP), are formed when milk proteins are catalyzed by proteolytic lactic acid bacteria, such as *Lactobacillus helveticus* [40]. IPP and VPP have been shown to promote antihypertensive effects by inhibiting angiotensin-converting enzyme (ACE), a key regulator of BP, fluid, and electrolyte balance [41]. These effects have been shown in-vitro [42] and in spontaneously hypertensive rats (SHR) [43]. In one study of SHR, investigators found that while supplemental IPP and VPP lowered BP, water supplemented with potassium, calcium, magnesium, and sodium also lowered BP. However, the greatest lowering of BP was seen among rats fed fermented milk [44]. Finally, a meta-analysis of 14 randomized feeding trials of probiotic milk interventions found modest overall reductions in SBP (3.10 mmHg) and DBP (1.09 mmHg) [45], with a stronger effect (SBP, 3.98 mmHg) in hypertensive individuals.

Yogurt is also a rich source of both calcium and vitamin D, which have been shown to work together in vascular smooth muscle cells to regulate BP via regulation of intracellular calcium concentrations [46,47]. In-vitro studies have also shown beneficial effects of these nutrients on inflammatory and atherosclerotic agents in hypertensive rats [48–50] but further studies in humans are needed to test these potential mechanisms.

In the current study, individuals who consumed more yogurt (and more dairy) also consumed less red and processed meat, sugar-sweetened beverages, refined carbohydrates, and added sugars. Therefore, the observed reduced risk of HBP associated with dairy and yogurt intakes could partly result from a replacement effect. Yogurt may be a marker of a healthy lifestyle and the observed inverse associations may be because of residual confounding with imperfect adjustment for other factors. Yogurt may support weight maintenance during the middle-adult years, thus indirectly benefitting BP by lessening aging-related weight gain [51]. Previous analyses in these same cohorts have shown an inverse association between yogurt consumption and weight gain whereas other dairy foods did not appear to have significant effects on weight [27]. The addition of

BMI as a potential causal intermediate in our multivariable model partially attenuated the results.

Our study has several important strengths including its large sample size that enabled us to categorize the participants more precisely. The high follow-up rates and availability of repeated measures of dietary intake, demographic and lifestyle variables are also important strengths. To our knowledge, this is the first longitudinal study with sufficient power to estimate the long-term dose–response relation of usual yogurt intake and incident HBP.

Our study also has some limitations. All three cohorts were predominantly Caucasian. Although the homogeneity of race, education, and socioeconomic status may help to reduce confounding, our results may not be generalized to other populations. There is strong evidence, for instance, of racial differences in HBP risk in the literature [52]. Another limitation relates to the use of FFQs, which are prone to a certain degree of measurement error. However, yogurt is usually eaten as an individual food and may be less susceptible to biased reporting and errors associated with the reporting of mixed dishes [53]. Finally, data on yogurt type were not available making it impossible to examine the specific effects of yogurt's protein or probiotic content.

Some of the current pooled analyses had high levels of heterogeneity. This could be because of the inherent differences among the cohorts in terms of various BP-related risk factors such as sex and age (mean baseline ages were 45, 36, and 52 years in the NHS, NHS II, and HPFS cohorts, respectively). Additionally, men have a higher risk of HBP than women until age 45, whereas older women have a higher HBP risk than men [54].

On the basis of the results of the current study, we conclude that higher total dairy intake especially in the form of yogurt was associated with a lower risk of developing HBP during the middle adult years. This association was particularly strong among adults with a generally healthy diet pattern.

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Conflicts of interest

There are no conflicts of interest.

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