Regular Yogurt Intake and Risk of Cardiovascular Disease Among Hypertensive Adults

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BACKGROUND
High blood pressure (HBP) is a major cardiovascular disease (CVD) risk factor. Clinical trials including Dietary Approaches to Stop Hypertension (DASH) have demonstrated beneficial effects of dairy consumption on risks of HBP and CVD. Yogurt, a fermented dairy product, may independently be related to CVD risk.

OBJECTIVE
To evaluate the association between yogurt consumption and CVD risk among hypertensive individuals in 2 large cohorts and to determine whether the association differs among those whose eating pattern more closely resembles the DASH diet.

METHODS
Overall, 55,898 female Nurses' Health Study (NHS) and 18,232 male Health Professionals Follow-Up Study (HPFS) participants with prevalent HBP were included. Cumulative average estimates of yogurt intake from validated food frequency questionnaires were related to verified self-reported CVD outcomes using Cox proportional hazards models. Hazard ratios and 95% confidence intervals (CI) were adjusted for CVD risk factors, medications, and diet covariates.

RESULTS
Yogurt intake was inversely associated with CVD risk (myocardial infarction and stroke) among hypertensive participants (P <0.01 in both cohorts). Among participants consuming ≥2 servings/week of yogurt, NHS women had a 17% (95% CI: 0.74–0.92) lower risk while HPFS men experienced a 21% (95% CI: 0.66–0.96) lower CVD risk compared to those who consumed <1 serving/month. Regular yogurt consumers with higher DASH diet scores had 16% (95% CI: 0.73–0.96) and 30% (95% CI: 0.57–0.85) CVD risk reductions in the 2 cohorts, respectively.

CONCLUSION
Hypertensive men and women who consumed ≥2 servings/week of yogurt, especially in the context of a healthy diet, were at lower risk for developing CVD.

Keywords: blood pressure; dairy; diet; dietary approaches to stop hypertension; hypertension; yogurt.

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High blood pressure (HBP) not only affects about 1 billion people worldwide but there is compelling evidence that it is a major cause of cardiovascular morbidity and overall mortality.[1] HBP is linked with an increased risk of cardiovascular disease (CVD) through a variety of mechanisms including arterial stiffness[2] and direct effects on vascular endothelial function.[3]

Higher dairy consumption has been associated with beneficial effects on CVD-related comorbidities such as hypertension,[4,5] type 2 diabetes, insulin resistance,[6,7] and dyslipidemia.[5] One of the earliest studies to show a beneficial effect of dairy intake on risk of HBP was the Dietary Approaches to Stop Hypertension (DASH) clinical trial, in which participants in the combination diet group (fruits and vegetables plus low-fat dairy) experienced the greatest BP-lowering effect compared to both the control Western diet and the fruits and vegetables only groups.[8] Later studies demonstrated that the DASH dietary pattern was associated with a reduced risk of both fatal and nonfatal CVD.[9,10]

Yogurt intake in the United States has increased substantially in the past decade.[11] Early studies suggested that regular consumption of fermented dairy products such as yogurt was associated with a lower risk of atherosclerotic vascular disease[12] and a reduction in arterial stiffness[13] in hypertensive subjects. A meta-analysis of 13 randomized controlled

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trials found that probiotic fermented milk (vs. placebo) was associated with a 3.98 mm Hg reduction in systolic blood pressure among hypertensive adults and a 2.09 mm Hg reduction among normotensives,[14] raising the possibility of a greater CVD benefit of yogurt consumption among hypertensives than nonhypertensives.[15]

While yogurt is known to be a nutrient-rich food and a source of probiotic bacteria, there are few large, longitudinal studies of yogurt's specific health effects rather than overall dairy consumption. To our knowledge, there is no published evidence on long-term yogurt intake and CVD risk among individuals with prevalent HBP. Our goal was to examine the association between yogurt intake and risk of CVD among those with prevalent HBP and to determine whether this association differs among those whose diet more closely resembles a heart-healthy dietary pattern.

METHODS

For the current analyses, participants included those with prevalent HBP from the Nurses' Health Study (NHS, N = 121,700, ages 30–55 at enrollment in 1980) and the Health Professionals Follow-Up Study (HPFS, N = 51,529, ages 40–75 at enrollment in 1986). The date of the first self-reported HBP diagnosis served as the baseline for these analyses. Hence, the baseline visit differed depending on when HBP was first reported. Participants without HBP were excluded, as were those with missing data on dairy intake, missing, or implausible energy intake (<500 or ≥3,500 kilocalories/day for NHS and <800 or ≥4,200 kilocalories/day for HPFS), or prevalent cancer, diabetes, or CVD (including revascularization, angina, myocardial infarction (MI), or stroke) at or before first diagnosis of HBP, leaving 55,898 and 17,984 NHS and HPFS participants, respectively, for the current analyses. Analyses were approved by the Institutional Review Board of Boston University School of Medicine.

Dairy and yogurt intake assessment

In the NHS, participants were asked to complete a mailed 61-item semiquantitative food frequency questionnaire (FFQ) in 1980 to report usual dietary intake in the preceding year. They were asked how often, on average, they consumed servings of each listed food item from the questionnaire using 9 possible response categories, ranging from "never or less than once a month" to "6 or more a day." An expanded 131-item FFQ was sent in 1984, 1986, and every 4 years thereafter until 2006. The same version of the FFQ was used from 1986 through 2006 for HPFS participants.[16]

The following foods were included in the estimation of total dairy intake in our analyses: milk (skim, low-fat, reduced-fat, and whole), yogurt, ice cream, sherbet, frozen yogurt, cottage/ricotta cheese, and other cheese. Servings of dairy foods were defined using MyPyramid servings from the United States Department of Agriculture (USDA).[17] Cream cheese and cream were excluded from the dairy variable we created as they did not meet the MyPyramid definition of a dairy food—one that is made from milk and retains its calcium content.[17] Finally, a DASH diet score was calculated for each participant.[9] While yogurt is a part of the usual DASH score, it was excluded from calculation of the score in these analyses.

Assessment of HBP

A participant who reported a HBP diagnosis on the enrollment questionnaire in 1980 (NHS) or 1986 (HPFS) was considered to have prevalent HBP. Those without HBP at enrollment were asked on each subsequent biennial questionnaire for any new diagnoses of HBP. Participants were considered to have prevalent HBP at first report and throughout the rest of the study. The validity of self-reported HBP has been examined in both the NHS and HPFS cohorts.[18,19] In the NHS, 77% of 51 cases of self-reported HBP in the validation study had either systolic blood pressure or diastolic blood pressure levels >160 or 95 mm Hg *via* standard BP measurement.[18] In the HPFS, a medical record review of a random sample of 100 participants reporting a diagnosis of HBP in 1988 confirmed the diagnosis in all participants.[20] Further, self-reported HBP among participants in the validation study was highly predictive of subsequent cardiovascular events.[19]

CVD outcome ascertainment

The assessment and diagnosis of CVD in these cohorts has been previously described.[21] For the current analyses, the primary outcomes include major CHD (nonfatal and fatal MI) and stroke (nonfatal and fatal) cases. As a secondary outcome, cases of revascularization are included.

On each biennial questionnaire, participants reported any interim physician-diagnosed events including MI, stroke, and revascularization. Permission was requested to access medical records to confirm all reported new diagnoses. World Health Organization criteria (diagnostic symptoms, electrocardiographic findings, or elevated cardiac enzyme concentrations) were used to confirm nonfatal MI.[22] Nonfatal stroke was confirmed using computed tomography, magnetic resonance imaging results or the National Survey of Stroke criteria (i.e., medical record confirmation of a neurological deficit with sudden or rapid onset that persisted more than 24 hours or until death).[23] Fatal MI and stroke were validated *via* physician review of death or medical records. CVD events in which no medical records were available but were deemed probable were included in these analyses, as was previously shown.[21]

Covariates assessment

A large number of potential confounding variables were explored including sociodemographic factors, family history, and other diet and lifestyle factors. Questionnaires were used to collect data on smoking status, physical activity (estimated as metabolic equivalent tasks [METs] per week), other lifestyle factors, and family history of HBP and MI.

Body mass index was calculated as the self-reported weight (in kg) divided by the height squared (in meters).

Statistical analyses

Yogurt intake for each participant was estimated as the cumulative average intake starting at the time of the first HBP diagnosis and stopping at the time of first occurrence of one of the following censoring events: date of CVD diagnosis, date of death, loss to follow-up, or end of follow-up (30 June 2010 for NHS and 31 January 2010 for HPFS). The calculation of cumulative average intakes has been previous described in detail.[24] This methodology is used to minimize exposure measurement error and is intended to reflect changes in yogurt intake over time. The DASH diet score was also computed from cumulative average of each score component. Due to concerns about changes in self-reported dietary intakes following certain diagnoses, secondary analyses were conducted in which dietary intakes were not updated following after exams at which participants reported the occurrence of angina, revascularization, or elevated cholesterol.[24,25] In these cases, cumulative average dietary intakes were carried forward to the exam prior to the occurrence of one of these events. We compared these results with our primary analyses in which cumulative average intake was calculated up to the stop censoring date and found that the hazard ratios (HRs) were virtually identical. Thus, our primary analyses are presented in the results of this manuscript.

HRs and 95% confidence intervals (CI) were calculated using Cox proportional hazards models to adjust for potential confounding factors. HRs for the risk of MI, stroke, and revascularization associated with average yogurt intake (categorized as <once/month, once/month to <once/week, once/week to <twice/week, and ≥twice/week) were first estimated. Since MI and stroke were the primary outcomes of interested, we estimated HRs for this combined outcome as well as for total CVD (MI, stroke, or revascularization). Finally, risk of each CVD outcome was estimated according to combined categories of yogurt intake and DASH diet scores. For these latter analyses, both yogurt intake and the DASH diet score were dichotomized (lower vs. higher) and

Table 1. Baseline characteristics of participants according to usual yogurt intake

	NHS (*N* = 55,898)				HPFS (*N* = 18,232)			
	Yogurt intake categories (1C s/d)							
	<1/month	1/month–<1/week	1–<2/week	≥2/week	<1/month	1/month–<1/week	1–<2/week	≥2/week
n	21,474	10,565	11,827	12,032	9,920	3,369	2,751	2,192
Age[2], year	58.7 (10.1)	58.5 (9.8)	58.4 (9.8)	58.5 (9.9)	60.9 (10.0)	58.9 (9.9)	59.3 (10.1)	60.6 (10.2)
Activity, MET-hours/week	13.0 (18.5)	14.5 (19.0)	15.8 (22.0)	18.3 (22.4)	25.7 (35.3)	28.4 (33.5)	30.9 (34.5)	34.4 (42.5)
BMI, kg/m^2	26.8 (5.3)	27.1 (5.3)	27.0 (5.2)	27.0 (5.3)	24.6 (7.8)	24.7 (7.9)	24.7 (7.7)	24.2 (7.9)
Calories, kcals/day	1,598 (526)	1,629 (518)	1,702 (522)	1,805 (542)	1,918 (599)	1,970 (603)	2,019 (596)	2,135 (630)
Alcohol, g/day	6.8 (12.2)	6.2 (11.1)	5.9 (10.2)	5.8 (9.5)	13.9 (17.7)	11.7 (15.1)	11.3 (14.0)	10.9 (14.1)
DASH diet score	22.4 (4.6)	23.8 (4.5)	24.6 (4.4)	25.7 (4.4)	22.6 (4.9)	24.5 (4.8)	25.2 (4.8)	26.7 (4.6)
Total fiber, g/day	17.2 (5.1)	18.3 (5.3)	18.7 (5.3)	19.4 (5.4)	20.8 (7.3)	22.5 (6.8)	23.3 (7.2)	24.2 (7.0)
Fruits/vegetables, s/day	4.4 (1.8)	4.8 (1.9)	5.1 (1.9)	5.5 (2.0)	5.1 (2.4)	5.8 (2.6)	6.1 (2.6)	6.7 (2.9)
Red and processed meats, s/day	1.2 (0.93)	1.1 (0.86)	1.1 (0.83)	0.93 (0.76)	1.2 (0.84)	1.0 (0.79)	0.98 (0.75)	0.88 (0.73)
Total dairy, s/day	1.3 (1.0)	1.5 (1.0)	1.7 (1.1)	2.1 (1.2)	1.3 (1.0)	1.4 (1.0)	1.5 (0.99)	2.0 (1.2)
Yogurt, s/day	0.00 (0.02)	0.06 (0.06)	0.14 (0.16)	0.45 (0.44)	0.00 (0.01)	0.06 (0.06)	0.15 (0.15)	0.48 (0.40)
Current smoker, %	23.2	15.2	12.2	11.1	10.0	5.1	4.3	3.5
Antihypertensive medication use, %	44.3	46.0	47.6	49.0	55.2	52.3	51.4	48.8
HBP family history, %	48.2	52.8	55.4	53.3	48.0	49.5	53.0	49.5
MI family history, %	21.2	20.5	19.7	20.3	34.0	32.7	32.6	35.1
Current postmenopausal hormone use, %	23.7	28.0	29.7	30.9	N/A	N/A	N/A	N/A

Values are mean (SD) for continuous variables and % for categorical variables. Abbreviations: BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; HBP, high blood pressure; HPFS, Health Professionals Follow-Up Study; MET, metabolic equivalent task; MI, myocardial infarction; NHS, Nurses' Health Study.

then cross-classified, yielding 4 mutually exclusive exposure categories: (i) low yogurt + low DASH diet score (reference group); (ii) low yogurt + high DASH diet score; (iii) high yogurt + low DASH diet score; (iv) high yogurt + high DASH diet score. The dichotomous cutpoints used were selected using sensitivity analyses to optimize analytic power and to remain consistent with FFQ and usual yogurt serving sizes: yogurt (<2 vs. ≥2 servings/week in the NHS; <1 vs. ≥1 serving/week in the HPFS) and DASH diet score (<25 vs. ≥25). Twenty-five was chosen as the cutpoint for the DASH diet score as it was around the median in both cohorts (24).

The following potential confounders were explored in the proportional hazards models: age, race, family histories of HBP, diabetes, and MI, antihypertensive medication use, hypercholesterolemia, physical activity, smoking status, cigarette pack years, alcohol intake, postmenopausal hormone use (in NHS), aspirin and multivitamin use, body mass index (baseline and updated every 2 years), and cumulative average intakes of the following dietary factors: total energy intake, carbohydrates, total fat and fat subtypes (saturated, monounsaturated, polyunsaturated, omega-3, trans fatty acids), protein (total, animal, and plant), whole grains, fiber (total, cereal), nuts, fruits and vegetables, sugar-sweetened beverages, potatoes, beans, red and processed meats, sodium, potassium, calcium, magnesium, and vitamin E. Only covariates that changed the HRs by >10% were retained in the final models. These included: age, race, physical activity, MI family history, antihypertensive medication use, and intakes of total energy, total fiber, trans fats, and other dairy foods (milk and cheese). Fixed

Table 2. Yogurt intake and subsequent risk of major CHD, stroke, and CABG in 2 cohorts

				Risk of major CHD				
	NHS				**HPFS**			
Yogurt intake[a]	**Cases**	**IR**	**Age-adjusted HR (95% CI)**	**Multivariable HR (95% CI)[b]**	**Cases**	**IR**	**Age-adjusted HR (95% CI)**	**Multivariable HR (95% CI)[b]**
<1/month	961	303	1.00	1.00	705	634	1.00	1.00
1/month–<1/week	334	228	0.79 (0.70–0.90)	0.85 (0.75–0.97)	197	516	0.91 (0.77–1.06)	0.94 (0.80–1.10)
1–<2/week	252	199	0.69 (0.60–0.79)	0.75 (0.65–0.87)	134	530	0.91 (0.75–1.09)	0.93 (0.77–1.12)
≥2/week	217	177	0.64 (0.55–0.75)	0.70 (0.60–0.82)	96	481	0.80 (0.64–0.99)	0.81 (0.65–1.02)
P for linear trend[c]			<0.001	<0.001			0.03	0.06
	NHS				**HPFS**			
				Risk of stroke				
<1/month	848	268	1.00	1.00	349	313	1.00	1.00
1/month–<1/week	337	230	0.90 (0.79–1.02)	0.98 (0.86–1.11)	86	224	0.81 (0.64–1.03)	0.85 (0.67–1.08)
1–<2/week	302	239	0.87 (0.76–0.99)	0.97 (0.84–1.11)	40	158	0.54 (0.39–0.76)	0.58 (0.41–0.81)
≥2/week	262	214	0.83 (0.72–0.95)	0.94 (0.81–1.09)	42	210	0.71 (0.51–0.98)	0.75 (0.54–1.05)
P for linear trend[c]			<0.01	0.44			<0.01	0.04
				Meta-analysis				
	Risk of major CHD				**Risk of stroke**			
<1/month	1,666	389	1.00	1.00	1,197	280	1.00	1.00
1/month–<1/week	531	287	0.83 (0.76–0.92)	0.88 (0.80–0.98)	423	229	0.88 (0.79–0.98)	0.95 (0.85–1.06)
1–<2/week	386	254	0.76 (0.68–0.85)	0.81 (0.72–0.91)	342	225	0.82 (0.72–0.92)	0.90 (0.79–1.02)
≥2/week	313	219	0.69 (0.61–0.78)	0.74 (0.65–0.84)	304	213	0.81 (0.71–0.92)	0.91 (0.79–1.04)
P for linear trend[c]			<0.001	<0.001			<0.001	0.12
I^2			69.0	30.2			63.7	69.4

Abbreviations: BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; CHD, Coronary Heart Disease; CI, confidence interval; CVD, cardiovascular disease; HBP, high blood pressure; HPFS, Health Professionals Follow-Up Study; HR, hazard ratio; IR, incidence rate per 100,000 person-years; MI, myocardial infarction; NHS, Nurses' Health Study.

[a]Cumulative average of yogurt intake was calculated from first report of HBP up to the first of the following events: CVD diagnosis, lost to follow up, death, end of study.

[b]Adjusted for age, race, smoking (defined as never, past, current with 1–14 cigs/day, current with 15–24 c/day, 25+ c/day), family history of MI, physical activity (continuous from baseline), BMI, BP-lowering medication use, and intakes of total energy, alcohol, trans fatty acids, fiber, milk, and cheese.

[c]Linear trend across yogurt intake categories was quantified with a Wald test for linear trend by assigning the median value to each category and modeling it as a continuous variable.

effects meta-analyses were used to pool estimates from both cohorts. All analyses were performed with SAS software (version 9.4; SAS Institute, Cary, NC).

RESULTS

The baseline characteristics of NHS and HPFS participants with prevalent HBP are shown according to yogurt intake in Table 1. Those with the highest yogurt intakes (≥2 servings/week) tended to be more physically active, drank less alcohol, and were less likely to smoke. Higher yogurt intake was also associated with a healthier diet as indicated by a higher DASH diet score, higher fiber and fruit and vegetable intakes, as well as lower intakes of red and processed meats. Both studies had similar distributions of the DASH diet scores (mean/median around 23/24).

In Table 2, there were 1,764 cases of incident MI (major CHD) and 1,749 strokes in the NHS. In the HPFS, there were 1,132 reported MIs and 517 strokes. Higher intakes of yogurt (≥2 servings/week) were associated with a 30% reduction (95% CI: 0.60–0.82) in risk of MI among NHS women (P trend <0.001) and a 19% reduction (95% CI: 0.65–1.02) in HPFS men (P trend = 0.06). Estimates for stroke risk were weaker than those for MI among women. When revascularization procedures (CABG) was examined separately (Supplementary Table 1), there were 3,300 and 2,148 cases in NHS and HPFS, respectively. Higher yogurt intake in women was associated with a 16% lower risk of undergoing revascularization (P trend <0.01) while there was no significant association observed among HPFS men (Supplementary Table 1). In separate analyses (not shown) restricted to cases of ischemic stroke only, results were similar to those of total stroke presented in Table 2 but the power of these analyses was very low given the small numbers of ischemic strokes in HPFS.

We examined our primary outcome (incident major CHD or stroke) first (Table 3) before investigating the secondary outcome including revascularization procedures (Supplementary Table 1). In both cohorts, participants consuming 1–<2 cups or ≥2 servings/week of yogurt had an approximately 20% lower risks of major CHD or stroke during the follow-up period (P for trend <0.01 in both cohorts). When revascularization was added to the total CVD outcome variable, the risk estimates were attenuated for both men and women, but remained significant for both cohorts (P for trend <0.01 for both).

Table 4 shows the independent and combined associations of higher yogurt intake and diet quality (as measured by the DASH diet score) with major CHD and stroke risk. Among women in the NHS cohort, a higher DASH score alone was unassociated with risk of major CHD or stroke. For each

Table 3. Risk of incident major CHD or stroke according to usual yogurt intake

	Risk of incident major CHD or stroke							
	NHS				HPFS			
Yogurt intake[a]	Cases	IR	Age-adjusted HR (95% CI)	Multivariable HR (95% CI)[b]	Cases	IR	Age-adjusted HR (95% CI)	Multivariable HR (95% CI)[b]
<1/month	1,793	568	1.00	1.00	1,026	928	1.00	1.00
1/month–<1/week	661	452	0.84 (0.77–0.92)	0.91 (0.83–0.99)	279	733	0.89 (0.77–1.01)	0.92 (0.80–1.05)
1–<2/week	542	429	0.77 (0.70–0.85)	0.85 (0.77–0.94)	170	675	0.79 (0.67–0.93)	0.82 (0.69–0.96)
≥2/week	479	392	0.74 (0.67–0.82)	0.83 (0.74–0.92)	135	679	0.77 (0.64–0.92)	0.79 (0.66–0.96)
P for linear trend[c]			<0.001	<0.001			<0.01	<0.01
	Meta-analysis							
<1/month	2,819	662	1.00	1.00				
1/month–<1/week	940	510	0.85 (0.79–0.92)	0.91 (0.84–0.98)				
1–<2/week	712	470	0.77 (0.71–0.84)	0.84 (0.77–0.91)				
≥2/week	614	432	0.75 (0.68–0.82)	0.82 (0.75–0.90)				
P for linear trend[c]			<0.001	<0.001				
I^2			0.0	0.0				

Abbreviations: BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; HBP, high blood pressure; HPFS, Health Professionals Follow-Up Study; HR, hazard ratio; IR, incidence rate per 100,000 person-years; MI, myocardial infarction; NHS, Nurses' Health Study.

[a]Cumulative average of yogurt intake was calculated from first report of HBP up to the first of the following events: CVD diagnosis, lost to follow up, death, end of study.

[b]Adjusted for age, race, smoking (defined as never, past, current with 1–14 cigs/day, current with 15–24 c/day, 25+ c/day), family history of MI, physical activity (continuous from baseline), BMI, BP-lowering medication use, and intakes of total energy, alcohol, trans fatty acids, fiber, milk, and cheese.

[c]Linear trend across yogurt intake categories was quantified with a Wald test for linear trend by assigning the median value to each category and modeling it as a continuous variable.

Table 4. Associations between independent and combined yogurt intake and DASH diet scores with risk of CVD

Risk of major CHD								
	NHS				**HPFS**			
Yogurt/DASH diet score[a]	**Cases**	**IR**	**Age-adjusted HR (95% CI)**	**Multivariable HR (95% CI)[b]**	**Cases**	**IR**	**Age-adjusted HR (95% CI)**	**Multivariable HR (95% CI)[b]**
Low/low	963	263	1.00	1.00	595	591	1.00	1.00
Low/high	584	261	0.84 (0.76–0.94)	0.96 (0.86–1.07)	379	606	0.85 (0.74–0.97)	0.90 (0.78–1.04)
High/low	90	174	0.74 (0.60–0.92)	0.78 (0.62–0.97)	69	551	1.01 (0.78–1.29)	1.01 (0.79–1.30)
High/high	127	179	0.65 (0.54–0.79)	0.75 (0.61–0.91)	89	471	0.70 (0.56–0.87)	0.73 (0.58–0.93)
Risk of stroke								
	NHS				**HPFS**			
Low/low	907	248	1.00	1.00	268	266	1.00	1.00
Low/high	580	259	0.87 (0.79–0.97)	1.01 (0.90–1.13)	187	298	0.90 (0.74–1.09)	0.93 (0.76–1.15)
High/low	114	221	0.95 (0.78–1.16)	1.02 (0.84–1.25)	26	207	0.85 (0.56–1.27)	0.86 (0.57–1.30)
High/high	148	208	0.76 (0.64–0.90)	0.91 (0.76–1.10)	36	190	0.61 (0.43–0.87)	0.63 (0.44–0.91)
Risk of major CHD or stroke								
	NHS				**HPFS**			
Low/low	1,854	508	1.00	1.00	841	840	1.00	1.00
Low/high	1,142	512	0.85 (0.79–0.91)	0.97 (0.89–1.05)	554	890	0.87 (0.78–0.97)	0.91 (0.81–1.03)
High/low	202	393	0.85 (0.73–0.98)	0.90 (0.77–1.04)	93	746	0.96 (0.77–1.19)	0.97 (0.78–1.21)
High/high	277	391	0.72 (0.63–0.81)	0.84 (0.73–0.96)	122	649	0.67 (0.55–0.81)	0.70 (0.57–0.85)
Meta-analysis								
	Risk of major CHD				**Risk of stroke**			
Low/low	1,558	333	1.00	1.00	1,175	251	1.00	1.00
Low/high	963	336	0.85 (0.78–0.92)	0.94 (0.86–1.02)	767	268	0.88 (0.80–0.96)	0.99 (0.90–1.09)
High/low	159	248	0.84 (0.72–1.00)	0.87 (0.74–1.03)	140	218	0.93 (0.78–1.11)	0.99 (0.83–1.18)
High/high	216	240	0.67 (0.58–0.77)	0.74 (0.64–0.86)	184	204	0.73 (0.62–0.85)	0.85 (0.72–1.00)
Risk of major CHD or stroke								
Low/low	2,695	579	1.00	1.00				
Low/high	1,696	595	0.85 (0.80–0.91)	0.95 (0.89–1.02)				
High/low	295	462	0.88 (0.78–0.99)	0.92 (0.81–1.04)				
High/high	399	445	0.70 (0.63–0.78)	0.79 (0.71–0.89)				

Abbreviations: BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; HBP, high blood pressure; HPFS, Health Professionals Follow-Up Study; HR, hazard ratio; IR, incidence rate per 100,000 person-years; NHS, Nurses' Health Study.

[a]Cumulative average of yogurt intake was calculated from first report of HBP up to the first of the following events: CVD diagnosis, lost to follow up, death, end of study. Yogurt cutpoints are <2/week (low), ≥2/week (high) in NHS; <1/week (low), and ≥1/week (high) in HPFS. DASH diet score cutpoints are <25 (low) and ≥25 (high) in both cohorts.

[b]Adjusted for age, race, smoking (defined as never, past, current with 1–14 cigs/day, current with 15–24 c/day, 25+ c/day), family history of MI, physical activity (continuous from baseline), BMI, BP-lowering medication use, and intakes of total energy, alcohol, trans fatty acids, fiber, milk, and cheese.

outcome, the greatest risk reduction occurred among those jointly exposed to higher yogurt consumption and higher DASH diet score. Among HPFS participants, those with higher yogurt intakes and a higher DASH score had 27% (95% CI: 0.58–0.93) and 37% (95% CI: 0.44, 0.91) lower risks of major CHD and stroke, respectively. For the combined CVD outcome with major CHD and stroke, the lowest risk was again found among those with higher yogurt intakes and a higher DASH diet score. These HRs were attenuated when revascularization was added to the CVD outcome (Supplemental Table 2).

DISCUSSION

Higher yogurt consumption among hypertensive women and men in the NHS and HPFS cohorts was associated with a lower risk of MI and stroke and, among women, with a lower likelihood of undergoing a revascularization procedure. The strongest and most consistent results were associated with the lower risk of MI in both men and women. Further, the associations between yogurt consumption and CVD risk were stronger among participants with higher DASH diet scores.

The independent effect of the original DASH diet intervention[8] was also observed in other trials including the Exercise and Nutrition interventions for CardiOvasculaR hEalth (ENCORE) study of overweight, middle-aged hypertensive men and women.[26] That study found that compared to those consuming a typical American diet, those randomized to the DASH diet intervention had lower BP, brachial artery flow-mediated dilation, baroreflex sensitivity, and left ventricular mass after a 4-month intervention period.[26]

A number of studies including the numerous DASH trials have found dairy intake to be associated with reduced risks of both HBP and CVD.[8–10,26] Several prospective studies among those without HBP have found an inverse association between yogurt intake and markers of CVD.[27,28] In a 5-year prospective study, Australian women over the age of 70 who consumed >100 g/day of yogurt had significantly less common carotid artery intima–media thickness than those who consumed less yogurt.[27] A case–control study of Italian adults found a 45% lower odds of acute MI among those who consumed ≥7 cups of yogurt per week compared to nonyogurt consumers.[28]

In early clinical trials, the BP-lowering effect of dairy was largely attributed to its calcium content. However, it has been shown by others that factors in dairy other than or in addition to dietary calcium may explain the beneficial effects on BP and CVD risk.[29] Several small randomized controlled feeding trials have examined the effects of fermented milk products on CVD risk factors among hypertensive individuals.[13,30,31] For example, a randomized, placebo-controlled, double-blind trial with 89 hypertensive subjects tested the impact of adding the milk tripeptides, isoleucine-proline-proline (IPP), and valine-proline-proline (VPP) to *Lactobacillus helveticus*-fermented milk. The investigators added 1.2 mg of IPP and 1.3 mg of VPP per 100 g of milk for 12 weeks and then increased the dose to 5.8 mg IPP and 6.6 mg VPP per 100 g for an additional 12 weeks. This protocol led to reductions in arterial stiffness in the intervention group compared with control subjects who were given *Lactobacillus helveticus*-fermented milk without IPP or VPP supplementation.[30] Hirota *et al.* found that these same fermented milk tripeptides improved vascular endothelial function independent of their BP-lowering effects in a randomized trial of hypertensive men.[31]

Taken together, these studies suggest that fermented dairy products may lower CVD risk through effects on vascular stiffness as well as through direct effects on BP. Consequently, yogurt consumption may be associated with lower CVD risk by improving BP control among hypertensive individuals. These tripeptides may play a role in platelet aggregation and clot formation *via* their inhibition of angiotensin-converting enzyme in the renin–angiotensin system,[32] one of the major BP regulators in the body. Angiotensin-converting enzyme inhibition leads to lower concentrations of angiotensin II, a potent vasoconstrictor[32] that has also been shown to increase intracellular calcium in vascular smooth muscle cells and pH in platelets, leading to increased platelet aggregation.[33] Platelets from hypertensive patients produce more reactive oxygen species, thereby reducing the bioavailability of nitric oxide,[34] an important vasodilator and inhibitor of platelet aggregation.[35,36] In spontaneously hypertensive rats, fermented dairy-derived peptides have been shown to improve vascular response *in vitro* possibly by the stimulation of nitric oxide release.[37]

This is the first large prospective study to show a reduced risk of MI and stroke associated with regular yogurt consumption among hypertensive adults. This study has several important strengths including its prospective design and the use of updated repeated assessments of diet for estimating long-term intakes and repeated measures of potential confounding variables. This study also had several limitations. Since yogurt is highly correlated with an overall healthy diet and lifestyle, it is possible that some potential confounders associated with a healthy lifestyle were not measured or were imperfectly measured, leading to uncontrolled or residual confounding. Additionally, yogurt is a complex dairy product and we were not able to study specific types of yogurt such as those with different added probiotics. While few studies examined food sources of probiotics, some have shown that different probiotic combinations have unique effects on BP and CVD risk factors.[14] Future studies are needed to assess different types of yogurt. Finally, the small number of stroke cases in HPFS yielded inadequate statistical power to examine different types of stroke.

CONCLUSIONS

Our results suggest that higher long-term yogurt intake is associated with lower CVD risk among hypertensive men and women. Higher yogurt intake in combination with an overall heart-healthy diet as measured by the DASH diet score was associated with greater reductions in CVD risk among hypertensive men and women. These findings endorse that incorporation of yogurt into a healthy diet pattern for individuals with hypertension to aid in the prevention of incident CVD.

SUPPLEMENTARY MATERIAL

Supplementary materials are available at *American Journal of Hypertension* online.

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DISCLOSURE

The authors declared no conflict of interest.

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